UNSTABLE PLAQUE: MORPHOLOGY AND PHYSIOLOGY

2987 | BEDSIDE
Association between plaque instability assessed by optical coherence tomography and microvascular resistance
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Background: Microvascular resistance of coronary arteries reportedly represents myocardial damage and microvascular dysfunction. However, association between plaque morphology of the lesions in the vessel of interest and coronary physiological characteristics including microvascular resistance has not been elucidated. We aimed to investigate the association between plaque characteristics and microcirculatory disturbance using optical coherence tomography (OCT) and pressure wire.
Methods: We investigated 238 de novo intermediate coronary lesions of 213 patients with stable angina pectoris who underwent OCT and the index of microcirculatory resistance (IMR) measurement. OCT analysis included presence of fibroatheroma (FA), thin-cap fibroatheroma (TCFA), ruptured plaque (RP), fibrous cap thickness (FCT), maximum lipid arc (LA), and lipid length (LL). Pressure-temperature sensor tipped wire was placed at the distal of coronary artery across the lesion and hyperemic mean transit time was measured with thermal dilution method during hyperemia induced by intravenous injection of adenosine or adenosine 50-triphosphate. IMR was calculated by distal coronary pressure divided by the increase of the hyperemic mean transit time. Microcirculatory disturbance (MD) was defined as showing an IMR ≥ 29 according to the institutional 75 percentile value. OCT findings were compared between the lesion with MD (MD group) and those without MD (non-MD group).
Results: Of all, MD was observed in 64 lesions (26.9%). MD group demonstrated more frequent FA (84.4% vs 73.5%, p=0.039), TCFA (21.9% vs 11.5%, p=0.042) and RP (17.2% vs 6.3%; p=0.010). LA and LL were significantly greater in MD group than in non-MD group (LA: 211 degrees [IQR 165–241] vs 178 degrees [IQR 155–229], p=0.034; LL: 8.0mm [IQR 5.5–12.2] vs 6.5mm [IQR 4.5–10.0], p=0.024, respectively), whereas no significant difference was observed in FCT (133 μm [IQR 90–201] vs 137μm [IQR 90–201], p=0.499).
Conclusion: Unstable morphologies of intermediate stenosis were associated with increased microvascular resistance of the index territories in patients with stable angina pectoris, which may suggest the intriguing relationship between lesion instability and downstream microcirculation.

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Prediction of culprit lesions in patients with acute coronary syndrome by assessing the hemodynamic forces acting on plaques: a three-dimensional frequency-domain optical coherence tomography study
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Background: Acute coronary syndromes (ACS) are triggered by plaque rupture/erosion. However, the factors responsible for the location of plaque rupture/erosion within the coronary vasculature of a patient are unclear, and thus, the prediction of culprit lesions remains problematic. The hemodynamic milieu has a critical role in vascular pathology.
Purpose: To investigate the local distribution of hemodynamic forces in culprit against non-culprit lesions in patients with ACS prior to percutaneous coronary intervention using frequency domain optical coherence tomography (FD-OCT).
Methods: Three-dimensional coronary artery reconstruction using FD-OCT & coronary angiography was performed in the culprit vessel of 15 patients presenting with ACS (myocardial infarction: 7 patients; unstable angina: 8 patients). The culprit (n=15) and non-culprit (n=11) lesions were identified. Computational fluid dynamics techniques were applied to calculate the following hemodynamic parameters in consecutive 1-mm segments: (1) pressure gradient (i.e. pressure change over vessel length), (2) axial plaque stress (i.e. the longitudinal component of hemodynamic stress acting on lesions), and (3) endothelial stress (i.e. the tangential stress due to the friction of the flowing blood on the endothelial surface).
Results: Culprit lesions exhibited (1) smaller lumen area (p<0.001), (2) higher pressure gradient (p<0.001), (3) higher axial plaque stress (p<0.001) and (4) higher endothelial shear stress (p<0.001) compared to non-culprit lesions (Figure). The independent predictors of identifying culprit against non-culprit lesions were lumen area (odds ratio: 2.47 [95% confidence intervals: 1.43–4.27] per 1 mm2 decrease; p=0.001) and axial plaque stress (odds ratio: 1.09 [95% confidence intervals: 1.01–1.17] per 100 Pascal [Pa] increase; p=0.020).
Conclusions: In patients with ACS, there was a large imbalance of hemodynamic forces acting on the culprit lesions compared to the non-culprit ones. Lumen size and axial plaque stress independently predicted culprit coronary arteries. Combined assessment of anatomic and hemodynamic parameters could be helpful in identifying coronary plaques at risk for future ACSs.

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Relevance of optical coherence tomography-derived unstable plaque features and physiological stenosis severity determined by fractional flow reserve
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Background: The association between morphological unstable plaque features and physiological lesion severity remains elusive. This study aimed to investigate the relevance of optical coherence tomography (OCT)-derived high risk characteristics of coronary plaque in accordance with different degrees of physiological stenosis severity on the basis of fractional flow reserve (FFR) and anatomical severity by quantitative coronary angiography (QCA).
Methods: We investigated 250 de novo intermediate coronary lesions of 226 unstable angina patients who underwent OCT and FFR measurements. Lesions were divided into tertiles on the basis of FFR and angiographic diameter stenosis (%DS, respectively). OCT findings included minimal lumen diameter (MLD), fibrous cap thickness (FCT), and the presence of thin-cap fibroatheroma (TCFA). TCFA was defined as lipid-rich plaque (lipid arc ≥ 90 degree) with fibrous cap thickness < 70μm. Prevalence of OCT findings were compared among the tertiles of FFR and QCA.
Results: FFR categories were defined as follows: 1st tertile (FFR-T1) (FFR ≤ 0.81), 2nd tertile (FFR-T2) (0.74 ≤ FFR < 0.81), and 3rd tertile (FFR-T3) (FFR ≥ 0.81). Quantitative coronary angiography (QCA) categories were defined as showing %DS ≤ 51% (QCA-T1), 51% < %DS ≤ 59% (QCA-T2), and %DS ≥ 59% (QCA-T3). MLA showed graded difference in proportion to FFR severity (1.96mm2 [1.40–2.46mm2] in FFR-T1, 1.44mm2 [1.15–1.88mm2] in FFR-T2, and 0.93mm2 [0.70–1.38mm2] in FFR-T3, p<0.01). This trend was also shown in QCA terciles (1.79mm2 [1.37–2.51mm2] in QCA-T1, 1.44mm2 [1.03–1.93mm2] in QCA-T2, and 1.05mm2 [0.66–1.44mm2] in QCA-T3, p<0.01). FCT showed a trend to be thinner in the FFR-T3 (115μm [63–161μm]) than in FFR-T1 and FFR-T2 (145μm [87–229μm], p=0.034, and 142μm [90–206μm], p=0.015, respectively), although there was no significant differences in relation with QCA tertiles. TCFA was observed more frequently in FFR-T3 (24.7%) than in FFR-T1 and FFR-T2 (9.6%, p=0.016, and 9.8%, p=0.011, respectively) and it was also observed in QCA terciles.
Conclusion: The prevalence of TCFA was more than 2 times greater in physiologically severe stenosis than in intermediate and mild stenosis. Physiological stenosis severity correlated with plaque instability assessed by OCT, which may be relevant to worse clinical outcomes in lesions with physiological disturbance.

ACKNOWLEDGEMENT/FUNDING:
This work was supported by LighLab Imaging/St. Jude Medical and the George D. Behrakis Research Fellowship

3051 | BEDSIDE
IABP-SHOCK II risk score for patients with cardiogenic shock complicating acute myocardial infarction
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Background: Mortality in cardiogenic shock still approaches 50%. Early risk stratification is crucial in order to take correct treatment decisions. Aim of this study was to develop a risk prediction score for short-term mortality in patients with cardiogenic shock.

CARDIOGENIC SHOCK

Anatomic and hemodynamic parameters

Acknowledgement/Funding: This work was supported by LighLab Imaging/St. Jude Medical and the George D. Behrakis Research Fellowship

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with infract-related cardiogenic shock based on data from the largest available randomized clinical trial (Intraaortic Balloon Pump in Cardiogenic Shock (IABP-SHOCK II) trial).

**Methods and results:** The model was developed on the intention-to-treat population of the IABP-SHOCK II trial using a multivariable Cox proportional hazards regression analysis with forward selection technique. Variables related to mortality in univariable analysis (p < 0.1) were retained in the model. The optimal cut-off points for continuous variables were defined using the Youden index. The following 6 variables were included in the model: age > 73 years, stroke, stroke at admission > 10.6 mmol/l, creatinine at admission > 132.6 μmol/l, TIMI-flow after percutaneous coronary intervention (PCI) < 3, serum lactate at admission > 5 mmol/l. The scoring system (IABP-SHOCK II score) was determined by rounding the respective parameter estimates, attributing either 0 or 1 points to the variables. Overall, 480 patients were included in the final analysis. According to the score, the population was classified into three risk categories: low (0–2), intermediate (3/4) and high (5–9). The observed mortality rates were 23.9, 49.4 and 77.3% for the three risk levels, respectively.

Validation in the IABP-SHOCK II registry population (n=88) showed good discrimination with an area under the curve (AUC) of 0.79 (95% confidence interval [CI] 0.64–0.81). External validation in a cohort of patients with infarction-related cardiogenic shock included in a European multicentre study (CardShock trial (NCT01374867), n=148) showed similar results (AUC 0.79 [95% CI 0.64–0.81]). Figure 1 depicts the Kaplan-Meier curves with pairwise comparisons by log-rank test (1 vs. 2 p=0.08, 1 vs. 3 p=0.001, 2 vs. 3 p=0.003).

**Conclusion:** The validated IABP-SHOCK II risk score consists of six variables which are easy to obtain in daily clinical practice. It helps to stratify the patients’ risk for short-term mortality and thus, might facilitate clinical decision making.

### Trends in incidence and mortality in cardiogenic shock in the primary PCI era. a 14 year study

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**Introduction:** The incidence of cardiogenic shock (CS) is thought to have reduced with the advent of PCI (Percutaneous Coronary Intervention) as the treatment of choice for patients with ACS (Acute Coronary Syndrome), however mortality rates remain in the region of 50%.

We aim to investigate trends in the incidence of CS and associated mortality in a large sample of patients over a 14-year period.

**Methods:** Anonymous data of adult patients with CS admitted to hospitals in the North of England between 2000 and 2013 was obtained and processed using the ACALM algorithm (Algorithm for Co-morbidity, Associations, Length of stay and Mortality) study protocol. ACALM uses the ICD-10 and OPCS-4 coding systems to identify patients. We compared trends in the incidence and mortality of patients with CS over the 14 year time period, split into three groups.

**Results:** Over the 14 year period, out of total sample of 929565 patients, there were 413 (0.04%) patients with CS. The most common cause for CS remains ACS. The incidence of CS has decreased progressively since 2000. Despite similar baseline characteristics, the mortality rate at 14 days, 30 days and 1 year has decreased over the time period which has coincided with an increased proportion of ACS patients undergoing PCI during their index admission.

**Conclusion:** CS incidence has declined over the study period and mortality has improved compared to the early 2000’s. These trends have coincided with an increase in the role of PCI in ACS. During this period medical therapy and use of support devices has also improved. Therefore, dedicated and early PCI in CS patients may continue to improve outcomes, but further analysis is required to delineate the role of PCI.

### Outcome of elderly patients undergoing extracorporeal life support in refractory cardiogenic shock

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**Aims:** The current study presents data from a real-world cohort of patients with refractory cardiogenic shock (CS) undergoing extracorporeal life support (ECLS) with the aim to report clinical experience, objectify complications and survival in elderly patients.

**Methods:** Eighty-three patients with refractory CS underwent percutaneous ECLS implantation performed by interventional cardiologists. Follow-up was performed at hospital discharge as well as at 18 months (IQR 15–36). Good clinical outcome was defined as survival with a Cerebral Performance Category (CPC) of 1–2. Patients were grouped according to age (<60 years versus >60 years).

**Results:** Median age was 61 years (IQR 50–72) and 43 patients (51.8%) were above the age of 60. ECLS could be weaned in more than half of the cohort (n=47, 56.6%) with no differences between the age groups (p=0.53). Despite similar rates of initial haemodynamic stabilisation, in-hospital mortality was higher in patients >60 years of age (45.0% versus 18.6%, p=0.009). At long-term follow-up only 2 patients were alive in the group of patients >60 years. This resulted in a mortality rate of 95.3% in the elderly in comparison to 67.5% in patients younger than 60 years (p=0.001). Age was identified as an independent predictor for mortality (p=0.04).

**Conclusion:** Despite a high rate of initial successful ECLS weaning, long-term prognosis of patients with CS undergoing ECLS above the age of 60 years is very poor.

### Relationship of rate and rhythm control strategies to adverse outcomes in patients with atrial fibrillation: the EURObservational Research Programme Atrial Fibrillation (EORP-AF) Pilot Registry

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**Background:** A major consideration in atrial fibrillation (AF) management in-
volves symptoms control, using rate and rhythm control strategies. The impact on adverse outcomes of contemporary rate and rhythm control strategies remains controversial.

**Purpose:** To assess the relation of rate and rhythm control strategies on adverse outcomes in the 1-year follow-up observation from the EORP-AF General Pilot Registry.

**Methods and results:** Events considered for this analysis were defined as any thromboembolic event (TE) including stroke, transient ischemic attack, acute coronary syndrome, coronary intervention, cardiac arrest, peripheral embolism and pulmonary embolism; cardiovascular (CV) death; and all-cause death. From the original 3,119 patients, 1,036 (33.2%) were assigned to rate control only and 355 (11.4%) were assigned to rhythm control only [Table 1]. Baseline characteristics were reported in Table 1. Patients assigned to a rate control strategy were older (p<0.0001) and more likely female (p=0.0266). Paroxysmal AF was more commonly recorded in patients assigned to rhythm control compared to those assigned to rate control (p<0.0001). Patients assigned to a rate control strategy reported higher rates for any TE (3.5% vs. 2.4%, p=0.0245), CV death (3.9% vs. 1.7%, p=0.0437) and all-cause death (9.8% vs. 2.5%, p<0.0001). Kaplan-Meier analysis shows that patients assigned to rate control strategy had a higher risk for all-cause death (p<0.001). On Cox multivariable regression analysis, adjusting for baseline characteristics and comorbidities, a rate control strategy was associated with a higher rate of any TE, CV death and all-cause death at 1-year follow-up. Rate control is independently associated with an increased risk of all-cause death.

### 3065 | BEDSIDE

**Are cardiovascular risk factors associated with the incidence of atrial fibrillation?** A systematic review and field synopsis of 23 factors in 32 initially healthy cohorts of 20 million participants

**Background:** Established primary prevention strategies of cardiovascular diseases (CVD), such as coronary heart disease (CHD), are based on understanding of risk factors, but the extent to which the same risk factors are associated with the incidence of atrial fibrillation (AF) is unclear.

**Methods:** We conducted a systematic review (updated to October 2015) and field synopsis of population-based, consensused or electronic health record (EHR) cohorts that investigated the associations of one or more of 23 cardiovascular risk factors, and incident AF. For each risk factor we extracted relative risks (RR) and 95% confidence intervals [95% CI], and extent of risk factor adjustment. We used forest plots and “Swiss cheese” plots to visualise the number of reports with in-verse (RR [95% CI] crossed unity, then the association was classed as an inverse or direct trend.

**Results:** 73 publications were included (84 reports based upon 28 consented and 4 EHR cohorts), with 576 602 AF events in 20 420 175 participants. The number of reports ranged from 3 to 19 (median 10) per risk factor, with 66 (78.6%) published in 2010–2015. We found substantial heterogeneity in AF event definition, and quality of reporting with age range not reported in 30 reports (35.7%), lack of adjustment for six standard CVD risk factors in 63 reports (75.0%), and lack of adjustment for intercurrent CVD in 69 reports (82.1%). This prevented meaningful meta-analyses. For alcohol intake, we identified 10 reports, 10 disparate alcohol definitions, and only 3 reports which showed a direct association. Hypertension adjustment for intercurrent CVD in 69 reports (82.1%). This prevented meaningful meta-analyses. For alcohol intake, we identified 10 reports, 10 disparate alcohol definitions, and only 3 reports which showed a direct association. 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were successfully applied, which underscores the importance of maintaining si-
nus rhythm in patients with acute heart failure.

3067 | BEDSIDE
Acute atrial tachyarrhythmias due to tropical viral disease. A new world wide threat
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Background: Zika, Chikungunya and Dengue fever viruses are arthropod-borne diseases that have caused millions of infections globally. There are very few pub-
lished reports concerning the cardiac complications in general and arrhythmias in particular, due to Tropical virus disease.

Purpose: To investigate the occurrence of acute atrial tachyarrhythmias in their tropi-
cal virus disease.

Methods: Prospective multi-center observational study of 277 patients with a Zika, Chikungunya and dengue infection from a Venezuelan outbreak. Clinical evaluation, chest X-Ray, ECG, echocardiography, Holter, including virological eval-
uation, cardiac biomarkers, and cardiac MRI procedures were performed.

Results: Of the 277 patients examined, 117 were males with a mean age of 59±8. 91 developed palpitations. Acute atrial tachyarrhythmia’s (34%) including atrial fibrillation (>8 patients) and atrial tachycardia (11%). New onset symptomatic atrial fibrillation was observed in 15 cases (7%), after the acute episodes 12 were classified as paroxysmal, 4 persistent and 3 permanent. Myocarditis was present in all of them.

Conclusion: New onset atrial tachyarrhythmias occurred in approximately 7% of patients with Chikungunya, Zika and Dengue. Myocarditis was detected in all of them and in 45% of a with Chikungunya.

3068 | BENCH
Detection of fibrotic changes in the left atrium using DE-MRI in patients with and without atrial fibrillation
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Background: Left atrial fibrosis (LA fibrosis) detected using Late-Gadolinium En-
hancement MRI (LGE-MRI) has been introduced as an independent predictor for success of pulmonary vein isolation (PVI) in patients with atrial fibrillation (AF). Nevertheless, it is still unclear if AF leads into LA fibrosis or if AF is the clinical manifestation of an altered LA.

Methods: A total of 198 (119 male) consecutively enrolled patients with AFIB underwent LGE-MRI to assess for LA Fibrobcess. Each LGE-MRI was segmented by isolation the LA wall and quantified for the relative extent of fibrotic remodeling using a software tool. Patients were placed in four staging categories based on the degree of LA fibrosis: Utah I (<10% fibrosis), Utah II (≥10% to 20%), Utah III (≥20% to 30%) and Utah IV (≥30%).

Results: 144 patients (94 male, 62±10.8 years) suffered from AF while 54 pa-
tients (25 male, 59.4±14.7 years) were found with stable sinus rhythm (SR). Among these 42.0% were submitted to CCV. A CCV strat-
ification tended to occur more frequently and it may be associated with elevated in incidence of stroke.

Conclusion: Gender differences in clinical manifestation, therapeutic strategies, and risk of adverse outcomes of atrial fibrillation (AF) have been reported, but contemporary evidence in clinical cohorts is limited.

3070 | BEDSIDE
Liberal use of chemical cardioversion in patients with atrial fibrillation in the emergency department: is it a safe strategy?
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Background: Chemical cardioversion (CCV) in patients with atrial fibrillation (AF) may be a reasonable strategy in the setting of acute clinical conditions. However, CCV is often overused and it may be associated with increased risk of adverse outcomes.

Purpose: Evaluate CCV patterns in the emergency department (ED) and the incidence of stroke at 30 days.

Methods: 2181 consecutive patients with AF who were evaluated in our ED in a 12 month period. Among them, 423 patients were admitted for in-hospital man-
agement. We excluded all cases where cardioversion was considered safe: previ-
ous oral anticoagulation (OAC) for at least 3 weeks (n=148) and transesophageal echocardiography for exclusion of preexisting atrial thrombus (n=14). All patients had AF for at least 48h and CCV was always performed using amiodarone. Clinical indication for cardioversion was defined as the presence of circulatory shock, syncope, myocardial ischemia and/or acute heart failure. Finally, we evaluated the impact of the “CCV” versus “no-CCV” strategy in the stroke rate at 30 days.

Results: A total of 264 patients were included with a mean age of 72.7±13.5 years (45.8% males). Among these 42.0% were submitted to CCV. A CCV strat-
egy was associated with a higher proportion of patients in sinus rhythm at dis-
charge (54.1 vs. 46% p<0.001). There were no differences between the “CCV” and “no-CCV” groups regarding CHA2DS2-VASc score (median 4.0 [interquartile range 2.0–5.0] vs 4.0 [2.0–5.0] p=0.924), clinical indication for cardiover-
sion (47.7% vs 49.7%, p=0.804) or proportion of OAC prescription at discharge (43.2% vs 35.9%, p=0.251). Stroke rate at 30 days was significantly superior in the “CCV” group (0.3% vs 14.7% p=0.003). Among patients with stroke following CCV (n=11), median time until CCV was 112 (4–209) hours and 45.5% of these patients did not have clinical indication for cardioversion.

Conclusions: In this population a CCV strategy was overused, with only about one-half of these patients having clinical indication for cardioversion. A liberal use of CCV was associated with higher stroke rate at 30 days and therefore its use must be carefully weighed in clinical practice.
3071 | BEDSIDE
The CHA2DS2-VASc score strongly correlates with glomerular filtration rate and predicts decline in renal function over time in patients with atrial fibrillation and chronic kidney disease

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Introduction: Patients with atrial fibrillation (AF) frequently suffer from chronic kidney disease (CKD). Declining kidney function may complicate the management of anticoagulation in these patients.

Purpose: To study the predictive value of the CHA2DS2-VASc score, a stroke-risk stratification model in AF, for kidney function and kidney disease progression in patients with AF and CKD.

Methods: A cohort of 18,539 patients with AF and CKD treated in the primary care setting was prospectively followed within an electronic database (n=124,149 eGFR measurements, mean number of measurements per patient: 6.8, median age: 78.5 years, median follow-up: 1.44 years (25th-75th percentile: 0.52–2.79)). Baseline kidney function and the kidney function trajectory over time was analysed by multi-level mixed-effects regression modelling.

Results: The mean baseline eGFR was 52.0 ml/min/1.73m² (95% CI: 51.8–52.3), and declined by 1.03ml/min/1.73m²/year (95% CI: 0.86–1.19, p<0.0001). Higher CHA2DS2-VASc scores (median: 4 points, range: 0–8) were associated with both a lower baseline eGFR (p<0.0001), and a faster progression of eGFR decline (p=0.002). The mean baseline eGFR decreased from 61.88 ml/min/1.73m² in patients with a score of 0 points to 41.26 ml/min/1.73m² in patients with a score of 8 points. The annual decline in eGFR increased from 0.57ml/min/1.73m²/year (95% CI: 1.18–1.74) in patients with a score of 0, to 1.46 ml/min/1.73m²/year (95% CI: 1.18–1.74) in patients with a score of 8. After 5 years of follow-up, patients with a CHA2DS2-VASc score of 0, 2, 4, 6, and 8 points had lost 6.0%, 9.4%, 12.8%, 16.3%, and 19.7% of their initial eGFR, respectively (Figure 1, p<0.0001).

Conclusions: The CHA2DS2-VASc score represents a strong clinical determinant of kidney function and renal decline over time in patients with AF and CKD. These results highlight the impact of comorbidities on kidney disease progression and have important implications for the management of anticoagulation in patients with CKD.

Acknowledgement/Funding: Data acquisition from IMS was supported by a grant from Bayer Pharma AG.

3072 | BEDSIDE
Short lasting supraventricular bursts as a risk factor for development of atrial fibrillation

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Background: According to the latest European Society of Cardiology’s guidelines for atrial fibrillation (AF) the definition of AF is an irregular heart rhythm without p-waves lasting at least for 30 seconds. The definition is based on convention and expert opinion, not scientific data. A high incidence of supraventricular ectopic beats (SVEB) is a risk factor for later development of AF.

Purpose: To evaluate if the number of SVEBs, or supraventricular bursts consisting of ≥4 SVEBs in row predicts later development AF.

Methods: Participants with supraventricular bursts (≥4 SVEBs in row) were identified from the STROKESTOP study, a mass screening study for AF including 7500 individuals 75/76 yrs old. In the STROKESTOP study participants were asked to perform intermittent 30 seconds long ECG registrations twice daily for 14 days. Individuals free of AF during the study, but with ≥4 SVEBs in a row and who had not developed AF at start of this study, n=47, were invited to undergo repeat AF screening after a period of two years. Total number of SVEBs, length of supraventricular burst (ie number of SVEBs in a row), and number of supraventricular bursts (≥4 SVEBs in a row) from the initial study were noted. A matched control group, n=50, without supraventricular bursts was identified within the study. Univariate analysis using binary logistic regression was performed and in addition multivariable analysis of significant parameters, to evaluate risk of development of AF. C-statistics was calculated.

Results: Of the 47 individuals screened, 21 (45%) were diagnosed with newly detected AF and had on average 54 SVEBs compared to 1 SVEB in the control group (p<0.001). On average individuals in the group with supraventricular bursts had 2.8 SVEB episodes, lasting on average 6 beats. In the control group 4 cases (10%) of AF were detected.

Comparing the group with newly detected AF with the group where AF was not detected no CHA2DS2-VASc parameters differed significantly, nor height or weight, but only length of supraventricular burst-episode, number of episodes of supraventricular bursts and total number of SVEBs. Using univariate analysis these remained significant, however using multivariable analysis only length of supraventricular burst episode, and total number of SVEBs remained significant. C-statistics for prediction of AF using length of supraventricular burst and total number of SVEBs was 0.78 (95% CI 0.67–0.89).

Conclusion: Within two years almost half of individuals with supraventricular bursts had developed AF. The total number of SVEBs and length of supraventricular bursts can be used to predict development of AF.

3073 | BEDSIDE
Biatral structural characteristics and association with epicardial adipose tissue in patients with paroxysmal atrial fibrillation initiated by right atrial ectopy

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Background: Paroxysmal atrial fibrillation (PAF) initiated by right atrial (RA) ectopy is rare. Whether epicardial adipose tissue (EAT) is associated with AF initiated by RA ectopy and structural contributors to RA ectopy remains unclear.

Purpose: We investigated biatral structural characteristics and the association with EAT in patients with PAF initiated by RA ectopy.

Methods: The RA, left atrium (LA), right and left atrial appendage (RAA, LAA) volumes, and EAT volumes surrounding each atrium were measured using 64-slice multidetector computed tomography (MDCT) in patients with PAF initiated by RA (RA-ectopy group, n=8, Age: 52±13) and PV (PV-ectopy group, n=32, Age: 63±7) ectopy.

Results: The LA volume index was significantly larger in the PV-ectopy group, than in the RA-ectopy group (81.3 [95% CI, 74.2–88.5] vs. 64.5 mL/m² [95% CI, 54.8–74.2]; P=0.04), whereas the RA volume index did not significantly differ between the groups (73.8 [95% CI, 66.8–80.3] vs. 68.1 mL/m² [95% CI, 57.1–79.1]; P=0.47). The LA volume index was significantly larger whereas the RA volume index was significantly smaller in the PV-ectopy group, than in the RA-ectopy group.

Computed tomography parameters

<table>
<thead>
<tr>
<th>PV-ectopy (n=32)</th>
<th>RA-ectopy (n=8)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LA volume index (mL/m²)</td>
<td>81.3 (74.2–88.5)</td>
<td>64.5 (54.8–74.2)</td>
</tr>
<tr>
<td>LAA volume index (mL/m²)</td>
<td>10.1 (9.0–11.3)</td>
<td>6.5 (4.5–8.5)</td>
</tr>
<tr>
<td>RA volume index (mL/m²)</td>
<td>73.6 (66.8–80.3)</td>
<td>68.1 (57.1–79.1)</td>
</tr>
<tr>
<td>RAA volume index (mL/m²)</td>
<td>10.3 (9.1–12.4)</td>
<td>14.1 (11.6–16.6)</td>
</tr>
<tr>
<td>LA/LAA volume ratio</td>
<td>12.5 (11.4–13.5)</td>
<td>9.8 (7.7–11.9)</td>
</tr>
<tr>
<td>LAA/RAA volume ratio</td>
<td>14.5 (12.6–16.5)</td>
<td>21.0 (18.6–23.5)</td>
</tr>
<tr>
<td>LAA/RA volume ratio</td>
<td>1.12 (0.89–1.35)</td>
<td>2.45 (1.36–3.54)</td>
</tr>
<tr>
<td>LA-EAT (cm³)</td>
<td>15.5 (13.1–17.9)</td>
<td>7.4 (4.8–10.0)</td>
</tr>
<tr>
<td>LAA-EAT (cm³)</td>
<td>16.0 (13.9–18.1)</td>
<td>9.3 (7.5–11.1)</td>
</tr>
</tbody>
</table>

LA, left atrium; LAA, left atrial appendage; RA, right atrium; RAA, right atrial appendage; EAT, epicardial adipose tissue.
group (10.1 [95% CI, 9.0–11.9] vs. 16.5 mL/m² [95% CI, 11.6–16.6]), respectively. The LA-EAT and RA-EAT volumes were significantly larger in the PV-ecopy group, than in the RA-ecopy group (LA-EAT: 15.5 [95% CI, 13.1–17.9] vs. 7.4 cm³ [95% CI, 4.8–10.0]; P < 0.001; RA-EAT: 16.0 [95% CI, 13.9–18.1] vs. 9.3 cm³ [95% CI, 7.5–11.1]; P = 0.001).

Conclusions: A large RAA, rather than RA structural remodeling, might be associated with AF initiation by RA ecotomy. PAF initiated by RA ecotomy was less associated with EAT surrounding the atrium than typical PAF initiated by PV ecotomy.

MAY INTRA CORONARY IMAGING IMPROVE CLINICAL OUTCOMES?

3074 | BEDSIDE
Clinical impact of optical coherence tomography findings on culprit plaque in acute coronary syndrome: the OCT-FORMIDABLE study registry
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Background: Aim of this study was to evaluate the clinical impact of the culprit plaque features assessed by Optical Coherence Tomography (OCT) in patients with Acute Coronary Syndrome (ACS).

Methods: The OCT-FORMIDABLE registry enrolled retrospectively all consecutive patients who perform OCT on culprit plaque in patients with ACS in 9 European centres. The primary endpoint was the correlation of culprit plaque characteristics at OCT with incidence of major adverse cardiovascular events (MACEs), defined as the composite of death from cardiac causes, non-fatal MI, clinically driven target vessel revascularization. The evaluation of the impact of plaque characteristics on therapy (both stent and medical treatment) efficacy was the secondary endpoint.

Results: 285 patients were included in the study. Mean age was 60±12.8 years old, 20.6% of the patients were of female gender. Main clinical presentation was ST-elevation myocardial infarction (STEMI, 49.8%). At OCT analysis culprit plaque rupture (CPR) was present in 65.3% of cases, 61.1% presented thin cap fibroatheroma, while 33.8% presented necrotic core with macrophage infiltrations (NCMI). During follow-up (11.7±13.7 months) 12.3% of the patients experienced MACEs.

At the multivariate analysis presence of CPR (HR 3.8, 1.5–10, p < 0.01) and NCMI (HR 3.2, 1.5–6.5, p < 0.01) were independent predictors for MACEs while the impaired membrane of a second generation drug eluting stent (DESs, HR 0.3, 0.1–0.6, p < 0.01) and dual antiplatelet therapy with prasugrel or ticagrelor at discharge (HR 0.4, 0.1–0.9, p = 0.03) were protective. The protective impact of second generation drug eluting stents and of new antiagregant drugs was reported only in patients with CPR, in patients without any of the baseline clinical or procedural features impacted on MACEs.

Conclusions: CPR and the presence of NCMI are independent predictors of worse outcome. Patients with CPR seem to benefit more of an intensive therapy, both from a pharmacological and interventional point of view. (NCT02486861)

3075 | BEDSIDE
Simple alternative to fractional flow reserve (FFR)
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Background: Instantaneous wave free ratio (iFR) can be used to assess the functional severity of coronary artery stenosis similar to FFR but independent of adenosine induced hyperaemia. However, results of the ADVISE II trial showed poor correlation between iFR and FFR when lesions fell between an intermediate zone (iFR >0.86 and <0.93). This situation arises in approximately 35% of cases necessitating a conversion to FFR assessment. Adenosine is the gold standard to induce hyperaemia in FFR procedures. However, it has several side effects and adds significant cost. Saline solution and contrast media have been shown to increase shear stress and ischemia induced vasodilatation. They may represent a simple, readily available and instantaneously accessible alternative to adenosine in functional assessment of coronary artery stenosis (CAS).

Purpose: To determine if hyperaemia induced iFR using intracoronary saline (iFRs) or contrast media iFR (iFRc) correlates well with adenosine mediated FFR. In addition, if they can be used as an alternative in the functional assessment of coronary artery lesions.

Methods: Patients with CAS associated with an IFR in the intermediate zone (≥0.86 and <0.93) were prospectively included in the study. Each stenosis was evaluated with baseline measurements: Ps/Pa, iFR, iFRs (saline solution volume = 10 ml), iFRc (contrast media volume = 8 ml) and adenosine mediated FFR. Lesions were deemed significant if FFR was ≥0.8. Reproducibility of iFRs and iFRc and the correlation between iFR and FFR, iFRs and FFR, iFRc and FFR was assessed. For both iFRs and iFRc, we established the threshold value for determining a lesion’s functional significance.

Results: Thirty coronary lesions were studied (30 patients). Reproducibility of iFRs and iFRc showed an excellent intra-class correlation coefficient of 0.94 (95% confidence limits: 85%). Pearson correlation coefficients were: 0.51 (p=0.04), 0.82 (p<0.0001) and 0.78 (p<0.0001) for FFR and iFR, FFR and iFRs, and FFR and iFRc respectively. ROC analysis also showed excellent accuracy and established cut-off values of <0.78 for iFRs and <0.77 for iFRc in predicting an FFR value of <0.80 (cf. figure). AUC for iFRs = 0.99 [95% CI: 95–100%], sensitivity 86%, specificity 100% and AUC for iFRc = 1 [95% CI: 100%], sensitivity 100%, specificity 100%.

Conclusion: Functional assessment of CAS by iFR is enhanced with the use of both intracoronary saline and contrast media. They compare favorably to adenosine mediated FFR. These agents are readily accessible, immediately available in any cath lab, safe and less costly. Our study establishes a cut-off value of 0.78 for intracoronary saline iFR and 0.77 for contrast media iFR for determining the functional significance of a coronary lesion.
pared two patient groups: those with all lesions >0.80 (“defect group”, n=254, 63%) and those with at least one lesion <0.80 (“perform group”, n=149, 37%). The primary end point was the rate of all cause death, non-fatal myocardial infarction, and unplanned revascularization.

Results: Median clinical follow-up was 1023 days (IQR 724 - 1284). Twenty-three patients died for follow-up. Overall incidence of adverse events at 1 and 3 years of follow-up were 14% and 25%, respectively. Event rates in the “defect” and “perform” groups were 10% and 21% at 1 year, and 23% and 32% at 3 years, respectively (log-rank test p=0.03). On univariable analysis, FFR functional group, age, diabetes, chronic renal dysfunction, ACS presentation and reduced left ventricular ejection fraction proved to be associated with higher risk of adverse events. After multivariable adjustment, chronic renal dysfunction (HR 2.62, 95% CI: 1.62 - 4.23, p<0.0001), ACS (HR 1.88, 95% CI: 1.18 - 2.99, p=0.008) and FFR functional group (“defect”) (HR 1.57, 95% CI: 1.04 - 2.36, p=0.03) were independent predictors of adverse events.

Conclusions: Our data indicate that evaluation of coronary artery disease with FFR predicts cardiac long-termizing outcome among all-comers patients referred for cardiac catheterization. In particular, patients without functionally significant coronary disease constitute a subset at lower risk of adverse cardiac events.

3077 | BEDSIDE
The pathophysiology of mental stress induced myocardial ischaemia

Background: Mental stress (MS) triggers myocardial ischaemia at cardiac workloads that are lower than those that cause exercise-induced ischaemia in the same patient. Clinical relevance is highlighted by observational studies demonstrating that MS is a proatherogenic event when large populations are exposed to acute MS for example by earthquakes and publicised national sports events. In contrast, even in patients with known coronary artery disease and exertional angina, exercise is safe and beneficial. These differences may reflect fundamental differences in underlying pathophysiology during MS that maybe amenable to targeted therapy.

Methods: Simultaneous intracoronary pressure and flow velocity data were acquired in a target artery from 15 patients with significant coronary artery disease (FFR<0.8 and/or stenosis >70%) and 13 controls (unobstructed coronaries) during MS. Studies were performed in the morning after an overnight fast in order to standardise circadian variation. Oral nitrate preparations, calcium channel antagonists and beta-blockers were stopped at least 24 hours in advance. All data were standardised to the same patient. Clinical relevance is highlighted by observational studies demonstrating that MS is a proatherogenic event when large populations are exposed to acute MS for example by earthquakes and publicised national sports events. In contrast, even in patients with known coronary artery disease and exertional angina, exercise is safe and beneficial. These differences may reflect fundamental differences in underlying pathophysiology during MS that maybe amenable to targeted therapy.

Results: At peak MS rate pressure product (RPP), a marker of myocardial oxygen demand, increased by 4346±2331mmHg.bpm (p=0.0001). Systolic and diastolic blood pressures increased by 27.52±12.67mmHg (p=0.0001) and 13 controls (unobstructed coronaries) during MS. Studies were performed in the morning after an overnight fast in order to standardise circadian variation. Oral nitrate preparations, calcium channel antagonists and beta-blockers were stopped at least 24 hours in advance. All data were acquired at rest and at peak MS. Mental stress involved a 6-minute mental stress test consisting of mental arithmetic and the Stroop test. Coronary flow averaged peak velocity (APV), microvascular resistance (MR) and Buckberg index (BI) were calculated. Wave intensity analysis also differentiated waves that accelerate and decelerate coronary flow.

Conclusions: Exposure to mental stress is associated with an increase in myocardial oxygen demand. This is met with an increase in coronary flow in patients with unobstructed coronaries. A paradoxical rise in microvascular resistance does occur in response to MS and this abnormal response correlates with the extent of atherosclerosis in the vessel.

3078 | BEDSIDE
Validation of a novel catheter for thermodilution-derived measurement of absolute coronary blood flow and microvascular resistances
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Background: While coronary angiogram detects only 5 to 10% of the volume of the coronary tree, no direct measurement is currently available to measure the microcirculation, which represents the remaining 90 to 95%. A novel infusion catheter was developed to directly measure absolute coronary blood flow and microvascular resistances.

Purpose: To validate the reproducibility of flow and microvascular resistance measurements with the new catheter by correlating duplicate measurements at the left anterior descending (LAD), circumflex (LCx) and right coronary artery (RCA) (test-retest repeatability).

Methods: A novel monorail infusion catheter with a double lumen associated with a pressure temperature sensor wire is able to assess coronary blood flow and microvascular resistances. Coronary flow is calculated with the following formula: \( Q = \frac{Q_i}{S} \times \frac{\rho \times \text{TI}}{T} \), where \( Q \) is the coronary flow (ml/min), and \( \rho \) is the density of saline at room temperature (ml/mM). TI is the saline injection temperature (degrees Celsius) and T is the temperature at the distal part of the coronary artery. Myocardial resistances are equal to the distal pressure divided by the absolute myocardial flow in mmHg/ml/min.1. Figure Hyperemia was obtained with the infusion of saline itself. Test retest stability of the measurements was studied after re-instrumentation of the coronary artery.

Results: Coronary blood flow (Q) and myocardial resistance (R) were measured in duplicate in 46 vessels from 27 patients. There were 23 LAD, 7 LCx and 16 RCA. Median (25th-75th value) hyperemic coronary flows in the LAD, the LCx and the RCA were 155 (129–236), 128 (110–187) and 161 (127–195) ml/min respectively. Median (25th-75th value) microvascular resistances in the LAD, the LCx and the RCA were respectively: 0.425 (0.359–0.532), 0.537 (0.493–0.593) and 0.472 (0.378–0.653) mmHg ml min−1. Test/retest repeatability of the measurements after re-instrumentation of the coronary artery showed a good reproducibility for both coronary blood flow and microvascular resistance (Spearman’s ρ correlation coefficient for Q was 0.902, P<0.001 and for R was 0.880, P<0.001) (Figure).

Conclusions: Direct measurement of coronary blood flow and microvascular resistances to assess coronary microcirculation is reproducible and safe with this novel coronary infusion catheter. These measurements might be proposed to evaluate the effect of new treatment targeting the coronary microvasculature.

Acknowledgement/Funding: PX is supported by an EAPCI interventional cardiology research grant and a Hellenic Cardiovascular Society (HCS) grant for 2016

3079 | BEDSIDE
Vascular healing is delayed after drug-eluting stent implantation in patients with acute coronary syndromes caused by plaque erosion compared to plaque rupture: an optical coherence tomography study
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Background: Presentation with acute coronary syndrome (ACS) is an important risk factor for poor vascular healing after drug eluting stent (DES) implantation. DES is the predominant mechanism underlying ACS, and the vascular response after DES implantation for plaque rupture has been extensively studied. Little is known, however, about the outcome after DES implantation for plaque erosion.

Purpose: To compare the vascular healing process after stent implantation between plaque rupture (PR) and plaque erosion (PE).

Methods: Sixty-five ACS patients who underwent culprit lesion optical coherence tomography (OCT) imaging both before and after stent implantation at baseline as well as at 6–months were included in this study. Patients were divided into two
groups: plaque rupture (PR, n=19) and plaque erosion (PE, n=24). Plaque characteristics, pre-stent thrombus burden, and post-stent intrastent structure (ISS) volume were analyzed. The ratio of uncovered to total stent struts per cross-section area (RUTTS), and neointimal thickness and area were measured at follow-up.

Results: There were significant differences in pre-stent thrombus burden and post-stent ISS volume between the PR and PE groups. Compared with PR, PE showed a significantly lower pre-stent thrombus score (34.2±19.2 vs. 68.6±44.2, p<0.009) at baseline and a smaller ISS volume (0.7±0.9 mm² vs. 2.1±1.9 mm², p<0.019) on post-procedure OCT imaging. At 6-month follow up, PE showed a higher incidence of RUTTS >0.3 (12.7±14.4% vs. 2.0±4.5%, p<0.003), thinner neointima (0.05±0.02 mm vs. 0.12±0.08 mm, p<0.002), and smaller neointimal area (0.5±0.2 mm² vs. 1.2±0.9 mm², p<0.004) compared with PR (Figure). In the multivariate logistic model, presence of plaque erosion was the only independent predictor for RUTTS >0.3.

Conclusions: Plaque erosion was associated with a less favorable healing response following DES implantation when compared to plaque rupture, with a higher incidence of RUTTS >0.3 at 6 months. Longer duration of dual anti-platelet therapy may be beneficial particularly in patients with plaque erosion who were treated with drug eluting stent.

3080 | BEDSIDE
Comparison of the diagnostic accuracy of instantaneous wave-free ratio and fractional flow reserve for the detection of myocardial ischemia as defined by myocardial perfusion imaging (MPI).

Methods: One hundred and eleven coronary lesions in 89 patients who had undergone multi-detector row coronary CT angiography and MPI were analyzed. The diagnostic accuracy of IF and FFR for the diagnosis of myocardial ischemia were by means of ROC curves. The diagnostic accuracy of IF and FFR for the detection of myocardial ischemia as defined by MPI was analyzed by using the area under the ROC curves (AUC).

Purpose: To investigate the diagnostic accuracies of IF and FFR for the detection of myocardial ischemia as defined by MPI.

Results: The number of lesion vessel was 79 (71.2%) in the left anterior descending (LAD) coronary artery, 17 (15.3%) in the left circumflex (LCX) coronary artery, and 15 (13.5%) in the right coronary artery (RCA). All of these 111 lesions were measured both FFR and IF, the average of IF and FFR were 0.89±0.10. The IF and FFR for the LAD, LCX, and RCA were 0.89±0.10, 0.89±0.10, and 0.89±0.10, respectively.

Conclusions: Although IFR and FFR have equivalent diagnostic performance especially in LAD, using FFR is thought to be desirable for the evaluation of ischemia as defined by MPI in the case of non-LAD.

3081 | BEDSIDE
Association between prior aspirin use in patients presenting first acute coronary syndrome and culprit lesion morphology assessed by optical coherence tomography.

Methods: A total of 433 consecutive patients with their first presentation of ACS who underwent OCT examination for culprit lesion before balloon angioplasty or stent implantation were investigated in the present study. OCT analysis included presence of intraluminal thrombus, fibroatheroma, thin-cap fibroatheroma, ruptured plaque and fibrous cap thickness. Clinical characteristics and OCT findings were compared between patients who were given aspirin at least 7 days prior to the onset (ASA group) and those who were naïve to aspirin (non-ASA group).

Conclusions: ASA use predicted more frequent in ASA group than non-ASA group (80.6% vs 54.4%, p<0.01). In OCT analysis, ASA group had less frequent intraluminal thrombus (35.8% vs 72.1%, p<0.01). There were no significant differences in plaque characteristics including fibroatheroma (89.6% vs 91.5%, p=0.691), TCFA (40.3% vs 53.7%, p<0.003), ruptured plaque (35.8% vs 40.5%, p=0.468), and FCT (76.0 ± 30.0 μm vs 83.5 ± 30.0 μm, p=0.266). After adjusting for significant differences in baseline characteristics including history of hypertension, dyslipidemia, and prior use of statin, propensity score matched cohort included 53 ASA group and 53 patients in non-ASA group. In the matched cohort, intraluminal thrombus was significantly less frequent in ASA group than non-ASA group (12.5% vs 21.6%, p=0.002), whereas no significant difference was observed in fibroatheroma (92.5% vs 90.6%, p=0.100), TCFA (41.5% vs 49.1%, p=0.559), ruptured plaque (32.1% vs 43.4%, p=0.316), and FCT (74.3 ± 29.3 μm vs 78.3 ± 29.3 μm, p=0.575).

Conclusion: In cases of first ACS presentation, patients with prior aspirin use were more likely to present with non-STElevation ACS with less frequent intraluminal thrombus, whereas no significant difference was observed in underlying plaque characteristics.

3082 | BEDSIDE
Effect of early statin therapy on fibrous-cap thickness in patients with acute coronary syndrome: The ESCORT study

Background: Statin can contribute to stabilization of coronary plaques. This is a prospective randomized study. A total of 61 patients started taking pitavastatin 4 mg/day on the day of admission (early statin group: n=31) or 7 days after the onset (late statin group: n=30).

Methods: This is a prospective randomized study. A total of 61 patients started taking pitavastatin 4 mg/day on the day of admission (early statin group: n=31) or 7 days after the onset (late statin group: n=30). OCT was performed to assess fibrous-cap thickness (FCT) in non-culprit lesions at admission (baseline), 3-week follow-up, and 6-month follow-up.

Results: At 3-week follow-up, the FCT significantly increased in the early statin group (81.1 ± 27.5 μm vs 52.6 ± 15.4 μm, p<0.001) whereas no significant change was observed in late statin group (78.6 ± 27.4 μm vs 78.0 ± 27.4 μm, p=0.999). After adjusting for significant differences in baseline characteristics including history of hypertension, dyslipidemia, and prior use of statin, propensity score matched cohort included 25 patients in early statin group and 25 patients in late statin group. In the matched cohort, FCT (75.6 ± 27.2 μm vs 75.1 ± 27.3 μm, p=0.716) and FCT (74.9 ± 27.2 μm vs 74.8 ± 27.2 μm, p=0.897) were significantly less frequent in early statin group compared with late statin group (41.5% vs 62.5%, p=0.02, respectively).

Conclusion: Early statin therapy significantly increased the fibrous cap thickness in patients with acute coronary syndrome.
group [140 [100–180] μm to 160 [125–205] μm; p < 0.01], whereas the FCT did not change in the late statin group [120 [100–150] μm to 120 [100–150] μm, p = 0.29]. Percent change in the FCT was significantly greater in the early statin group (110 [92–137] % vs. 98 [85–110] %, p < 0.01). The percent change in the FCT was negatively correlated with percent change in serum malondialdehyde-modified low-density lipoprotein levels (r = -0.43, p < 0.01). During 6-month follow-up the FCT increased in both groups, and percent change in the FCT between baseline and 6-month follow-up was comparable between the 2 groups.

Conclusion: Increase of FCT in coronary plaque was observed at 3 weeks after starting a statin therapy, and a further increase was obtained at 6-month follow-up. Statin might have an early beneficial plaque-stabilizing effects in patients with ACS.

Results: The comparison between stent diameters measured from fluoroscopy images and computational results showed a mean difference of -1.04% (max 9.9%) for BE and -0.06% (max 7.1%) for SE implantations. Presence of PVR was identified by the automatic code in 93% of BE and 85% of SE cases, while correct location in 93% and 75% of cases respectively. The sole patient who developed conduction abnormalities (Fig. 1b), from the SE cohort, showed the highest stress distribution, thus providing a potential computational parameter to monitor this risk.

P3085 | BENCH Cerebral hypoperfusions and hypertensive events during atrial fibrillation: a mechanism for cognitive impairment?

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Background: Atrial fibrillation (AF) is associated with an increased risk of dementia and cognitive decline, independent of clinical strokes/TIAs. Several mechanisms have been proposed to explain this association, but altered cerebral blood flow dynamics during AF has been poorly investigated: in particular, it is unknown how AF influences hemodynamic parameters of the deepest cerebral circulation.

Purpose: Aim of the present study was to study AF impact on cerebral circulation through a computational hemodynamic analysis.

Methods: Two coupled lumped-parameter models (systemic and cerebrovascular circulations, respectively) were used to simulate sinus rhythm (SR) and AF.

Figure 1. Top panel: representative pressure and flow rate time series are reported for the internal carotid artery-middle cerebral artery (ICA-MCA) pathway during SR (blue) and AF (red). Lower panel: absolute frequency of hypoperfusions (a) and hypertensive events (b) during AF along the ICA-MCA pathway; the abscissa indicates the number of consecutive beats characterizing the events. P(a): systemic arterial pressure; P(MCA,left): left middle cerebral artery pressure; P(CCA,left): left common carotid artery pressure; P(I/CCA,left): left internal carotid flow rate; Q(MCA,left): left middle cerebral artery flow rate; Q(d/m,left): left middle distal flow rate; Gipv: proximal venous flow rate.
For each simulation 5,000 cardiac cycles were analyzed, computing main statistics (mean and standard deviation) for different cerebral hemodynamic parameters.

Results: With respect to SR, AF triggered a greater variability (represented by the standard deviation) of the parameters, especially in the deepest circulation (cerebral arterioles and capillaries) (see Figure, lower panel). By contrast, neither hyperperfusion nor hypertensive events occurred during SR.

Conclusion: During AF, the higher variability of the cerebral hemodynamic variables increases proceeding towards the peripheral circulation, reaching the maximum extent at the arteriolar and capillary levels and possibly resulting in local transient periods of excessive pressure or reduced blood flow. Thus, the impact of AF per se on cerebral hemodynamics candidates as a relevant mechanism into the genesis of AF-related cognitive impairment/dementia.

P3086 | BEDSIDE
Can computational fluid dynamics (CFD) predictions of FFR really agree with invasive FFR in intermediate stenoses? Lessons from a study using optical coherence tomography (OCT) and invasive measures

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Background: Computational fluid dynamics (CFD) modelling can estimate lesion specific FFR values (FFRCFD) from computed tomography coronary angiography (CTCA) images. The upper limit of accuracy of this technique may therefore be limited by i) the luminal characterisation ability of CTCA; and ii) the reliability of CFD on estimated boundary conditions of coronary flow and pressure.

Purpose: To assess the upper limits of agreement between FFRCFD and invasive FFR in intermediate coronary stenoses, using gold standard luminal imaging and patient specific boundary conditions of resting and hyperaemic flow. Pearson’s correlation coefficient of per-vessel FFRCFD values with FFR values was 0.57 (p=0.007). In the sensitivity analysis of the CFD simulations to varying volumetric flow rate levels, an increase of flow rate by 1% decreased FFRCFD and standard FFR values by 0.40, 0.35 and 0.20 in severe, intermediate and mild stenoses respectively.

Conclusions: In intermediate stenoses, using close to exact conditions for CFD (gold standard luminal imaging and patient specific boundary conditions), the diagnostic accuracy of FFRCFD was 71.4%. A major limitation of the concept of CFD is the requirement to estimate hyperaemic volumetric flow rate as a boundary condition. In this study, changes within the physiological range for hyperaemic flow conditions altered FFRCFD values by as much as 40%.

Acknowledgement/Funding: Medical Research Council Fellowship Grant (Dr Cook)

P3087 | BENCH
Study of the impact of electrical heterogeneities in the right and left atrium on atrial fibrillation perpetuation

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Introduction: Electrical heterogeneity in the atria has been consistently linked with the initiation and perpetuation of atrial fibrillation (AF). The present model-based study investigated the contribution of action potential duration (APD) heterogeneities in the left atrium (LA) and right atrium (RA) on the perpetuation of the reentrant activity during AF.

Methods: A computer model with a geometry based on computed tomography and a Courtemanche atrial cellular model was implemented. Self-terminated AF episodes were initiated via ramp pacing in a model with modified channel conductance, homogeneous tissue and 4:1 anisotropy ratio. Once AF was observed, random patchy heterogeneities with shorter APD were separately introduced in the LA and the RA. Percentage of heterogeneities was progressively increased from 20% to 80% of each atrium size (characteristic length scale of patches was 7.5mm). For each simulation, the following values were assessed: average AF duration, the number of sustained AF episodes (lasting more than 50s), number of wave-fronts (WF) and AF cycle length (AFCL). The results were averaged across the atria surface over 130 simulations (26 AF initial conditions and 5 random localizations of heterogeneities).

Results: For the model with no heterogeneities, #WF was 8.82±3.67, AFCL 278±52ms and the average AF duration 15.42±9s. For low percentage of heterogeneities there were no significant differences between RA, LA and the model with no heterogeneities. For high percentage of heterogeneities the results showed that a significant right-to-left atrial APD gradient was associated with more sustained AF episodes, longer duration, higher #WF and shorter AFCL compared to the left-to-right APD gradient (sustained AF episodes: 95% vs. 92%, p<0.04; duration: 48±9 vs. 23.8±21s, p<0.05; #WF: 11.72±3.3 vs. 9.7±3.1, p<0.04; AFCL: 209±69ms vs. 225±64ms, p<0.05).

Conclusion: High inter-atria differences in APD significantly affect the dynamics and the duration of the reentrant activity. Our findings are in line with previous studies reporting the right atrium as the dominant driver in some persistent AF cases.

Acknowledgement/Funding: This study was supported by the TMF Foundation.

P3088 | BEDSIDE
Systematic review of non-invasive computed tomography-derived FFR (FFR-CT) studies to guide integration of FFR-CT into mainstream clinical practice


Background: How to optimally integrate FFR-CT into clinical practice is not known. Overall diagnostic accuracy values provide only an overview across entire ranges of disease severity, in study populations that can differ from clinical cohorts. To interpret FFR-CT values on a patient-by-patient basis, diagnostic accuracy needs to be evaluated across narrow ranges of disease severity, in a sample-independent manner.

Purpose: To formulate a strategy for integrating non-invasive computed tomography-derived FFR (FFR-CT) into mainstream clinical practice.

Methods: A systematic review was performed of all studies that i) quantified physiological stenosis severity with both FFR-CT and invasive FFR (blinded); and ii) displayed a scatter plot of FFR-CT and invasive FFR values. Data were digitized to extract the individual data points for analyses of diagnostic performance. A per-quantile analysis of FFR-CT diagnostic accuracy was performed in each 0.10 FFR-CT disease quantile from 0.20 to 1.00. FFR-CT ≤0.80 and FFR ≤0.80 was used as the diagnostic cut-point, with invasive FFR as the reference standard.

Results: 4 studies (422 vessels) met the inclusion criteria. Mean age was 62.9 years (72% male). The overall diagnostic accuracy of FFR-CT was 77.5%, however, at the extremes of disease severity, FFR-CT values ≥0.90 and <0.50 demonstrated 93% and 85% agreement with invasive FFR respectively. Con-
versely, in the middle zone of FFR-CT 0.70 to 0.90, diagnostic accuracy fell to 70%, reaching a nadir of approximately 50% in the FFR-CT range 0.70 - 0.80. **Conclusions:** Interpretation of FFR-CT values on a patient-by-patient basis is aided by knowing the diagnostic accuracy of the technique in different ranges of disease severity. Extreme zone FFR-CT values have good diagnostic agreement with invasive FFR, reliably categorizing stenoses without the need for confirmatory invasive FFR assessment. However, middle zone FFR-CT values have markedly lower diagnostic accuracy and confirmatory invasive FFR is therefore recommended. Currently, FFR-CT does not support virtual PCI planning in any values below the cutoff for ischemia, as the numerical match for invasive FFR is poor. **Acknowledgement/Funding:** Medical Research Council Fellowship Grant (Dr Cook)

**P3089 | BEDSIDE**

Computational hemodynamic assessment of coronary lesions from computed tomography angiography: a novel approach

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**Background and aim:** Fractional Flow Reserve (FFR) obtained by Invasive Coronary Angiography (ICA) is an established index for assessing the functional significance of a coronary lesion and making decisions for coronary revascularization. Developments in Computed Tomography Angiography (CTA) also allow calculation of various functional indices for determining stenosis severity. In this study, we propose a novel approach to assess the haemodynamic status of the lesion and make decisions for revascularization, supported by known diagnostic accuracy of the technique in different ranges of disease severity.

**Methods and results:** 34 Patients with stable angina and intermediate (20–90%) pre-test likelihood of coronary artery disease (CAD) undergoing ICA and CTA with FFR measurement were included. 3D reconstruction was performed in 3 coronary arteries having a stenosis severity >30% and ≤70% on ICA and FFR measurements ranging from 0.45 to 1.0. After pre-processing of the initial CTA images and rough estimation of the artery borders and the arterial centerline, we have performed accurate centerline and lumen area detection, followed by reconstruction of the 3D surfaces. In the generated 3D models, we have employed blood flow simulations using the Finite Element Method, applying a laminar and incompressible flow and considering blood as a Newtonian fluid, we have calculated the virtual Functional Assessment Index (vFAI), which has been previously shown to correlate well with FFR derived from ICA. Nine vessels (26.4%) had FFR values lower than the 0.80 threshold. There was a good correlation between calculated vFAI and FFR values (r=0.916, P<0.001). In addition, there was a good agreement between the two measurements by the Bland-Altman method of analysis (mean difference=-0.042, SD=0.045). The limits of agreement were from -0.131 to 0.046, with 95% confidence intervals of -0.174 to -0.089 for the lower limit and 0.004 to 0.089 for the upper limit.

**Conclusions:** The proposed method can help clinicians to assess non-invasively the functional severity of a coronary lesion detected by CTA thus reducing possible false positive results and better selecting patients for invasive angiography and possible revascularization.

**P3090 | BEDSIDE**

Daily patterns of blood pressure values and prevalence of hypertension in professional drivers from the European RACER-ABPM study

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**Introduction:** Professional drivers are a group exposed to many cardiovascular risk factors. Non-systematic working hours, prolonged stress, low physical activity, along with irregular, in most cases, unhealthy meals are immanent aspects of the normal working schedule of most of those patients. These contribute to the development of overweight and obesity, which are one of the most important risk factors of cardiovascular disease.

**Purpose:** The aim of the current analysis was to establish prevalence of arterial hypertension in a group of continuous professional drivers – subpopulation of the RACER study cohort.

**Methods:** The RACER study is a prospective, study focused on assessing cardiovascular risk factors in professional drivers of the Central Europe. Patients included into the study were screen for the classical and non-classical cardiovascular risk factors. All patients had an ambulatory blood pressure monitoring (ABPM) performed for the diagnosis of hypertension and assessment of the daily variability of the values.

**Results:** Out of the whole RACER study population, 144 drivers were included into the RACER-ABPM study. Out of this group 135 (95.7%) were male, and the mean age was 50.2±9.3 years, and mean body mass index was 32.3±3.0 kg/m². Family history of cardiovascular disease was noted in 21.3% of patients, 28.1% were current smokers and 2.9% had diabetes. Arterial hypertension was previously diagnosed in 39 (27.9%) patients. In ABPM, the mean 24-hour blood pressure values were 130.3±14.3 and 80.9±9.9 for systolic and diastolic blood pressure respectively and 46.1% of patients could be categorized as dippers. Based on the ABPM results, arterial hypertension was diagnosed in 104 (73.8%) of patients. Patients with hypertension tend to be more often male and have family history of cardiovascular disease. There were no other differences in the population with and without arterial hypertension.

**Conclusions:** Arterial hypertension is highly prevalent in professional drivers. Also abnormal day-to-night blood pressure values patterns are often seen in this group. Arterial hypertension is one of the most important cardiovascular risk factors therefore proper and early diagnosis and treatment could significantly improve prognosis in this group.

**P3091 | BEDSIDE**

Association of urinary sodium excretion with ambulatory blood pressure in healthy adults

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**Purpose:** Many studies have shown a relationship between urinary sodium excretion and blood pressure (BP), mainly among middle-aged to elderly individuals and using conventional BP measurements. In the current study, we aimed to evaluate the relationship of ambulatory BP with 24-h urinary sodium excretion in a large sample of healthy adults.

**Methods:** Our analysis included 2788 individuals from two population-based studies in the Principality of Liechtenstein (n=2010) and in Switzerland (n=778). Participants included into the study were screen for the classical and non-classical cardiovascular disease, diabetes, a body mass index (BMI) >35 kg/m² or intake of BP lowering treatment were excluded. In Switzerland, 24-h urinary sodium excretion was used as a measure of sodium intake, while in the Principality of Liechtenstein it was calculated from fasting morning urinary samples using the Kawasaki formula. 24-h ambulatory blood pressure measurements were obtained from each individual.

**Results:** Median age, BP, sodium excretion (sodium chloride excretion) and estimated glomerular filtration rate in the studies in the Principality of Liechtenstein and in Switzerland were 35 and 44 years, 123/76 and 118/77 mmHg, 4.2 and 3.2 g/d (10.7 and 8.1 g/d), and 110 and 99 ml/min/1.73m², respectively. In multivariable linear regression models, no significant linear associations were observed between sodium excretion and systolic BP, as shown in the Table. There was no
evidence of a non-linear relationship using piece-wise linear regression models (Table). Similar findings were obtained for diastolic BP.

Methods: A total of 2,424 subjects [1,566 men and 858 women, mean age: 49.6±5.2 years (between 40 and 59 years)] who underwent health examinations were included. Bed time, sleep quantity (time in bed, TIB), and sleep quality were assessed using the Pittsburgh Sleep Quality Index (PSQI). The presence of hypertension was defined as current treatment of antihypertensive medication.

Results: In the male group, bed time was significantly earlier in subjects with hypertension (n=239) than in subjects without hypertension (n=1,327) (23:10 min ± 76 min vs. 23:28 min ± 67 min, p<0.001), whereas there was no difference in TIB between the two groups. The global PSQI score was significantly higher in subjects with hypertension than in subjects without hypertension (5.3±2.5 vs. 4.7±2.2, p=0.001). In the female group, the global PSQI score was significantly higher in subjects with hypertension (n=50) than in subjects without hypertension (n=808) (5.7±3.1 vs. 4.9±2.3, p<0.05), whereas there was no difference in bed time between the two groups. Multiple logistic regression analyses revealed that after adjusting for age, gender, body mass index, smoking, and alcohol intake, both bed time (OR, 0.92; 95% CI, 0.86–0.98; p<0.05) and the global PSQI score (OR, 1.11; 95% CI, 1.04–1.18; p<0.05) were significantly associated with the presence of hypertension in the male group, whereas the significance was lost in the female group.

Conclusions: These results suggested that quality, rather than quantity, may be associated with the presence of hypertension in middle-aged men. Furthermore, those with hypertension tend to go to sleep earlier.

P3093 | BEDSIDE
Sleep quality as well as sleep quantity may be important factors contributing to the development of hypertension.

Conclusions: In this large cohort of healthy adults, 24-h urinary sodium excretion was not associated with 24-h ambulatory BP. These results differ from prior studies among older individuals.

P3095 | BEDSIDE
Visceral adiposity index is increased in pre-hypertension: the Polish Norwegian Study (PONS)

Methods: Blood pressure patterns remain to be adequately explored and warrant further investigation.

Abstract P3092 – Table 1. Mean 5-year changes in NT-proBNP and BP

<table>
<thead>
<tr>
<th>ATN</th>
<th>NT-proBNP, % (95% CI)</th>
<th>ΔSBP, mm Hg (95% CI)</th>
<th>P</th>
<th>ΔDBP, mm Hg (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>WL</td>
<td>Men</td>
<td>32 (19 to 43)</td>
<td>-0.001</td>
<td>-2.0 (−4.0 to -0.0)</td>
<td>0.005</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>34 (26 to 44)</td>
<td>0.001</td>
<td>-1.4 (−2.9 to 0.1)</td>
<td>0.003</td>
</tr>
<tr>
<td>WS</td>
<td>Men</td>
<td>19 (14 to 23)</td>
<td>-0.001</td>
<td>0.9 (0.3 to 1.5)</td>
<td>0.006</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>11 (7 to 15)</td>
<td>-0.001</td>
<td>1.8 (1.0 to 2.6)</td>
<td>0.001</td>
</tr>
<tr>
<td>WG</td>
<td>Men</td>
<td>11 (5 to 18)</td>
<td>0.001</td>
<td>2.6 (1.9 to 3.6)</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>4 (0 to 19)</td>
<td>0.131</td>
<td>3.6 (2.6 to 4.6)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

BP: blood pressure; WL: weight loss; WS: weight stable; WG: weight gain; CI: confidence interval; SBP: systolic blood pressure; DBP: diastolic blood pressure.

Lifestyle and blood pressure 611

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Lifestyle and blood pressure / PCI complications

P3096 | BEDSIDE
Obesity and female sex are associated with development of left ventricular hypertrophy in treated hypertensive outpatients: the campania salute network

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Background: The aim of this study was to evaluate incident left ventricular (LV) hypertrophy (LVH) in a treated hypertensive population.

Methods: From the Campania Salute Network registry, we identified 4290 hypertensives (age 50.3±11.1 years, 40% women) without LVH at baseline. LVH was defined as left ventricular mass index (LVMI) above the threshold for LVH (≥50 g/m².7 in women and ≥50 g/m².7 in men).

Results: After a follow-up (FU) of 47.4 months (interquartile range 26.5–85.1), 915 patients (21.3%) exhibited LVH. These patients were older, more frequently females, obese (both p < 0.0001) and diabetic (p = 0.03). At baseline, patients developing LVH during FU presented with lower heart rate and glomerular filtration rate (GFR/REPi both p < 0.0001), higher fasting glucose, body mass index (BMI), longer history of hypertension and shorter duration of FU (all p < 0.001). During FU average systolic BP was higher and heart rate lower in patients developing LVH during FU as compared to patients developing LVH during FU vs. optimal BP and 3.11 (2.57–3.77) for being HTN vs. preHTN. Compared to a VAI <1.9, the odds ratio of a VAI >2.1 was 1.36 (95% CI 1.19–1.55) for being preHTN vs. optimal BP and 1.98 (1.73 –2.27) for being HTN vs. preHTN.

Conclusion: VAI is independently associated with preHTN and HTN status. Potentially, identifications of preHTN individuals with increased VAI may guide targeted aggressive prevention interventions.

Acknowledgement/Funding: The Polish-Norwegian Research Fund (PNRF-CA1-10-07)

P3097 | BEDSIDE
If something goes wrong: a detailed analysis of the full spectrum of PCI-related complications in a large-scale, prospective registry study

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Background: Improvements in stent technology and adjunctive therapy as well as in operator experience and skills have led to a decreasing risk of major percutaneous coronary intervention (PCI)-related complications despite the increasing complexity of cases. Very few studies, however, have examined the full spectrum of complications. Methods: Between May 2005 and April 2008 a total of 47,407 consecutive patients were prospectively enrolled into the PCI-Registry of the Euro Heart Survey Programme. In the present analysis PCI-related complications in patients with acute coronary syndrome (ACS; n=24,389; 51.4%) and stable coronary artery disease (CAD; n=23,018; 48.6%) were evaluated.

Results: The incidence of PCI-related complications among patients with ACS and stable CAD is displayed in Table 1.

Table 1

<table>
<thead>
<tr>
<th>Complication</th>
<th>ACS</th>
<th>Stable CAD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute segment closure</td>
<td>0.7%</td>
<td>0.4%</td>
</tr>
<tr>
<td>No flow/slow flow</td>
<td>1.9%</td>
<td>0.6%</td>
</tr>
<tr>
<td>Distal embolisation</td>
<td>0.4%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Early stent thrombosis</td>
<td>0.9%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Emergency CABG</td>
<td>0.2%</td>
<td>0.1%</td>
</tr>
<tr>
<td>Coronary perforation</td>
<td>0.3%</td>
<td>0.2%</td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>0.9%</td>
<td>0.2%</td>
</tr>
<tr>
<td>Deterioration</td>
<td>0.9%</td>
<td>0.2%</td>
</tr>
<tr>
<td>Heart block requiring pacing</td>
<td>1.1%</td>
<td>0.1%</td>
</tr>
<tr>
<td>Shock induced by procedure</td>
<td>0.2%</td>
<td>0.1%</td>
</tr>
<tr>
<td>Respiratory failure requiring ventilation</td>
<td>1.1%</td>
<td>0.1%</td>
</tr>
<tr>
<td>False aneurysm</td>
<td>0.7%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Arterial occlusion or dissection</td>
<td>0.1%</td>
<td>0.1%</td>
</tr>
<tr>
<td>Infection at puncture site</td>
<td>0.3%</td>
<td>0.1%</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>1.0%</td>
<td>0.4%</td>
</tr>
<tr>
<td>Renal failure requiring dialysis</td>
<td>0.8%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Non-fatal stroke</td>
<td>0.4%</td>
<td>0.1%</td>
</tr>
<tr>
<td>Post-procedural non-fatal MI</td>
<td>2.2%</td>
<td>0.2%</td>
</tr>
<tr>
<td>In-hospital death</td>
<td>2.5%</td>
<td>0.2%</td>
</tr>
</tbody>
</table>

Conclusions: In clinical practice there is a wide spectrum of PCI-related complications. As expected, the rate of serious complications was significantly higher among patients with ACS.

P3098 | BEDSIDE
High-dose statin therapy is effective at preventing the development of contrast-induced nephropathy in patients undergoing percutaneous coronary intervention for acute coronary syndromes: a meta-analysis

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Background: Contrast-induced nephropathy (CIN) is often encountered following percutaneous coronary intervention (PCI) in patients with acute coronary syndromes (ACS) and is associated with high in-hospital morbidity and mortality. Statins may prevent the development of CIN, however their efficacy in patients with ACS has not been evaluated.

Purpose: We conducted a meta-analysis of randomized controlled trials (RCTs) to assess statin efficacy in the prevention of CIN in patients undergoing PCI for ACS.

Methods: PubMed, EMBASE, MEDLINE and the Cochrane Central Register were searched for RCTs from inception to September 2014 to compare high-dose statins (rosuvastatin 40mg/day, atorvastatin 80mg/day or simvastatin 80mg/day) with low-dose statins (atorvastatin 10mg/day, simvastatin 10mg/day) or placebo treatment in patients with ACS, undergoing PCI. Study-specific odds ratios (ORs) were calculated, and between-study heterogeneity was assessed using the I² statistic. We used a random effects model meta-analysis to pool the OR.

Results: Seven RCTs, including 5174 patients were included in the analysis. CIN
Radial artery spasm: prevalence, prevention and safety vasodilators agents in a prospective randomized meta-analysis


Background: Radial artery spasm (RAS) remains a major limitation for transradial approach (TRA). The aim of our study was to compare the efficacy and safety of different vasodilators in the prevention of RAS in patients undergoing TRA.

Methods: Between February 2011 and January 2013, patients with stable angina who planned elective PCI were assigned into a 1:1:1 ratio to control, continuous infusion of nicorandil were not significantly different to that in control.
P3102 | BEDSIDE

Pre-procedural risk score for contrast induced-acute kidney injury development in ST elevation myocardial infarction patients undergoing primary percutaneous coronary intervention

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Background: Risk scores for the prediction of Contrast Induced-Acute Kidney Injury (CI-AKI) in patients with ST-Elevation Myocardial Infarction (STEMI) undergoing primary Percutaneous Coronary Intervention (pPCI) include variables related to the procedure, whereas reliable pre-procedural risk scores are lacking.

Purpose: We aimed to determine the prognostic significance of bleeding events and subsequent 30-day and 1-year mortality after pPCI reproducibly predicted the risk of CI-AKI in two different populations. The score identified patients at risk for atrial fibrillation (AF) in this age group is debated.

Material and methods: The subjects in this study were men who participated in the Gothenburg Population Study of men born in 1943, a cohort consisting of randomly selected men born 1943 and living in the city of Gothenburg. They were first examined in 1993 and underwent a re-examination in 2014. Questionnaires were used for the diagnosis of OSA.

Results: Out of 412 men screened, 121 (29.3%) had moderate or severe obstructive sleep apnea (OSA) in men aged >70 years from the general population. The role of OSA as a risk factor for atrial fibrillation (AF) in this age group is debated.

P3104 | BEDSIDE

Severe sleep apnea is associated with atrial fibrillation in older men from the general population

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Background: Data on the prevalence of obstructive sleep apnea (OSA) in men aged >70 years from the general population are limited. The role of OSA as a risk factor for atrial fibrillation (AF) in this age group is debated.

Purpose: This study investigated: (1) the prevalence of OSA in elderly men of similar age randomly recruited from the general population; and (2) to what extent a diagnosis of OSA is associated with AF in this population.

Material and methods: The subjects in this study were men who participated in the Gothenburg Population Study of men born in 1943, a cohort consisting of randomly selected men born 1943 and living in the city of Gothenburg. They were first examined in 1993 and underwent a re-examination in 2014. Questionnaires were used for the diagnosis of OSA.

Results: Out of 412 men screened, 121 (29.3%) had moderate or severe obstructive sleep apnea (OSA), with an AHI (apnea-hypopnea index) ≥15/h, while 191 did not.

Differences in sleep parameters between the groups.

Whole Cohort No atrial fibrillation Atrial fibrillation p-value

Apnea Hypopnea Index; AHI 11.8±0.6 11.2±0.6 15.0±1.6 0.002
Oxygen Desaturation Index; ODI 10.1±0.6 9.6±0.6 13.6±1.7 0.002
Mean pulse (bpm) 61.0±0.5 60.4±0.5 64.5±1.6 0.016

Conclusions: Blowing scales vary significantly identify rates of severe bleeding after pPCI, and several are independently associated with increased 30-day and 1-year mortality.

Acknowledgement/Funding: The CHAMPION trials were funded by The Medicines Company.
This French longitudinal cohort study was based on the national hospitalization database covering hospital care from 2009 to 2012 for the entire country. All patients were included in order to compare characteristics among IS patients with no AF, known AF and new AF. From patients with IS and no AF at baseline (or in their prior history), we calculated incidence rates of newly diagnosed or incident AF.

Results: We included 336,291 patients with IS (50.3% male; median age: 74±15 years). Of those, known AF was present in 95,832 (28.5%) and new AF was recorded during follow-up in 14,095 (4.2%). Characteristics, cardiovascular risk factors and comorbidities in IS patients with no AF, known AF and new AF are listed in table. Cardiovascular risk factors seen in patients with IS and known AF were even more prevalent amongst patients with new AF after IS. The fact that patients with so-called “new AF” more often had a history of transient ischemic attack suggests that AF was previously unknown rather than being “true” new-onset AF.

Conclusions: Obstructive sleep apnea is common in elderly men from the general population, and there is a three-fold higher probability for having AF in those with severe OSA. Longitudinal studies in elderly are warranted to determine whether OSA is a risk factor for development of AF, and to what extent AF can be prevented by relevant treatment of OSA.

Acknowledgement/Funding: The Swedish Heart-Lung Foundation.

P3106 | BEDSIDE
Pre-existing cardiovascular comorbidities underlie newly diagnosed atrial fibrillation after acute ischemic stroke

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Background: Many ischemic strokes (IS) occur in patients with atrial fibrillation (AF) and 20% of all strokes are attributed to AF. Whether cardiovascular risk factors in IS patients with newly diagnosed AF (new AF) during follow-up are similar to patients with known AF is not well established. New AF possibly reflects underlying cardiovascular comorbidities but might also be triggered by “neurogenic” mechanisms in patients with IS.

Methods: This French longitudinal cohort study was based on the national hospitalization database covering hospital care from 2009 to 2012 for the entire country. All patients were included in order to compare characteristics among IS patients with no AF, known AF and new AF. From patients with IS and no AF at baseline (or in their prior history), we calculated incidence rates of newly diagnosed or incident AF.

Results: We included 336,291 patients with IS (50.3% male; median age: 74±15 years). Of those, known AF was present in 95,832 (28.5%) and new AF was recorded during follow-up in 14,095 (4.2%). Characteristics, cardiovascular risk factors and comorbidities in IS patients with no AF, known AF and new AF are listed in table. Cardiovascular risk factors seen in patients with IS and known AF were even more prevalent amongst patients with new AF after IS. The fact that patients with so-called “new AF” more often had a history of transient ischemic attack suggests that AF was previously unknown rather than being “true” new-onset AF.

<table>
<thead>
<tr>
<th>Characteristics of patients with IS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Male gender</td>
</tr>
<tr>
<td>CHA2DS2-VASc score</td>
</tr>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>Diabetes</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
</tr>
<tr>
<td>Heart failure</td>
</tr>
<tr>
<td>Coronary artery disease</td>
</tr>
<tr>
<td>Pulmonary disease</td>
</tr>
<tr>
<td>Kidney disease</td>
</tr>
<tr>
<td>History of transient ischemic attack</td>
</tr>
</tbody>
</table>

Conclusions: Obstructive sleep apnea is common in elderly men from the general population, and there is a three-fold higher probability for having AF in those with severe OSA. Longitudinal studies in elderly are warranted to determine whether OSA is a risk factor for development of AF, and to what extent AF can be prevented by relevant treatment of OSA.

Acknowledgement/Funding: The Swedish Heart-Lung Foundation.

P3107 | BEDSIDE
Presence of diabetic complications does not incrementally increase risk of ischemic stroke in diabetic patients with atrial fibrillation

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Background: Conventional stroke risk prediction tools used in atrial fibrillation (AF) incorporate the presence of diabetes mellitus (DM) as a risk factor. However, it is unknown whether this risk is homogenous or dependent on the presence of diabetic complications, such as diabetic retinopathy, nephropathy, and neuropathy, which might reflect incrementally more advanced DM. The present study examined the risk of ischemic stroke in diabetic patients with and without end-organ damage.

Method: The present study used the National Health Insurance Research Database in Taiwan with detailed healthcare data on all-comers to the Taiwanese national health care system from January 1, 1996 to December 31, 2011. AF and DM were identified when listed as discharge diagnoses or confirmed more than twice in the outpatient department. Patients on antithrombotic agents were excluded. The clinical endpoint was ischemic stroke confirmed on imaging.

Results: Among the 50,180 non-anticoagulated AF patients with DM, the majority had no microvascular complications (72.7%), while 2.6% had diabetic retinopathy, 8.4% had diabetic nephropathy, and 16.1% had diabetic neuropathy. The primary outcome occurred with an incidence of 47.44 events per 1,000 person-years of follow-up. When compared with DM patients without microvascular complications, those with diabetic retinopathy, nephropathy, or neuropathy had higher incidences of ischemic stroke (46.52 vs. 50.72, 47.66, or 51.97 per 1,000 person-years, respectively). However, after adjusting for confounding factors, the differences were no longer significant. When stratified according to the CHA2DS2-VASc score (range 1–9), there were no differences in the adjusted hazard ratios for each diabetic complication when compared to no diabetic complication at each score with regards to the risk of ischemic stroke (Figure).

Conclusions: In a large nationwide AF cohort with DM, risk of ischemic stroke...
I. Grazhdankin1, D. Losik1, D. Ponomarev1, A. Strelnikov1, E. Pokushalov1
MI. More rigorous monitoring strategies and relevant intervention are needed.

Conclusion:

Background: Cardiac arrhythmias (CA) following the myocardial infarction (MI) can be associated with major adverse cardiovascular events. A timely detection of post-MI arrhythmias may lead to early intervention and bring benefit to the patients. The data on the "real incidence" of post-MI arrhythmias remained limited.

Objective: We aimed to continuously monitor the rate and burden of CA by implanting cardiac loop-recorder (ILR) in patients with a preserved LVEF after AMI.

Methods: In this prospective observational study, patients who underwent PCI and had LVEF ≥ 40% within 7 days following MI were enrolled to receive ILR implantation. Primary outcome was the incidence of new-onset AF (defined by the ILR device’s algorithm) during a follow up (FU) of 2 years.

Results: Of 827 consecutive patients with ACS, 50 (6%) eligible patients were finally recruited (mean age 57.8±8.3, 88% male). During the FU period, AF was found the most frequently detected arrhythmia, 29 (58%) of the patients developed new-onset AF, with a cumulative rate of all arrhythmias by 72%. The rate of AF events was increased in a time-dependent manner (16% at 3 months to 50% at 12 months), and the peak cumulative AF burden was detected between 3–6 months. Only 11% of symptomatic episodes were confirmed as AF, and 93% of patients with AF were asymptomatic. The Cox regression analysis further found that baseline troponin level and female-gender were risk factors of new-onset AF post-MI.

Conclusion: AF is a frequent but largely underestimated cardiac arrhythmia after MI. More rigorous monitoring strategies and relevant intervention are needed.

P3109 | BEDSIDE
Risk of new onset atrial fibrillation following an acute coronary syndrome: data from the GRACE registry

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Background: Atrial fibrillation (AF) is a frequent complication of an acute coronary syndrome (ACS) and is associated with an increased risk of in-hospital and long-term mortality. Yet, many studies lack recent electrocardiographic (ECG) assessments in hospital and core-lab verification of AF, which is important for accurate prognostication.

Purpose: To determine whether patients presenting with ACS who developed new-onset AF had an increased risk of death or a composite major adverse cardiovascular events (MI), or stroke when compared to patients with and without prior AF.

Methods: Among 7282 patients (median age 66; 33.4% female) presenting with an ACS (ST-segment elevation MI (STEMI) 37.6%, non-STEMI 32.3%) in the Global Registry of Acute Coronary Events (GRACE), individuals were categorized based on whether they presented with a history of prior AF (8.5%), new-onset AF (9.2%) or no AF (82.3%; reference) according to core lab ECG assessments (presentation ECG, 24–48 hour ECG and case report form). The three groups were mutually exclusive and included all patients. The core ECG lab was blinded to clinical data and outcomes. Multivariable models were constructed to estimate whether new-onset AF was independently associated with death in-hospital and at 6 months or MACE at 6 months.

Results: Patients with prior AF on average were older and had higher rates of established cardiovascular disease compared with new-onset or no AF patients. The mean CHADS2-VASc score of patients with prior AF was 4, with new-onset AF was 3 and without AF was 2 (P-global <0.001). At the index ACS, new-onset AF patients presented with higher risk ACS as reflected by higher GRACE scores, rates of STEMI and rates of cardiac arrest on presentation compared with prior AF or no AF patients. New-onset AF and prior AF patients had higher rates of 6-month mortality compared with patients without AF (22.3% and 21.3% vs. 7.5%, P-global <0.001). Adjustment for prognosticators, including those in the GRACE risk model, revealed that new-onset AF was independently associated with higher mortality in-hospital and at 6-months as well as MACE at 6-months compared with patients without AF (Figure). Furthermore, the adjusted risk of mortality in hospital and at 6 months as well as MACE at 6 months was similar among patients with new-onset or prior AF (all P for pair-wise comparisons >0.46).

Conclusion: The risk of death and MACE following ACS in patients with new-onset and prior AF appear similar and significantly increased compared with patients without AF. Knowledge of mortality and ischemic risks in patients with AF during ACS may allow clinicians to better risk stratify patients with ACS and guide diagnostic and therapeutic decisions.

Acknowledgement/Funding: The Global Registry of Acute Coronary Events (GRACE) was supported by an unrestricted grant from Sanofi-Aventis, Paris, France.
Hypertension in patients with Atrial Fibrillation: the EUROS observational research programme on atrial fibrillation (EORF-AP) pilot registry

G.A. Dan1, E. Badila1, E. Weiss1, C. Laroche2, G. Boriani3, A. Dan4, L. Tavazzi5, A.P. Maggioni5, H.J. Crijns6, R. Popescu7, G.Y.H. Lit8, 1University of Medicine and Pharmacy Carol Davila, Bucharest, Romania; 2European Society of Cardiology, EURObservational Research Programme Department, Sao-Paulo-Antipolis, France; 3University of Bologna, Experimental, Diagnostic and Speciality Medicine, Institute of Cardiology, Bologna, Italy; 4Columbia University Hospital, Cardiology, Bucharest, Romania; 5QMV Care and Research, Etterre Sansvinin Health Science Foundation, Maria Cecilia Hospital, Cotignola, Italy; 6ANMCO Foundation For Your Heart, Florence, Italy; 7Maastricht University Medical Centre (MUMC), Cardiology, Maastricht, Netherlands; 8University of Birmingham Centre for Cardiovascular Sciences, City Hospital, Birmingham, United Kingdom

Background: Atrial fibrillation (AF) is commonly found in hypertensive patients and the relationship between the two is bidirectional, with an incremental effect on adverse outcomes.

Purpose: To study clinical features, treatment patterns and 1-year outcomes amongst AF patients with hypertension (HTN), compared to normotension (NT) AF patients in the EURObservational Research Programme Atrial Fibrillation (EORF-AP) Pilot Registry, a prospective multi-national survey conducted by the European Society of Cardiology in 9 European countries.

Methods: Of 3119 enrolled AF patients, 2194 were diagnosed with HTN (AF-HTN) and 909 were NT (AF-NT) (16 patients had unknown HTN status). We compared baseline clinical features, management strategy and 1-year outcomes in terms of all-cause death, cardiovascular (CV) death, and any thrombosis-related event (TE: stroke, transient ischemic attack, acute coronary syndrome, coronary intervention, cardiac arrest and peripheral or pulmonary embolism) in HTN vs. non-HTN patients.

Results: The AF-HTN patients had more prevalent CV risk factors and comorbidities (mean CHA2DS2-VASc score in 4 AF-HTN, vs. 2 in NT AF; p<0.0001). Crude rates of all-cause death and any TE event was higher in AF-HTN. Kaplan-Meier analysis curves for death by hypertensive status showed no significant differences between AF-HTN vs. AF-NT (log rank test, p=0.210). On logistic regression analysis, HTN did not emerge as an independent risk factor for outcomes.

Conclusion: AF patients with a history of HTN have a higher prevalence of comorbidities and this conferred a higher risk for a composite endpoint of all-cause/CV death and thromboembolic events. HTN did not emerge as independently associated with a higher all-cause 1-year mortality.

ION CHANNELS: FROM THE MOLECULAR LEVEL TO INTEGRATIVE BIOLOGY

P3110 | BEDSIDE

Hypertension in patients with Atrial Fibrillation: the EUROS observational research programme on atrial fibrillation (EORF-AP) pilot registry

G.A. Dan1, E. Badila1, E. Weiss1, C. Laroche2, G. Boriani3, A. Dan4, L. Tavazzi5, A.P. Maggioni5, H.J. Crijns6, R. Popescu7, G.Y.H. Lit8, 1University of Medicine and Pharmacy Carol Davila, Bucharest, Romania; 2European Society of Cardiology, EURObservational Research Programme Department, Sao-Paulo-Antipolis, France; 3University of Bologna, Experimental, Diagnostic and Speciality Medicine, Institute of Cardiology, Bologna, Italy; 4Columbia University Hospital, Cardiology, Bucharest, Romania; 5QMV Care and Research, Etterre Sansvinin Health Science Foundation, Maria Cecilia Hospital, Cotignola, Italy; 6ANMCO Foundation For Your Heart, Florence, Italy; 7Maastricht University Medical Centre (MUMC), Cardiology, Maastricht, Netherlands; 8University of Birmingham Centre for Cardiovascular Sciences, City Hospital, Birmingham, United Kingdom

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Conclusion: AF patients with a history of HTN have a higher prevalence of comorbidities and this conferred a higher risk for a composite endpoint of all-cause/CV death and thromboembolic events. HTN did not emerge as independently associated with a higher all-cause 1-year mortality.

ION CHANNELS: FROM THE MOLECULAR LEVEL TO INTEGRATIVE BIOLOGY

P3111 | BENCH

SCN10A/Nav1.8 channels contribute to arrhythmogenesis in the human failing heart

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In heart failure, enhanced persistent current through Na channel (late INa) prolongs action potential duration (APD) and increases diastolic sarcoplasmic reticulum (SR) Ca2+ leak. We have shown that Ca/CaM modulation Kinase II (CaMkII) increases late INa in heart failure via Nav1.5 phosphorylation, thereby producing arrhythmias. Here, we studied whether in the human failing heart augmented late INa and arrhythmogenic consequences are due to neuronal sodium channel Nav1.8. Additionally we investigated a possible association between Nav1.8 and CaMkII. The protein levels of Nav1.8 were significantly increased 2-fold in ventricular homogenates from patients with hypertrophy (Hy, n=9) and heart failure (HF, n=8) compared to non-failing (HF, n=10). In parallel, expression levels of cardiac sodium channel Nav1.5 were decreased. Co-immunoprecipitation revealed a significant increase in association of Nav1.8 with CaMkII in HF compared to NF (n=3 vs. 3). Whole-cell patch clamping showed a potent reduction in late INa integral and APD after addition of novel Nav1.8 specific blockers, either A-803467 (30 nM) or PF-01247324 (1 μM) in ventricular human failing myocytes. Furthermore, using confocal microscopy (Fluo4 AM), we studied the diastolic SR Ca2+ leak. In HF, both A-803467 and PF-01247324 resulted in a significant decrease of CaSpF (58%), while in Hy CaSpF was not changed. Additionally, we measured late INa and CaSpF in mice lacking Nav1.8 (SCN10A–/–) vs. wild-type (WT). In WT, the addition of isoproterenol (ISO, 30 nM) resulted in a significant increase of INa and CaSpF. In SCN10A–/–, the addition of ISO did not change late INa and CaSpF. These findings indicate that Nav1.8 contributes to arrhythmogenesis in the human failing heart.

Abstract P3110 – Table 1. Major events during 1-year follow-up de- : 1 University of Medicine and Pharmacy Carol Davila, Bucharest, Romania; 2European Society of Cardiology, EURObservational Research Programme Department, Sao-Paulo-Antipolis, France; 3University of Bologna, Experimental, Diagnostic and Speciality Medicine, Institute of Cardiology, Bologna, Italy; 4Columbia University Hospital, Cardiology, Bucharest, Romania; 5QMV Care and Research, Etterre Sansvinin Health Science Foundation, Maria Cecilia Hospital, Cotignola, Italy; 6ANMCO Foundation For Your Heart, Florence, Italy; 7Maastricht University Medical Centre (MUMC), Cardiology, Maastricht, Netherlands; 8University of Birmingham Centre for Cardiovascular Sciences, City Hospital, Birmingham, United Kingdom

<table>
<thead>
<tr>
<th>Events</th>
<th>Males</th>
<th>Females</th>
<th>Total</th>
<th>p-value HTN vs. non-HTN</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15592</td>
<td>1035</td>
<td>2621</td>
<td>1084</td>
<td></td>
</tr>
<tr>
<td>All cause death + any TE</td>
<td>157 (10.4%)</td>
<td>97 (10.2%)</td>
<td>254 (10.3%)</td>
<td>113 (11.1%)</td>
</tr>
<tr>
<td>CV death – any TE or bleeding</td>
<td>114 (8.0%)</td>
<td>69 (7.7%)</td>
<td>183 (7.9%)</td>
<td>75 (7.8%)</td>
</tr>
</tbody>
</table>

Acknowledgement/Funding: NMRC/CBER/002/2012; NHUS (NUHSRO/2014/061)AP/Partner/02; President's Graduate Fellowship from NUS; NMRC CS-IRG; NUS Start-up grant.
polared areas have been reported because of the occurrence of virtual anodes in the cardiac tissue. Although mathematical modelling studies have suggested the importance of virtual anodes in determining the success for electrical defibrillation, there is no experimental evidence that hyperpolarisation can defibrillate the heart. Because electrical stimulation of tissue always induces simultaneous depolarisation and hyperpolarised areas without proper control over spatial extent and level of membrane potential change. Here we present a novel optogenetic method to induce isolated hyperpolarisation in cardiomyocytes expressing the light-activated proton pump Archaerhodopsin3-3 (ArchT) and addressed the effectiveness for defibrillation in a mouse model of ventricular tachycardia.

Methods: Transgenic mice with cardiac expression of ArchT in fusion to EGFP were generated by crossing breeding MHC-Cre with Ai46D mice expressing ArchT-EGFP after Cre-Mediated removal of a flxed-STOP cassette. Expression of ArchT was induced by intraperitoneal injection of the light sensitive ion channel responsiable for Is HCN4. Hearts were isolated (and denervated) at the two time points and Langendorff-perfused (n=8) – the intrinsic HR was 97 beats/min slower at ZT0 compared to ZT12 (P <0.01). Therefore, the cardiac rhythm in HR is intrinsic to the heart. To study the underlying mechanism, patch clamp experiments were conducted on sinus node myocytes isolated at the two time points. A key pacemaker current is the I{f} current (If) and this was measured during 5 s hyperpolarizing pulses from a holding potential of -35 mV. There was a circadian rhythm in If. For example, If was measured at -125 mV) at ZT2 was 17.8±2.9 pA/pF (n=10), whereas at ZT14 It was doubled at 35.0±6.3 pA/pF (n=6; P <0.05). This circadian rhythm in If could be blocked by the light-activated proton pump ArchT-3.0 and the light-sensitive ion channel responsible for If is HCN4. Sinus node biopsies were collected at ZT0 and ZT12 and the expression level of clock genes and HCN4 was measured at the mRNA level by quantitative PCR; in addition, expression of HCN4 protein was measured by Western blot. Consistent with previous reports (e.g. OCK and HCN1 and HCN4) were expressed and varied in a circadian manner (n=8; P < 0.05). HCN4 mRNA was 89% higher at ZT0 compared to ZT12 (n=7; P <0.05), whereas HCN4 protein was 49% lower at ZT0 compared to ZT12 (n=7; P <0.05); a time lag of hours is expected between mRNA, protein and ionic current. In silico analysis of 10 kb of the HCN4 promoter revealed the 7 conserved consensus (EBOX) binding sites for the BMAL1:CLOCK heterodimer. Chromatin immunoprecipitation enrichment of these sites was observed by over-expressing BMAL1 in vitro.

Conclusion: We have shown circadian rhythms in CLOCK, BMAL1, HCN4 mRNA. HCN4 protein. If, the intrinsic HR in vitro and the normal HR in vivo. It is concluded that the well known circadian rhythm in HR is not the result of vagal tone and instead could be the result of a circadian rhythm in transcription of the HCN4 gene driven by a circadian clock in the sinus node.

Acknowledgement/Funding: BHF, MRC, Wellcome Trust, Biotechnology and Biological Sciences Research Council.
Characteristics in the transitional tissue did not change with PHT, but further downstream there were conduction disturbances in 5 out of 6 PHT hearts: in 3 hearts there was Wenckebach conduction in the compact node and in 2 hearts there was decremental conduction in the penetrating bundle. Control hearts showed normal 1:1 conduction. Consistent with our electrophysiological findings, the AV node showed downregulation of K+ channels responsible for depolarizing/inward currents (HCN4, Cav2.1, Cav2.3, Cav3.1 and Cav3.2) and key repolarizing K+ currents (Kv1.4, Kv4.2, Kv4.3, KCNH2). The former would tend to shorten action potential duration and this is likely to be countered by the latter. Connexin expression (Cx40, Cx43 and Cx45) in the AV node did not change in PHT.

Conclusion: In PHT, detrimental conduction in the AV node is a result of ion channel remodelling and this is the likely cause of AV node dysfunction and heart block.

Acknowledgement/Funding: British Heart Foundation

**P3117 | BENCH**

Combined use of transgenic LQT2, LQT5 and LQT5-5 rabbit models with decreased repolarization reserve as novel tool for pro-arrhythmia research


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**Purpose:** For this aim, different transgenic LQT5 rabbit models with impaired repolarization reserve were generated (LQT2, HERG-G628S, loss of IKr; LQT5, KCNQ1-G529R, decreased fks; double-transgenic LQT2–5, loss of IKr/decreased fks).

**Methods:** In vivo telemetric ECG (QTc, QTd observed/GT expected) and ex vivo monophasic action potential measurements in Langendorff-perfused hearts (action potential duration (APD75), triangulation (APD90-APD30), and spatial dispersion of repolarization (APDmax-APDmin)) were performed to assess the effects of several K+ channel blockers on cardiac repolarization in wild type (WT), transgenic LQT2, LQT5, and LQT2–5 rabbits.

**Results:** At baseline, QTc (ms) was similar in LQT5 (135.3±5) as in WT (137.2±6) but was significantly prolonged in LQT2 and LQT2–5 rabbit models (162.9±11 and 167.9±15, p<0.05 vs. WT). Slight IKr-blockade by low dose dofetilide (0.02mg/kg, im) prolonged QT in only in LQT5 (QTi (%), 104.5±3%, p<0.05 vs. baseline) but not in WT, nor in LQT2 and LQT2–5 rabbits that lack IKr. IK1-blocker BaCl2 (0.3mg/kg, im) prolonged QT in all groups (QTi (%), WT 105.7±3.3, LQT5 104.9±4.1, LQT2 110.8±4.8, LQT2–5 104.9±2.6, p<0.05 vs. baseline). Ex vivo, IKr-blocker dofetilide (1mM) prolonged APD75 in all groups (changes (ms), WT +8.5±2.7, LQT5 +6.0±2.7, LQT2–5 +12.4±3.2, all p<0.05 vs. baseline) except for LQT2 lacking IKr. APD75 prolongation induced by IKs-blocker HMR-1556 (100μM) was more pronounced in LQT2–5 as in WT or LQT5 (changes (ms), LQT5–2 vs. WT +9.8±3.2 vs. WT +6.0±2.3 or LQT5 +5.2±2.8). IK1-blocker BaCl2 (10μM) or combined IK1/IKs-blockade by BaCl2+HMR prolonged APD75 significantly more in LQT2–5 and LQT2–5 than in WT (BaCl2: LQT2–5 +24.5±7, LQT2–5 +24.2±8 vs. WT +13.9±6, BaCl2+HMR: LQT2–5 +34.6±10, LQT2–5 +28.0±5 vs. WT +16.7±3, all p<0.05). Spatial dispersion of repolarization was increased significantly by BaCl2+HMR only in LQT2 (change +7.4±4.4 ms; p<0.05 vs. baseline) but in none of the other genotypes.

**Conclusion:** LQT2–5 rabbit models with pronounced reduction of repolarization reserve are very sensitive to K+ channel blockers demonstrating not only QT prolongation but also increased APD triangulation and dispersion. The combined use of different transgenic LQT5 rabbit models with different extents in reduction of repolarization reserve may provide further insights into pro-arrhythmic mechanisms of K+ channel blocking drugs.

Acknowledgement/Funding: German Heart Foundation F02/14 and Hungarian Scientific Research Fund 110896

**NOVEL PHARMACOLOGICAL THERAPY IN CHRONIC HEART FAILURE**

**P3118 | BENCH**

Contribution of central donepezil to prevention of cardiac dysfunction and improvement of long-term survival in chronic heart failure rats after myocardial infarction

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**Introduction:** We have shown that oral administration of donepezil, an acetylcholinesterase inhibitor, improves prognosis in chronic heart failure (CHF) rats with extensive myocardial infarction (MI), but its mechanisms remain unclear. The present study aimed to examine whether central infuion of donepezil, without systemic administration, would effectively prevent cardiac remodeling and dysfunction and improve long-term survival in CHF rats.

**Methods:** Survived rats for one week after extensive MI were implanted with a blood pressure transmitter and a micro-infusion pump which connected to a cerebroventricular cannula. Animals were randomly assigned to central saline (CST) or donepezil (CDT) infusion group. Donepezil was administered at a dosage of 0.1 mg/kg/day (one fiftieth of an oral dose used in the previous studies) for 120 days. We evaluated cardiac remodeling and function (CST: n=14, CDT: n=13) after 6 weeks treatment, and also examined 160-day survival rate (CST: n=25, CDT: n=25).

**Results:** Although there was no significant difference in the MI size between the two groups, CDT markedly improved 160-day survival (88% vs. 32%, P<0.002; figure), through the prevention of cardiac remodeling [bwight [2.77±0.07 vs. 2.97±0.05kg, P<0.05]; myocardial interstitial fibrosis (4.9±0.8 vs. 9.0±0.9, P<0.01)] and cardiac dysfunction [left ventricular (LV) shortening fraction max. 3885±15 vs. 3183±177 mmHg/s, P<0.05; cardiac index, 181±15 vs. 145±11 ml/min/kg, P<0.05]; LV end-diastolic pressure (LVEDP), 23±1 vs. 28±1 mmHg, P<0.05] compared with CDT group. CDT decreased plasma levels of BNP (359±8 vs. 429±27 pg/ml, P<0.05), angiotensin II (80±10 vs. 138±33 pg/ml, P<0.05), and norepinephrine (741±215 vs. 1566±217 pg/ml, P<0.05) compared with CDT group. These results indicated that central infusion of donepezil repro-duced most of the beneficial effects of oral donepezil treatment in CHF rats.

**Conclusion:** The central mechanism plays a main role in the donepezil treatment which prevents the progression of cardiac remodeling and improves long-term prognosis in CHF rats.
tion (LVEF; 48±4.5 vs. 33±4.5%, p<0.001) and cardiac output (CO; 26±6.7 vs. 14±2.8; p<0.001) compared to the TAC placebo group (TAC_P). After 3 weeks of drug administration, the heart function of the TAC_RIO group recovered and achieved the heart performance of sham placebo mice, whereas the TAC_P group showed a further decrease (TAC_RIO vs. TAC_P: FS 30.5±4.3 vs 14.4±2%; LVEF 56±31.7% vs. 30.6±4%; CO 88.6±4.8 vs. 141±2.3; p<0.001). The heart function in the TAC_RIO group remained stable until the end of the study eight weeks after TAC. The left ventricular mass (LVM) increased in both TAC groups to the same extent until the 6th week after surgery. In week 7 and 8 after surgery, LVM of TAC_RIO decreased whereas LVM in TAC_P showed a further increase (127.2±17.3 vs. 159±21 mg, 129.8±18.5 vs. 156.6±4.2; p<0.001). In line with the reduced LVM in week 8, Sirius red staining of the heart revealed a lower extend of fibrous tissue in TAC_RIO than in TAC_P.

Conclusions: We could demonstrate the strong beneficial effect of sGC stimulation in pressure overload induced HF. The stimulation of sGC not only improves the heart function, but also reduced the hypertrophic response to TAC.

P3121 | BEDSIDE
Magnesium orotate improves symptoms, exercise capacity and quality of life in patients with valve prosthesis: results from a randomized, open-label, case-control 2-year study
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Background: Successful surgery for valvular heart disease prolongs life and generally improves symptoms and cardiac function. Nevertheless, myocardial dysfunction and impaired quality of life (QoL) may not improve postoperatively. We aimed to assess safety and efficacy of nonsteroidal anabolic magnesium orotate (MO) in a long-term treatment of heart failure in operated valvular heart disease.

Methods: Magnesium orotate (52–60 mg, 3–2 times/day) was given to 35 cardiac surgery patients (age: 58.3±2.2 years; 64% males; 65% NYHA class III, 35% NYHA class II; 38% concomitant CAD, 22% CABG; median (IQR) 6 min walk distance (6-MWD) 351 (156–448) m; mean (SD) left ventricular ejection fraction (LVEF) 53.5 (2.1)% 2–4 weeks after conventional aortic (n=113) or mitral (n=87) valve surgery. NYHA class at 6 weeks after surgery: 35% NYHA FC II; 38% concomitant SCAD, 22% CABG; median (IQR) 6-min walk distance (6-MWD) 351 (156–448) m; mean (SD) left ventricular ejection fraction (LVEF) 53.5 (2.1)% 2–4 weeks after conventional aortic (n=113) or mitral (n=87) valve surgery.

Results: In a follow-up of 24 months, 24 patients had a mean 6-MWD increase of 192 m (p<0.001), with a clinically viable drug for the inhibition of CaMKII has not yet emerged.

P3122 | BENCH
Get the right balance: a novel vasopressin receptor antagonist equally blocks human V1a and V2 receptors and inhibits the release of plasminogen activator inhibitor-1 from cardiomyocytes
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Background/Introduction: Plasma Vasopressin levels are markedly increased in patients with heart failure. Vasopressin can induce water retention by renal V2 receptor activation as well as arterial vasconstriction and subsequent increase of afterload via V1a receptor activation. Therefore, selective V2 receptor antagonists (e.g. tolvaptan or satavaptan) induce aquaresis but may cause compensatory vasopressin release and thus activation of unblocked V1a receptors, leading to vasoconstriction, increased afterload stress, and worsening ventricular function.

Purpose: We identified a novel dual acting V1a/V2 vasopressin receptor antagonist, BR-6819 and aimed to investigate its effects on vasopressin induced arterial vasoconstriction, platelet aggregation and release of pro-fibrotic biomarker proteins.

Methods: Ki values of BR-6819 and tolvaptan were determined in radioactive receptor binding assays using membranes of recombinantly expressed human V1a or V2 receptors. Aortic rings (3 mm) from male Wistar rats were used for determination of inhibitory potential versus vasopressin (1 nM) induced aortic constriction in organ baths containing Krebs-Henseleit solution equilibrated with 95% O2, 5% CO2 at 37°C. Vasopressin mediated platelet aggregation in human platelet-rich plasma (PRP) from nonsmoking healthy volunteers (n=4–8) was determined turbidimetrically using an aggregometer. Plasminogen activator inhibitor-1 (PAI-1) protein release was determined using a commercial ELISA (American Diagnostica) from supernatants of vasopressin induced (1 nM) cardiomyocytic rat H9c2 cells.

Results: BR-6819 was found to possess almost identical Ki values at human V1a (1.3±0.2 nM) and V2 (0.5±0.1 nM) receptors, whereas tolvaptan showed a 102 fold higher V1a Ki which indicates a 102 fold higher selectivity for V2 receptors. Platelet aggregation assays using PRP from human donors revealed IC50 values of 95 nM and 1705 nM for BR-6819 (n=4 donors) and tolvaptan (n=8 donors), respectively. BR-6819 and tolvaptan inhibited vasopressin induced contraction of isolated rat aortic rings with IC50 values of 27 nM and 230 nM, respectively. BR-6819 dose-dependently reduced the vasopressin induced expression of PAI-1 from rat cardiomyocytic H9c2 cells while the V2 selective compound satavaptan exhibited no effect on the expression of this pro-fibrotic marker.

Conclusion: Based on its balanced V1a/V2 receptor activity BR-6819 may offer a new treatment option for patients with congestive heart failure by potential pre- and afterload reduction.

P3123 | BEDSIDE
The CaMKII inhibitor RA123456 attenuates heart failure and prevents ventricular and atrial arrhythmias in vivo
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Rationale: Excessive activation of Ca/calmodulin kinase II (CaMKII) is of critical importance in the development of heart failure (HF) as well as atrial fibrillation (AF). However, a clinically viable drug for the inhibition of CaMKII has not yet emerged.

Methods: We enrolled 24 patients with T2DM (HbA1c >6.0%) and stable HF who have been receiving appropriate medical therapy including diuretics. All patients underwent urine and seronic morphological examination before and after 3 days of ipragliflozin therapy (50mg/day).

Result: After 3 days of ipragliflozin administration, 24-hour urinary glucose excretion increased from 0.23±0.7 to 23±1.8 g/day (p<0.01) and fasting plasma glucose decreased from 116±30 to 103±15 mg/dl (p<0.01). Daily urinary volume increased from 1374±512 to 1687±734 ml (p<0.01) and body weight decreased (-0.68±0.72 kg, p<0.01) whereas serum creatinine concentration and estimated glomerular filtration rate (eGFR) remained unchanged. Although 24-hour urinary sodium excretion tended to increase from 94±40 to 113±55 mg/dl (p=0.061), sodium excretion as a percent of sodium intake did not significantly change. Changes in daily urinary volume correlated highly with changes in 24-hour urinary sodium excretion (r =-0.718, p<0.01), but weakly correlated with changes in urine osmolality and 24-hour urinary glucose excretion.

Conclusion: Short-term ipragliflozin therapy safely and effectively reduced body fluid without adverse effects on the neuroendocrine system and worsening renal function in patients with T2DM and stable HF. SGLT2 inhibitor has great potential as a novel natriuretic agent for HF treatment.

The CaMKII inhibitor RA123456 attenuates heart failure and prevents ventricular and atrial arrhythmias in vivo
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Purpose: Excessive activation of Ca/calmodulin kinase II (CaMKII) is of critical importance in the development of heart failure (HF) as well as atrial fibrillation (AF). However, a clinically viable drug for the inhibition of CaMKII has not yet emerged.
Objective: We tested the effects of RA123456 on the development of heart failure in a murine transverse aortic constriction model of heart failure. Furthermore, we evaluated the antiarrhythmic effects of the compound on stimulated arrhythmias in a transgenic mouse model of CaMKII overexpression.

Methods and results: Male CaMKII transgenic mice (median age 14 weeks) were administered the compound by an octapolar catheter (Millar) introduced via the right jugular vein into the right ventricular apex. 10 min after isoproterenol injection (2 mg/kg BW i.p.) burst stimulation (at decreasing intervals of 40–20 ms basic cycle length, duration 22.1s) at the right ventricle or right atrium was used to provoke atrial or ventricular arrhythmias. Administration of RA123456 (30 mg/kg BW) <4h before stimulation via gavage resulted in a significant reduction of the propensity for both atrial and ventricular arrhythmias. Atrial fibrillation was induced in 6 of 6 mice for vehicle vs. 1 of 6 for RA123456, p<0.05 chi-square test. Ventricular tachycardia was induced in 6 of 7 for vehicle vs. 2 of 7 for RA123456, p<0.05 chi-square test. Also, Male C57BL/6J mice (median age 12 weeks) were subjected to transverse aortic constriction (TAC) and left ventricular function was monitored by echocardiography. Two weeks after TAC, RA123456 was administrated by gavage qd (at 30 mg/kg KG) for 7 days. RA123456 significantly increased ejection fraction (EF) (22.4±2.1 vs. 34.8±2.5, n=8 vs. n=10, p<0.05, ANOVA), which correlated with a significant reduction in CaMKII autophosphorylation at threonine 287 (p-CaMKII) as assessed by Western blot. RA123456 p(CaMKII) levels were 0.1370±0.07 vs. 0.75±0.15 in control, n=8 vs n=9, (p<0.05, t-test).

Conclusion: RA123456 is an orally available CaMKII inhibitor that potently inhibits arrhythmogenesis and significantly reduces heart failure development in models.

Acknowledgement/Funding: This work was supported by SANOFI-AVENTIS R&D

P3124 | BEDSIDE
The effects of LCZ696 on left ventricular remodeling in hypertensive patients - Results of a double blind, randomized, multicenter trial
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Background: The angiotensin receptor neprilysin inhibitor LCZ696 (sacubitril/valsartan) improves cardiovascular mortality and reduces heart failure hospitalizations in patients with heart failure and reduced ejection fraction. Arterial stiffness and global aortic distensibility were evaluated by 3 T magnetic resonance imaging and pulse wave analysis, respectively.

Methods and results: A total of 351 heart failure patients were analyzed, 175 were randomized to the OLM group (N=175) and 176 to the LCZ696 group (N=176). Patients were ejection fraction ≤40%, left ventricular ejection fraction <35%, New York Heart Association (NYHA) Functional Classification III or IV were prospectively followed up. Univariate logistic regression analysis detected the age, LVEF, 6MWD at discharge. Univariate logistic regression analysis detected the age, LVEF, 6MWD at discharge. Consequently, we studied 159 patients aged 67.0±11.7 years (114 males and 45 females). We determined significant factors affecting the readmission and their cut-off values using univariate and multivariate logistic regression analyses and the area under the receiver operating characteristics curves (AUC).

Results: Of 4049 eligible patients who were referred to CR, 2079 (51.3%) participated (30% patients and 41% caregivers). Independent predictors to participate in the CR program included STEMI, age ≤75, men gender, non-DM, non-smoker, no prior CABG, and no PVD. CR as compared to non-CR patients had lower rates of 1-year hospital re-admission (11.9% vs. 22.0%, p<0.001) and mortality (0.5% vs. 1.7%, p=0.027). Multivariate analysis revealed that CR was an independent predictor protecting from mortality (OR 0.53, 95% CI 0.44–0.65, p<0.001). Other predictors of mortality included prior CABG (OR 1.53), DM (OR 1.36), and hypertension (OR 1.31), all p<0.001.

Conclusions: Follow-up acute MI, only half of eligible patients who were referred to CR elected to participate. Patients who participated in CR program had a significantly lower readmission rates and lower mortality. Participation in CR rehabilitation program should be vigorously encouraged to all patients after MI.
discharge and its predictive cut-off value were 0.77 and 390 meters, respectively (Figure). When CHF patients showed 50 meters or less in the 6MWD increase during hospitalization, the diagnostic odds ratio and relative risk for readmission were 17.6 (95% CI: 7.5 - 41.1, \(P < 0.001\)) and 2.7 (95% CI: 2.1 - 3.3, \(P < 0.001\)), respectively. When they showed 390 meters or less in the 6MWD at discharge, the diagnostic odds ratio and relative risk for readmission were 4.8 (95% CI: 2.4 - 9.7, \(P < 0.001\)) and 2.7 (95% CI: 1.7 - 4.3, \(P < 0.001\)), respectively.

Conclusion: The 6MWD increase during hospitalization was shown as a strong predictor for readmission due to decompensated CHF and its predictive cut-off value was 50 meters in CHF patients.

**P3127 | BEDSIDE**

Participation in exercise-based cardiac rehabilitation is associated with improved levels of risk factors in myocardial infarction survivors

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**Background:** The efficiency of exercise-based cardiac rehabilitation (CR) to positively affect cardiovascular (CV) risk factors and to decrease CV morbidity and mortality is well documented. However, patients who have been studied so far have predominately been low-risk middle-aged men. Therefore, there is a need to study the effects of exercise-based CR in a broader setting. The Swedish myocardial infarction (MI) registry, SWEDHEART, provides data from an unselected MI patient population, with nationwide coverage and one year follow-up data available on >80% of those >75 years of age.

**Purpose:** To examine the association between participation in exercise-based CR in a “real-life” setting and changes in levels of risk factors after one year of follow-up in post-MI patients.

**Methods:** The registry-based cohort included in the study consisted of 19,236 patients (75% men, mean age 62±10.7 years) who suffered an MI between 2011–2013 and attended a follow-up visit at one year thereafter. We compared groups based on participation (yes/no) in the physiotherapist-led exercise-program that is a part of routine exercise-based CR programs offered in Sweden (43.3% participation rate). Using multivariate regression analysis adjusting for age, sex, comorbidities and medication we studied the association between participation in the exercise-program and changes in CV risk level factors [blood pressure (BP), lipids, fasting blood glucose (FBG), weight/MI, self-reported physical activity and smoking] between baseline (time of MI) and the one year follow-up visit.

**Results:** A more pronounced decrease in systolic BP (−20.0 mmHg vs. −18.1 mmHg, \(P = 0.001\)), total cholesterol (−1.2 mmol/L vs. −1.0 mmol/L, \(P = 0.001\)), LDL cholesterol (−1.2 vs. −1.0 mmol/L, \(P = 0.005\)) and triglycerides (−0.2 vs. −0.1 mmol/L, \(P = 0.02\)) was observed in participants compared to non-participants. No significant changes were seen in diastolic BP, HDL or FBG levels. Participants gained less weight (+0.1 vs. +0.4 kg, \(P = 0.001\)) and were more physically active at one year (3.8 vs. 3.3 periods of 30 minutes of physical activity/week, \(P = 0.006\)). Participants who had smoked at baseline were more often smoke-free at one year compared to smoking non-participants (36% vs 49%, \(P < 0.001\)). In gender-based post-hoc analysis both sexes showed improvements in risk factors.

**Conclusion:** In a large unselected cohort of MI survivors, participating in exercise programs as a part of CR was associated with improvements in levels of CV risk factors after one year follow-up. The results support findings from previous studies in selected populations. Further studies are needed to confirm long-term benefit on CV morbidity and mortality in unselected populations.

**P3128 | BEDSIDE**

Determinants and outcome of drop-out in outpatient cardiac rehabilitation

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**Background:** The effect of adherence to cardiac rehabilitation (CR) on outcome is not entirely clear.

**Purpose:** Therefore, we aimed to assess the impact of premature withdrawal of CR on outcome in coronary artery disease (CAD) patients.

**Methods:** 1024 CAD patients who entered CR between September 2007 and January 2013 were prospectively enrolled in the study. One-hundred patients who dropped out for medical reasons were excluded, resulting in 924 patients with acute coronary syndrome (n=388), elective percutaneous coronary intervention (n=129) or coronary artery bypass graft (n=407). Drop-out was defined as attending <50% of the training program, which has a maximum of 45 sessions. Differences in clinical characteristics and a combined end-point of all-cause mortality and rehospitalisation for a coronary event, cerebrovascular accident or heart failure, were assessed according to drop-out.

**Results:** Patients attended 36±12 training sessions on average, with 18% dropping out in the first half of the program. A median follow-up period of 33 months (interquartile range [24-51]) was completed after start of CR, which was equal between both groups of patients. Also a similar demographic and clinical profile was observed in both groups with a comparable age, gender distribution, left ventricular function and baseline exercise capacity. However, patients who withdrew prematurely from CR had more comorbidities such as chronic obstructive pulmonary disease (p=0.049) and peripheral arterial disease (p=0.011) and were more frequently smokers at start of CR (p=0.025). These patients were also more frequently singles (p=0.07), more dependent on others to get to CR (p=0.026) and tended to report more anxiety-related problems on the Hospital Anxiety and Depression Scale (p=0.081) at start of CR. Furthermore, two years after starting CR, patients who dropped out had a significantly higher event rate than their counterparts who attended the program for more than half of the sessions. (21% versus 12%, \(P = 0.001\)).

**Conclusion:** Drop-out was associated with an adverse outcome in CAD patients, with a higher event rate for the combined end-point of mortality and rehospitalisation among those patients that withdrew prematurely from the CR program. Therefore, patients should be encouraged to sustain their program, in particular those with comorbidities and a vulnerable psychosocial background which seems to play a predisposing role in drop-out.

**P3129 | BEDSIDE**

The benefits of cardiac rehabilitation in coronary artery disease: does the weight matter?


**Background:** Cardiac rehabilitation programs (CRP) are medically supervised exercise-based interventions for patients (pts) who experience a cardiac event. It has been recognized that CRP improved coronary heart disease (CHD) risk factors (RF) and functional capacity. Obesity is a major CHD RF. On the other hand, obese pts may have some difficulties in CRP performance. The aim of this study was to compare obese and non-obese pts regarding their baseline clinical profile and response to a CRP.

**Methods:** We analysed data from a prospectively collected registry of 433 consecutive pts who underwent CRP after an acute coronary syndrome (ACS) from January 2009 to October 2015. Pts were divided in two groups according to their body mass index (BMI): BMI ≥30kg/m² (obese) and BMI <30kg/m² (non-obese). Exercise performance was assessed using both duration and metabolic equiva-
lents (MEs) achieved in standard exercise test (ET) using Bruce protocol before and after CRP.

Results: Ninety-nine (22.9%) pts were obese. No differences concerning age (54.1±10.1 vs 54.7±9.6 years) or gender (79.8% vs. 86.7% males) were found between groups. Obese pts had a mean waist circumference 108.4±6.1 cm in males and 102.1±7.6 cm in females, while non-obese pts presented a mean waist circumference of 93.8±5.5 in men and 81.5±7.4 cm in women. Among CHD RF, hypertension and diabetes were more frequent in obese pts (64.6% vs. 40.1%, p<0.001 and 29.6% vs. 16.3%, p=0.003, respectively). Obese pts also showed higher levels of depression symptoms at admission (p=0.005). The index coronary event affected 1 coronary artery in more than half of pts in both groups. Echocardiography showed a slightly higher mean fractional ejection in obese compared to non-obese (55.5±10.8% vs 51.7±12.0%, p=0.012). Baseline functional capacity was lower in obese group both in duration (7.0±12.3 min vs 8.3±12.23 min; p<0.001) and intensity (7.6±7.32 METs vs 8.9±12.18 METs; p=0.001). Both groups significantly improved their functional capacity with obese pts showing higher relative improvement in both duration (+36.7% vs. 28.8%, p<0.043) and intensity (+32.4% vs. 25.9%, p=0.079).

Conclusion: Obesity is an epidemic in western countries. It is tightly linked to CHD. Overweight should be a main focus in both primary and secondary prevention. Response to exercise training exerts similar, if not higher, benefits in obese pts and this group should be priority in CRP.

P3130 | BEDSIDE
Peak oxygen uptake during exercise testing and long-term cardiovascular events in patients with coronary artery disease undergoing cardiac rehabilitation: a population-based study

Background: Measurement of percentage of predicted peak oxygen consumption (%VO2) during cardiopulmonary exercise testing has been shown to predict mortality in patients with coronary artery disease (CAD). Its association with major adverse cardiovascular events (MACE) has not been determined.

Purpose: To test the hypothesis that decreased exercise capacity (represented by %VO2) is associated with long-term MACE in patients with CAD in the community.

Methods: We performed a community-based retrospective longitudinal study on stable CAD patients entering Phase II cardiac rehabilitation between the years 2002 through 2012 and who completed a symptom-limited graded VO2 treadmill exercise test. VO2 was computed using a Medical Graphics CPX/D metabolic cart after collecting expired gases. %VO2 was estimated using the Astrand equation for men and the Jones equation for women. The composite outcome of MACE included acute coronary syndromes (myocardial infarction or unstable angina), coronary artery bypass graft, percutaneous coronary revascularization, ventricular arrhythmias requiring hospitalization, stroke or death from any cause, and was ascertained using a record linkage system. Cox proportional hazard models were included in an Excel database for analysis.

Results: Our cohort included 887 patients, 77% males, mean age 63±12 years. After a mean follow-up of 5 years, 172 patients had a MACE (#): MI (50), unstable angina (33), CABG (14), PCI (93), ventricular arrhythmia (5), stroke (17) and death (25). Normal or increased exercise capacity was related to lower rate of MACE (HR 0.43, 95% CI 0.21–0.79, p=0.04) compared those with %VO2 ≥100% to those with %VO2 <100%. The lower the %VO2 the higher the rate of MACE (See table). Per each 1 mL/kg/min decrease in %VO2 the risk for MACE increased 1% (HR 1.01, p=0.02).

Model 1 | Model 2
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Conclusion: Patients with normal or increased exercise capacity had reduced rates of MACE events. The lower the %VO2 the higher the rate of MACE, suggesting that exercise capacity at time of cardiac rehabilitation predicts cardiovascular outcomes.

Acknowledgement/Funding: Supported in part by the European Regional Development Fund-Projekt FNUSA-ICRC (No. Z.1.05/1.00/2012.01), NIH grant (R01HL65176 and R01HL65176)

P3131 | BEDSIDE
Cost effectiveness analysis of a cardiac rehabilitation program after an acute coronary syndrome
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Background: Enrolment in a cardiac rehabilitation (CR) programme after an acute coronary syndrome is recommended in ESC current guidelines for the management of ST and non ST elevation acute coronary syndromes (IIA level of recommendation). Regardless, there are important economic and social restrictions to these treatments.

Purpose: To assess a cost effectiveness analysis of a cardiac rehabilitation program after an ACS in preventing cardiovascular events and its impact in quality of life.

Methods: Retrospective analysis of all consecutive patients discharged after an ACS from a secondary hospital in Spain during 2013 and 2014. Demographic and clinical variables as well as main costs of treatment, hospitalization, were included in an Excel database for analysis. Only direct costs were taken in count as indirect costs were not available. Health care provider perspective.

Results: 226 p were included in the study; 38 of them enrolled a cardiac rehabilitation programme. Differences between groups are resumed in the table. There was no difference in myocardial infarction or death at follow up between groups. Mean follow up was 563 days. After multivariate analysis we found that patients enrolled to a cardiac rehabilitation programme were more frequently male, younger and with no peripheral arterial disease. Cost effectiveness analysis showed cardiac rehabilitation programme improve QALYs at a lower cost (dominates standard care, more effective, less costs). Incremental costs were -54294 € with a gain of 6,84 QALYs per 100 patients treated (see picture).

Baseline characteristics and events

<table>
<thead>
<tr>
<th>Cardiac rehabilitation group</th>
<th>Non-CR group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>p ≤ 0.001</td>
</tr>
<tr>
<td>Female gender</td>
<td>p = 0.013</td>
</tr>
<tr>
<td>Peripheral arteropathy</td>
<td>p = 0.001</td>
</tr>
<tr>
<td>Complete revascularization</td>
<td>p = 0.009</td>
</tr>
<tr>
<td>DAPT duration</td>
<td>p &gt; 0.19</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>p = 0.237</td>
</tr>
<tr>
<td>Angor pectoris</td>
<td>p = 0.014</td>
</tr>
<tr>
<td>Death</td>
<td>p &gt; 0.001</td>
</tr>
</tbody>
</table>

Cost effectiveness

Conclusion: Enrolment in a cardiac rehabilitation programme after an ACS seems to be highly cost effective. People referred to these programmes are younger, mainly male, and with no peripheral artery disease. Efforts by authorities and clinicians to widespread this therapy to female and older patients should be made.

BASIC MECHANISMS IN PULMONARY HYPERTENSION

P3132 | BENCH
A new experimental model of pulmonary arterial hypertension-KDR knock out
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Background: Pulmonary arterial hypertension (PAH) is a severe and progressive disease characterized by obstruction of small pulmonary arteries leading to increased pulmonary vascular resistance. The key pathologic finding in this disease is a negative pulmonary vascular remodeling process with total vessel
occlusion and a monoclonal expansion of collateral endothelial cells. It has been proposed that impaired vascular endothelial growth factor (VEGFA) signaling plays a significant role in this process. Aim of our study was to investigate whether inhibition of VEGF-R2 (KDR) by direct gene manipulation may replicate classical pulmonary vasculopathy.

Methods: We utilized mice with conditional VEGF-R2-KDR knock-out in endothelial cells (KDR−/−). KDRflox/flox/Tie-2Cre and KDRflox/flox/Tie-2 were injected intraperitoneally with tamoxifen for three weeks to induce the knock-out. KDR−/− mice and wild type littermates were housed in an environmental chamber with FiO2 of 10% or under normoxia for 2, 4, and 6 weeks. We investigated the effect of KDR deletion and chronic normobaric hypoxia on pulmonary hemodynamics and right ventricular hypertrophy.

Results: There was no difference in mice might, heart weight and heart weight to body weight ratio between study and control mice. After KDR knockout mice revealed a significant increase in VEGF and BMP serum levels. Real-time PCR indicated a significant downregulation of the BMP pathway as consequence of KDR knockout. Knockouts showed significantly increased right ventricular pressures (RVPs’s) and Fulton indices after 4, and 6 weeks under normoxic and hypoxic conditions, compared with wild type controls (Fig.1), whereas there was no significant difference in systemic arterial pressure between both groups. Knockout mice showed a significant increase in pulmonary arterial wall thickness and significant increased α-SMC positive area measured by tissue FACS.

Conclusion: Classical pulmonary arterial hypertension was induced in C57/BL6J mice by direct ablative gene manipulation of KDR.

P3134 | BENCH Preventive effects of novel urotensin II receptor antagonist in experimental pulmonary arterial hypertension J.H. Lee 1, B.K. Park1, H.W. Seo 2, M.Y. Lee 1, E.M. Lee 1, J.H. Lee 1, T.G. Kim1, J.Y. Hong 3, K.S. Oh 1, B.H. Lee 1. 1Korea Research Institute of Chemical Technology, Bio & Drug Discovery Division, Daejeon, Korea Republic of; 2KEPCO Medical Center, Seoul, Korea Republic of

Background: The pathophysiologic implications of urotensin II (U-II) action on the urotensin II receptor (UT) in pulmonary arterial hypertension (PAH) have been proposed recently. Besides, high expression levels of U-II in experimental models and human PAH, U-II has been shown to increase pulmonary vascular cell proliferation and inflammatory responses, which are critical for PAH development. However, the direct role of U-I and UT in PAH has not yet been clarified.

Purpose: The aim of the present study was to evaluate the preventive effects of a novel UT antagonist, KR36676, on pathophysiological changes in an animal model of PAH.

Methods: PAH was induced by a single subcutaneous injection of monocrotaline (MCT, 60 mg/kg) in rats. Animals randomly received KR36676 (30 mg/kg/day) or vehicle by oral gavage. Three weeks after MCT-injection, hemodynamic alterations, right ventricular hypertrophy, myocardial fibrosis, pulmonary vascular remodeling and expression of p-ERK, TNF-α, and NF-κB were determined.

Results: The MCT-induced increase in right ventricular systolic pressure, cardiac hypertrophy and fibrosis was effectively decreased by oral administration of KR36676. Morphometric and molecular analyses revealed that the pulmonary arterial wall thickness, pulmonary vascular cell proliferation (i.e. number of PCNA-positive cells), and TNF-α expression were significantly lower in KR36676-treated group compared with the vehicle-treated group. These preventive effects of KR36676 are achieved, at least, in part, by suppression of ERK1/2 and NF-κB signaling pathway.

Conclusions: A novel UT antagonist, KR36676, effectively prevents the progression of experimental PAH associated with pulmonary vascular remodeling and inflammation. Our findings provide evidence of therapeutic efficacy and underlying mechanisms of UT antagonist for PAH prevention.

Acknowledgement/Funding: This study was supported by the Bio & Medical Technology Development Program of the NRF funded by the Korean government (2011-0019397).

P3135 | BENCH Hemodynamic and anti-remodelling effect of the rho kinase inhibitor y-27632 in monocrotaline pulmonary arterial hypertension rat model S. Cantoni1, S. Cavalli1, G. Marchini1, S. Bertolini1, F. Pastore1, R. Nasini2, F. De Logu2, G. Villetti1, F. Facchinetti1. 1Chiesi Farmaceutici S.p.A., Department of Pharmacology and Toxicology, Parma, Italy; 2University of Florence, Department of Health Sciences, Section of Clinical Pharmacology and Oncology, Florence, Italy

Introduction: Pulmonary arterial hypertension (PAH) is a progressive and disabling disease with high mortality. Accumulating evidence showed that Rho-kinases (ROCK) serves as a point of convergence of various signalling cascades in the pathogenesis of PAH and plays a major role in the sustained vasconstrictor activity induced by many agonists, including endothelin. ROCK is also implicated in pulmonary arterial smooth muscle cell (PASMCC) proliferation and the regulation of cell motility, all of which are involved in the pulmonary vascular remodelling, including medial thickening of arterioles.

Purpose: To assess the effect of the ROCK inhibitor Y-27632 in monocrotaline (MCT)-induced PAH in rats, an experimental model commonly utilized to mimic clinical features of PAH group I.

Methods and results: Male wistar rats were randomized into three groups: sham (CTRL, n=6); MCT (n=15); Y-27632 (MCT+Y-27632, n=15). MCT groups and sham were subjected to a single subcutaneous (s.c.) injection of monocrotaline (MCT, 60 mg/kg) or vehicle (saline solution), respectively. Two weeks after, rats received treatment with Y-27632 (p.o., 100 mg/kg) once daily. After 28 days from the MCT induction, rats were subjected to haemodynamic measurements and, subsequently, sacrificed. Heart and lungs were collected for histological evaluation.

Results: MCT group developed RV hypertrophy (RV/LV+S). Changes in pulmonary vascular remodelling in lung were assessed by histological evaluation after H&E and alpha smooth muscle actin (alpha-SMA) staining. RV pressure (RVP) was increased in MCT rats (MCT vs CTRL: 117±23±1.1 mm Hg). However, Y-27632 treatment attenuated this change (MCT-Y-27632: 33±22 mm Hg) without affecting systemic pressure (CTRL: 124±8; MCT+Y-27632: 96±6 mm Hg).

Conclusions: The MCT group developed distal pulmonary artery mus-
P3136 | BENCH
Hyoxia-induced pulmonary hypertension is attenuated by hypoxia-inducible factor-α deletion in macrophage

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Background: Pulmonary hypertension develops with vascular constriction. The constricted vessels make gas exchange harder and blood oxygen level lower. Hypoxia condition induces infiltration of inflammatory cells in pulmonary arteries and mediate thickness. Hypoxia-inducible factor-α (HIF-α) is a regulator of transcription in hypoxic cells. It regulates hundreds of genes involved in inflammation, metabolism, proliferation and extracellular matrix reorganization. However, little is known about the mechanisms about the role of inflammatory cells and HIF-1α in pulmonary hypertension.

Purpose: We investigated HIF-1α knockout (KO) mice specifically in macrophage to determine the contribution of HIF-1α in macrophage on pulmonary vascular response to chronic hypoxia.

Methods: Macrophage from Monocyte specific HIF-1α KO (M-HIF1KO) mice were used. M-HIF1KO mice or its littermate control mice were put into hypoxia (10% O2) or normoxia for 3 weeks. The mice were assessed hemodynamic status, right ventricular hypertrophy and histology of lung. Macrophage infiltration around pulmonary arteries was assessed by immunohistochemistry with anti-MAC-2 antibody after 3 days hypoxia. Peritoneal macrophages from M-HIF1KO or control mice were incubated under hypoxia (1% O2) or normoxia for 8 hours and assessed gene expression involved in pulmonary hypertension.

Results: Control mice in 3 weeks hypoxia manifested significant elevation of right ventricular systolic pressure (RVSP) (36.7±1.6 mmHg vs. 22.2±1.6 mmHg in normoxia, p<0.05), right ventricular weight/left ventricular and intraventricular septum weight (Fulton index) (0.50±0.048 vs. 0.23±0.017 in normoxia, p<0.05) and percentage of small pulmonary arteries full muscularization (37.8±1.0% vs. 11.7±3.6% in normoxia, p<0.05). M-HIF1KO mice in hypoxia exhibited a significant reduction in all of these (RVSP: 27.50±1.3 mmHg, p<0.05, Fulton index: 0.38±0.025, p<0.05, muscularization: 27.8±1.18%, p<0.05) compared with control mice in hypoxia. Macrophage infiltration was also upregulated by hypoxia in comparison with per 40 vessels in normoxia (27.5±1.1 in normoxia, p<0.05), and the hypoxia-induced macrophage infiltration was suppressed in M-HIF1KO mice (27.0±0.6 cells per 40 vessels, p<0.05). Gene expression of peritoneal macrophage involved in vascular remodeling and macrophage migration (e.g., Vegf, Pdgfb, Glut1) was estimated in hypoxia-induced hypoxia and normoxia. Hypoxia induced these gene expressions was suppressed significantly in the peritoneal macrophage from M-HIF1KO mice compared with control mice.

Conclusion: These results indicate that HIF-1α in macrophage contributes to progress of pulmonary vascular remodeling and pulmonary hypertension in chronic hypoxia. Macrophage and Monocyte specific HIF-1α deletion may be the new therapeutic target to pulmonary hypertension.

P3137 | BENCH
Levosimendan prevents and reverts pressure-overload induced right ventricular failure

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Introduction: Levosimendan is an inotropic agent with pulmonary vasodilatory and cardioprotective properties. Levosimendan is used in the clinical setting of severe left ventricular failure, but the effects of levosimendan in RV failure secondary to pulmonary hypertension remains largely unexplored.

Purpose: To investigate the effects of chronic treatment with the calcium sensitizer levosimendan in an experimental model of pulmonary hypertension.

Methods: Angioproliferative pulmonary hypertension was induced in rats by combined exposure to the VEGF-receptor antagonist SU5416 and hypoxia (SUHx). The rats were randomized to pretreatment by levosimendan (3 mg/kg/day) before

SuHx (n=10, PREV), levosimendan given as reversal treatment after hypertrophy and failure had developed (n=10, REV), or vehicle treatment (n=10, VEH). A healthy control group received vehicle (n=10, CONTROL). Ten weeks after SuHx, RV function was evaluated by echocardiography, MRI, invasive pressure-volume measurements, histology, and biochemistry.

Results: SuHx induced pulmonary arterial hypertension resulting in RV hypertrophy, dilatation, and impaired RV function. Levosimendan treatment improved cardiac output (figure 1) and decreased RV afterload compared to VEH (VEH vs. PREV 219±33 vs. 132±20 mmHg/mL, p<0.05, VEH vs. REV 219±33 vs. 130±11 mmHg/mL, p<0.01). In the PREV group, levosimendan restored right ventricular-arterial coupling (VEH vs. PREV 0.9±0.1 vs. 1.8±0.3, p<0.05), increased capillary density (VEH vs. PREV 1025±73 vs. 1481±79 capillaries/mm2, p<0.01) and reduced pathologic gene expression of ANP and BNP compared to VEH (ANP, VEH vs. PREV 233±12 vs. 14±2 fold change compared to CONTROL, p<0.05, BNP, VEH vs. PREV 17±1 vs. 4±1 fold change compared to CONTROL, p<0.05).

Conclusion: Chronic treatment with levosimendan prevents the development of right ventricular failure and reverts established right ventricular failure in the SuHx model of pulmonary hypertension.

Acknowledgement/Funding: Danish Heart Foundation

P3138 | BENCH
Inhibition of nuclear factor-kappaB-mediated inflammation improves RV function in rats with pulmonary artery banding

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Background: In patients with pulmonary hypertension (PH), right ventricular (RV) dysfunction predicts poor prognosis. Although, inhibition of nuclear factor-kappaB (NF-κB) attenuated inflammation and prevented worsening of pulmonary vascular lesions in rats with PH, how the inhibition of NF-κB affects RV function remains unknown.

Purpose: In a rat model of RV pressure overload, we assessed the time course of NF-κB activation and RV function. We then examined the effect of NF-κB inhibitor on the RV inflammation and function.

Methods: We banded the main pulmonary artery using 18-gauge needle in Sprague-Dawley rats (8W: 180-220g). We inserted a Millar catheter into RV and measured RV function parameters. RV bands were placed to induce RV hypertension by immune-mediated inflammatory injury. RV function and inflammation were examined at Day 0, Day 3, Day 7, Day 14 and 28 after PAB (n=4–6, each group). We also measured the chronic effect of NF-κB inhibitor, pyridyldithiocarbamate (PDTC, 200mg/kg/day, orally, from Day 0 to 28, n=4–7, each group) on RV function and inflammation. Values are expressed as mean±SEM.

Results: PAB significantly increased RV systolic pressure (sham: 31±13±3mmHg vs. Day14: 78±8±5mmHg, p<0.01, and Day28: 69±3±2mmHg, p<0.01), and RV relaxation (sham: 21±7±3% vs. Day14: 12±3±1%, p<0.01, and Day28: 22±3±2%, p<0.01). RV output and diastolic pressure increased (sham: 38±7±3% vs. Day14: 50±8±3%, p<0.01, and Day28: 55±9±5%, p<0.01). In the PREV group, levosimendan restored right ventricular-arterial coupling (VEH vs. PREV 0.9±0.1 vs. 1.8±0.3, p<0.05), increased capillary density (VEH vs. PREV 1025±73 vs. 1481±79 capillaries/mm2, p<0.01) and reduced pathologic gene expression of ANP and BNP compared to VEH (ANP, VEH vs. PREV 233±12 vs. 14±2 fold change compared to CONTROL, p<0.05, BNP, VEH vs. PREV 17±1 vs. 4±1 fold change compared to CONTROL, p<0.05).

Figure: Representative photomicrographs showing the effects of NF-κB inhibitor, PDTC, on PAB-induced RV hypertension and fibrosis. Immunohistochemistry of RV in sham (left), vehicle (middle) and PDTC (right) at Day28. PAB-induced increase in p65 expression (arrow head, brown; upper) and CD68-positive macrophages (arrow, middle) were attenuated by PDTC treatment. PDTC reduced RV fibrosis scanned by Masson Trichrome (blue; lower). Scale bar indicate as 100μm.

Effects of PDTC on PAB
end-diastolic pressure (RVEDP) (sham: 1.5±0.9 vs. Day14: 5.0±1.0mmHg, p<0.05, and Day28: 7.2±0.8mmHg, p<0.01). PAB hypotrophied RV (RV/LV+septum ratio) (sham: 0.29±0.02 vs. Day14: 0.57±0.05, p<0.01) and activated p65 (NF-κB) (sham: 4.3±2.0 vs. Day14: 14.3±1.2ng/μg, p<0.05). PAB increased infiltration of inflammatory cells, mainly CD68 positive macrophages on Day1 (sham: 4.3±1.0 vs. Day1: 40.7±5.8cell/mm², p<0.01) and remained increased until Day28 (22.9±5.8cell/mm², p<0.05). PAB time dependently fibrosed air mass (Masson trichrome staining) (sham: 0.7±0.1 vs. Day14: 6.7±1.0%, p<0.01, and Day28: 8.4±0.6%, p<0.01). Chronic administration of PDB increased RVSP (vehicle: 70.0±2.7 vs. PDTC: 90.7±9.0mmHg, p<0.001) and +max dp/dt RVEDP (vehicle: 517±91 vs. PDBTC: 1303±221/sec, p<0.01) and decreased RVEDP (vehicle: 7.2±0.8 vs. PDBTC: 3.4±0.5mmHg, p<0.01) indicating improvement of RV function. PDB decreased activation of p65 (vehicle: 21.5±4.9ng/μg, p<0.01), and infiltration of CD68 positive macrophages (vehicle: 22.1±3.7 vs. PDBTC: 5.6±0.8cell/mm², p<0.01) and fibrosis (vehicle: 8.1±1.0 vs. PDBTC: 2.4±0.4%, p<0.01) (Figure) and mRNA levels of pro-inflammatory cytokines.

Conclusions: PDB significantly activates NF-κB and in turn deteriorates RV function. PDBTC prevents worsening of RV function through attenuating the infiltration of macrophage and fibrosis. Inhibiting NF-κB activation may serve as a new therapeutic target for the RV dysfunction associated with PH.

INSIGHTS ON THROMBOSIS AND ANTICOAGULANTS

P3139 | BEDSIDE
Familial clustering of venous thromboembolism - A Danish nationwide cohort study
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Background: Venous thromboembolism (VTE) poses a great burden for patients and healthcare systems worldwide, as the condition is the third leading cause of cardiovascular death. Thus, identification of high-risk patients, including those who are genetically exposed, is of utmost importance to improve current prophylactic regimes and treatment guidelines.

Purpose: To examine the relative risk of VTE in first-degree relatives compared with the general population.

Methods: By crosslinking Danish nationwide registers we identified patients with VTE between 1978 and 2012, and their familial relations. The first member in a family to acquire VTE was defined as the proband. All first-degree relatives to the proband were followed from the VTE date of the proband and until an event (VTE, death, emigration, or end of study 31st of December 2012, whichever came first). The relative risk of VTE was estimated by standardized incidence ratios (SIRs) using time-dependent Poisson regression models, with the general population as a fixed reference. The final model was adjusted for potential confounders: Age, sex, calendar year, comorbidities, and concomitant medication.

Results: We identified 38,862 maternal probands, 35,355 paternal probands, and 18,156 sibling probands. First-degree relatives to probands amounted; 70,767 children of maternal probands, 66,065 children of paternal probands, and 29,183 siblings to sibling probands. Having a parent or a sibling previously diagnosed with VTE was associated with an over 2-fold increased risk of VTE (adjusted SIR of 6.37 [CI: 6.28–6.47]). Noteworthy, the risk of VTE increased remarkably for all first-degree relatives when the proband was diagnosed with VTE at a young age (<10 years).

Conclusion: A family history of VTE was associated with a significantly increased risk of VTE among first-degree relatives as compared with the general population, and the risk was significantly increased when the proband was diagnosed at a young age (<10 years).

Acknowledgement/Funding: This study was funded by a grant from the Danish council of independent research

P3140 | BEDSIDE
Inhibitory effects of ticagrelor monotherapy on arachidonic acid induced platelet aggregation in patients with coronary heart disease
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Background: In a recent in vitro study it is indicated that besides inhibiting adenosine diphosphate (ADP) induced platelet aggregation (PA), ticagrelor also has an inhibitory effect on arachidonic acid (AA) induced PA without the need for co-administration with aspirin. The present study was a pilot study conducted to evaluate the inhibitory effect of ticagrelor monotherapy on AA induced PA in patients with coronary heart disease (CHD).

Methods: Patients with documented CHD receiving aspirin and clopidogrel for at least 1 year were enrolled into the study. Patients entered a washout phase with ticagrelor (90 mg bid) for 2 weeks and then were randomized in a 1:1 ratio to receive either ticagrelor 90 mg bid or ticagrelor/aspirin for 14 days. AA induced PA in the ticagrelor and ticagrelor/aspirin groups were 48.2±24.0% and 8.7±6.0%, respectively (P<0.001). Individual data of AA induced PA in the monotherapy group varied significantly. A small proportion of patients in the monotherapy group exhibited low AA induced PA (<20%). Patients in the ticagrelor group showed 13.0% inhibition of AA induced PA compared to 87% in the dual therapy group while measured by thrombelastography.

Conclusion: Inhibition of AA induced PA by ticagrelor/aspirin was significantly greater as compared to ticagrelor alone. Ticagrelor monotherapy exhibited mild inhibitory effect on AA induced PA in patients with CHD. In the attempt to use ticagrelor monotherapy in patients post PCI or ACS, this study can provide some useful reference.

Acknowledgement/Funding: funded Astrazeneca

P3141 | BENCH
Endothelial autophagy gene 7 (ATG7) modulates the expression of thrombomodulin and regulates thrombosis
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Background/Introduction: Thrombomodulin (TM), a transmembrane endothelial protein, is an essential regulator of hemostasis and prevents the development of thrombus formation. Upon atherosclerotic plaque rupture, endothelial cells (ECs) become activated and attenuate the expression of TM, resulting in pronounced thrombus formation. Furthermore, endothelial autophagy is important for the secretion of von Willebrand factor in mice and cultured cells.

Results: Out of the 60 patients who were randomized after the 2 weeks washout phase, 57 (ticagrelor, n=32; ticagrelor/aspirin, n=25) completed the final evaluation and entered the full analysis set. Demographics and baseline characteristics were well balanced between the 2 groups. At day 14 after randomization, the AA induced PA in the ticagrelor and ticagrelor/aspirin groups were 48.2±24.0% and 8.7±6.0%, respectively (P<0.001). Individual data of AA induced PA in the monotherapy group varied significantly. A small proportion of patients in the monotherapy group exhibited low AA induced PA (<20%). Patients in the ticagrelor group showed 13.0% inhibition of AA induced PA compared to 87% in the dual therapy group while measured by thrombelastography.

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Acknowledgement/Funding: funded Astrazeneca

P3142 | TABLES
Screening LTA-PA (%) 7.03 (2.89) 7.76 (2.55) 0.323 46.09 (15.89) 41.90 (11.68) 0.274 60.19 (13.72) 58.00 (14.59) 0.564
Baseline LTA-PA (%) 53.75 (20.01) 49.64 (23.49) 0.476 20.72 (14.30) 22.52 (11.94) 0.615 66.63 (13.71) 68.92 (16.96) 0.574
Day 14 LTA-PA (%) 48.22 (24.01) 8.67 (5.96) 0.0001 21.50 (7.86) 21.92 (10.21) 0.864 65.00 (14.22) 44.38 (17.71) 0.001

1: ticagrelor; T+A: ticagrelor and aspirin; LTA-PA: platelet aggregation rate measure by LTA; TEG-IPA: inhibition rate of platelet aggregation measure by TEG.
Purpose: Given that ECs play a central role in regulating thrombosis, we hypothesize that an intact endothelial autophagy machinery is essential for TM expression and thrombus formation, and that loss of endothelial autophagy results in increased TM expression and reduced thrombus formation.

Methods: We used small interfering RNA (siRNA) to knockdown and characterize the effects of ATG7 knockdown in HUVECs. Furthermore, we generated a novel mouse line in which ATG7 is conditionally deleted from ECs (EC-ATG7−/−) and utilized two established in vivo models of thrombosis to monitor thrombus formation in the mesenteric, and cremaster arteries.

Results: siRNA-mediated knockdown of ATG7 (siATG7) in HUVECs resulted in increased TM mRNA by over 9-fold (N=3; p<0.05). Similarly, siATG7 in HUVECs demonstrated a decrease in TM protein expression, as shown by Western blot analysis. We next examined the effect of loss of ATG7 on thrombosis in mice. Upon FeCl3-induced injury, time to mesenteric artery occlusion was significantly prolonged in EC-ATG7−/− mice compared with wild-type (WT) mice (26.6±1.8 and 20.0±1.4 min, respectively; p=0.008). Furthermore, we determined, via mean fluorescence intensity, that the size of thrombi in the cremaster arteries of EC-ATG7−/− mice was reduced compared with WT mice (8.2±2.9 and 1.8±0.7 AU, respectively; x109; p=0.049) after laser-induced injury.

Conclusions: Loss of endothelial ATG7 results in increased TM expression in vivo. EC-ATG7−/− mice exhibited extended occlusion times and reduced thrombus formation across all models of thrombosis. These results suggest that endothelial autophagy intricately regulates thrombus formation in a TM-dependent manner and represents a previously unrecognized target to modulate thrombosis susceptibility.

Acknowledgement/Funding: Canadian Institute for Health Research (CIHR; FRN140815) to JWY and Heart and Stroke Foundation of Canada (G-13-140815). The study is supported by the Norwegian Research Council (215756/430) and the Norwegian Cancer Society (R133-A90506). I. Seljeflot.

P3142 | BEDSIDE
Contemporary registry of intermediate and high risk pulmonary embolism patients presenting to a large tertiary medical center.

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Background: Patients with pulmonary embolism (PE) represent a challenging group of patients. While those with low risk PE can be managed mostly uneventfully, patients with intermediate and high risk PE mandate close monitoring and aggressive therapy, respectively, to prevent clinical deterioration. We present a consecutive cohort of intermediate and high risk patients treated in a large tertiary medical center.

Methods: Retrospective cohort of consecutive intermediate and high risk PE patients presenting to a large tertiary medical center.

Results: Overall 170 patients were evaluated. Of these, 144 were classified as intermediate risk PE and 26 as high risk PE. Mean age patient was 66.8±16, 45% males. Forty-two percent had a history of recent immobilization, 29% a history of venous thrombo-embolic event. The most common presenting sign was dyspnea (87%), followed by chest pain (45%), leg swelling (26%), and syncope. Upon imaging studies: 61% had right ventricular dysfunction, and 25% severe dysfunction. In the intermediate risk group, 15% (N=21) required escalation therapy as follows: 6 became hemodynamically unstable with low risk PE and underwent surgical pulmonary embolectomy. In the high risk group 42% underwent surgical pulmonary embolectomy and 39% received thrombolysis. Overall, in hospital mortality was 8%: 33% in the high risk group, and 6% in the intermediate risk group.

Conclusions: In contemporary practice, intermediate and high risk PE patients present a therapeutic challenge. These patients still suffer from a high mortality and complication rate mandating advanced close monitoring for detection of clinical deterioration in order to provide an adequate therapeutic response.

P3143 | BEDSIDE
Markers of thrombin generation in patients with ST-elevation myocardial infarction are associated with long term clinical outcome.

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Introduction: Thrombin generation and fibrin formation, in addition to platelet activation, play important roles in intracoronary thrombus formation, which may lead to acute myocardial infarction (AMI). Whether increased pro-coagulant activity during AMI is associated with clinical outcome is not clarified.

Aim: To investigate whether levels of the pro-thrombotic markers pro-thrombin fragment 1+2 (F1+2) and D-dimer measured in the acute phase of ST-elevation myocardial infarction (STEMI) are associated with later clinical outcome.

Material/Methods: Patients (n=971) with STEMI were included. Warfarin users were excluded for this purpose. Blood samples were drawn at a median time of 24 hours after onset of symptoms and 18 hours after percutaneous coronary intervention (PCI). The primary outcome was a composite of all-cause mortality, re-infarction, stroke, unscheduled revascularization or re-hospitalization for heart failure; secondary outcome was total mortality. The median follow up time was 4.6 years, recorded by telephone call and cross-checked with hospital records. Associations were calculated by trend analyses through quartiles and multivariate analyses were performed by logistic regression, with the variables dichotomized at median levels.

Results: The number of composite endpoints and total mortality was 195 (20.1%) and 79 (8.1%). Significantly higher levels of D-dimer were observed in patients both with combined endpoints and total mortality compared to those without events (both p<0.01), whereas F1+2 was higher with respect to total mortality (p=0.001).

There were significant trends for increased numbers of both events through quartiles of both markers. When dichotomizing levels at median values (F1+2 265 pmol/L, D-dimer 519 ng/mL) significantly increased risk of events was observed in univariate analyses (composite endpoint p=0.013 and 0.015 respectively, total mortality p=0.001, both). When adjusting for relevant covariates (age, gender, admission glucose, NT-proBNP and peak Troponin T) no significant associations were found with regard to the composite endpoint, whereas D-dimer was significantly associated with total mortality (OR 2.04, 95% CI 1.07–3.86, p=0.03) and F1+2 borderline significant (OR 1.87, 95% CI 0.93–2.98, p=0.08).

Summary/Conclusion: The hypercoaguable state in the acute phase of an AMI seems to be of significant importance for future clinical outcome, especially for mortality. Thus, anticoagulant treatment after AMI might still be discussed.

Acknowledgement/Funding: Stein Erik Hagen Foundation for Clinical Heart Research.

P3144 | BEDSIDE
Tecarfarin pharmacokinetics and pharmacodynamics—A novel CYP2C9 independent vitamin K antagonist.


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Tecarfarin is a novel vitamin K antagonist (VKA) anticoagulant, metabolized by carboxyesterase 2 (h-CE2). Unlike most drugs, it is not metabolized by the CYP450 system, markedly reducing drug-drug interactions. In order to evaluate the pharmacokinetic (PK), pharmacodynamic (PD), safety and tolerability profile of tecarfarin, we performed single ascending (SAD; n=66) and multiple ascending dose (MAD; n=43) studies in human volunteer subjects (HV).

In the SAD, tecarfarin was administered to 5 of 6 HVs (age 29.3 y ± 7.1; 11% female) in each of 11 SAD cohorts (0.2, 0.6, 1.5, 3.0, 4.5, 6.0, 8.0, 10, 20, 30, and 40 mg). CMAX was achieved at an average Tmax of 5.0 h ± 2.4 at the 40 mg dose. Mean elimination T1/2 was 89.9 h ± 12.8 at the 40 mg dose (range 87–136 h across all doses) with no dose dependence. There were no significant changes in INR, PT, or aPTT at any of the four daily measurements post-dose. Except for a consistent trend in decreasing factors II, VII, and X levels on Days 2 and 3 in the 30 and 40 mg cohorts, lower doses showed minimal changes from baseline in these same factors. The maximum decline in coagulation factors percent change from baseline for the 40 mg dose was 5.9% at 12 h for Factor II, 30.1% at 2 d for Factor VII, and 5.5% for Factor X at 2 d. Intersubject variability in CMAX and
AUC was assessed using the coefficient of variation (%CV). This ranged from 7.4%-36.4%, and 7.6%-33.9% respectively. In the MAD, teccfarin was administered to 5 of 6 Hvs (age 31.6 y + 8.1; 19% female) in each of 7 MAD cohorts (1, 3, 6, 10, 20, 30 and 40 mg). The starting dose was continued for 7–14 d or until the INR reached the target range (TR) of 1.7–2.0. If the TR was achieved prior to Day 14, the dose was down-titrated to achieve a steady state INR within the TR. Teccfarin elimination T1/2 ranged from 107–140 h with no dose dependence. The lower doses of teccfarin (1, 3, 6, and 10 mg) had little effect on the INR. The 20 mg dose brought 3 subjects into the TR, whereas the 30 and 40 mg doses brought all subjects into the TR, and all required down-titration to prevent exceeding the TR. The final dose required for steady state INR within the TR varied between 10 and 20 mg. Upon cessation of dosing, INR declined below the TR within 1–3 d. Vitamin K dependent factors and INR returned to baseline and mirrored the increase in INR levels. An example of the INR response in the 30 mg cohort and the percent change in factor activity from baseline are shown in the Figures. There were no serious adverse events in either study.

Conclusion: 1. Teccfarin is a VKA which establishes anticoagulation through depletion of the vitamin K dependent coagulation factors. 2. Maintenance dosing for INR TR 1.7–2.0 is between 10 and 20 mg. 3. Teccfarin has a relatively low coefficient of variance for CMAK and AUC, consistent with high bioavailability and tight protein binding.

P3148 | BEDSIDE
Presence of bacterial DNA in thrombus aspirates of patients with myocardial infarction

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Introduction: Infectious agents, especially periodontal bacteria, has been suggested to be involved in inflammation contributing to plaque instability and formation of coronary thrombus, leading to an Acute Coronary Syndrome (ACS). However, the relationship between bacterial infection and acute myocardial infarction (AMI) has not yet been completely clarified and more research in this field is warranted.

Purpose: The aim of this study is to detect bacterial DNA in thrombus aspirates and peripheral blood samples of patients who presented Acute Coronary Syndrome with ST segment elevation (STEMI) treated with Primary Percutaneous Coronary Intervention (PPCI).

Methods: We studied 109 consecutive patients with STEMI from whom removal of thrombus with aspiration catheter was obtained. Bacterial DNA detection was performed by prolonged real-time PCR using the LightCycler®480. We used 10 probes for the detection of: Aggregatibacter actinomycetemcomitans, Chlamydia pneumoniae, viridans group streptococci, Porphyromonas gingivalis, Fusobacterium nucleatum, Tannerella forsythia, Treponema denticola, Helicobacter pylori, Aeromonas hydrophila, Staphylococcus aureus, Prevotella intermedia, and Streptococcus mutans.

Results: Four different species have been detected in ten thrombi. The most frequent bacterial DNA found was from viridans group streptococci (6 patients, 5.5%), followed by DNA from Staphylococcus aureus (2 patients, 1.8%), one patient presented DNA from Porphyromonas gingivalis (0.9%) and another patient Prevotella intermedia (0.9%). The bacterial DNA was not detected in the peripheral blood samples of any patient.

Conclusions: Bacterial DNA from four species have been detected in the thrombus aspirates of patients with STEMI. No Bacterial DNA was detected in peripheral blood. This fact suggest that such bacteria could be latently present in the patients, or if symptoms are not properly recognized. Adequate knowledge and skills of the primary care team as well as optimal collaboration between primary care and secondary care are paramount to ensure accurate and timely diagnosis of AF and to reduce the risk of future cardiovascular complications through guideline-conformed shared management.

Purpose: This study looked at knowledge gaps and professional proficiency of cardiologists, neurologists & general practitioners/family physicians (GPs) from six European countries in the diagnosis and management of AF patients.

Methods and sample: This ethics-approved applied research study employed a mixed-methods approach combining both qualitative and quantitative methods. Participants were recruited from France, Germany, Italy, Poland, Spain, and the UK. Semi-structured qualitative Interviews were conducted with a sample of cardiologists (n=18), neurologists (n=6), and GPs (n=6). An ensuing quantitative survey was completed by cardiologists (n=276), neurologists (n=125) and GPs (n=130). Triangulation was used to combine qualitative and quantitative data, improving trustworthiness of the findings.

Results: The collaboration between specialists and GPs to jointly manage AF was reported as being low to moderate quality by both cardiologists (66%) and neurologists (63%). The quality of referrals received (as judged by the apprehension of information and the timeliness of referrals) was also found to be moderate by both groups of specialists (66% and 63% respectively). Significant differences between countries were noted. Reciprocally, 47% of GPs reported low to moderate quality of follow-up notes received from specialists after patient referral, again with wide variation across countries. Skills and confidence gap related to ensuring a proper diagnosis of AF were reported as contributing to delayed referral to specialty care and delayed initiation of treatment. Not only 65% of GPs but also 49% of cardiologists reported low to moderate skills in detecting potential AF. Not only a majority of GPs (86%) but also a large proportion of cardiologists (57%) reported low to moderate skills in using implantable devices to improve diagnostic standards in specific populations.

Conclusion: This study highlights the need for increased interprofessional collabor-
BLOOD PRESSURE PHENOTYPE AND TARGET ORGAN DAMAGE

3229 | BEDSIDE
Impact of visit-to-visit variability of blood pressure and coronary atheroma changes by 3-D IVUS and subsequent cardiovascular events

Background: Visit-to-visit variability in systolic blood pressure (SBP) was reported to be related to increased cardiovascular risk. Intravascular ultrasound (IVUS) is used as an end point in studies aimed at reducing progression or regression of coronary atheroma. However, the relationship between variability in blood pressure and atheroma volume changes by IVUS, or long-term clinical outcomes has been poorly defined.

Methods: Serial IVUS examinations were performed in 338 stable angina pec- toris patients undergoing percutaneous coronary intervention (PCI). After PCI for culprit lesions, intravascular ultrasound (IVUS) was performed in their non-culprit vessels to determine atheroma volume at baseline. After 12–16 months, IVUS of the originally examined coronary artery was performed during follow-up angiography. Five-year clinical outcomes, including major adverse cardiac- and cerebrovascular events (MACCE), and annual progression rate of atherosclerosis by volumetric IVUS, and visit-to-visit variability in SBP for five-years were evaluated.

Results: Atheroma volume increase by IVUS was 5.7%, and five-years MACCE rate was 22.6%. Patients with MACCE had larger annual atheroma progression than the rest of the population (20.6% vs. 2.3%, p < 0.001). Visit-to-visit variability in SBP was a strong predictor of subsequent increased coronary atheroma volume (eg, top-decile hazard ratio (HR) for SD SBP over five visits: 4.18, 95% CI 1.95–8.67, p < 0.01), independent of mean SBP, but dependent on precision of measurement (top-decile HR over five visits: 4.21, 2.58–7.64, p < 0.01). Maximum SBP reached was also a strong predictor of MACCE (HR for top-decile over five visits: 8.12, 3.46–10.11, p < 0.01, after adjustment for mean SBP). In addition, residual visit-to-visit variability in SBP on treatment was also a strong predictor of increased coronary atheroma volume and MACCE (top-decile HR for MACCE: 4.48, 1.92–6.48, p < 0.01).

Conclusions: Visit-to-visit variability in SBP and maximum SBP are strong predictors of increased coronary atheroma volume, independent of mean SBP. Increased residual variability in SBP in patients with treated hypertension is associated with a high risk of subsequent cardiovascular events.

3230 | BEDSIDE
Cardiovascular and metabolic predictors of incident arterial hypertensin in adolescents and young adults: the Strong Heart Family Study
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Aim: To assess whether any metabolic and/or cardiovascular (CV) characteristics predict development of hypertension (Htn) in a young population.

Methods: We measured baseline anthropometric, laboratory and echocardiographic characteristics of 1,629, 14-to-39 year-old normotensive participants of the 4th Strong Heart Study (SHS) examination (mean age: 26±7 years, 62% female, 63% obese) without prevalent CV disease. Htn was defined by use of antihypertensive medications or blood pressure (BP) above the 95th percentile of the normal distribution for age, sex, and height in participants<18 years, or BP ≥140/90 mmHg in adults≥18 years.

Results: At the time of the 5th SHS exam (after 4-year follow-up), Htn was found in 184 participants (11%). These participants were more likely male, older and diabetic, had higher baseline BMI, waist girth, systolic and diastolic BP, pulse pressure, heart rate, LDL cholesterol and triglycerides, urinary albumin/creatinine ratio and C reactive protein levels than participants remaining normotensive (all p < 0.05). Higher baseline cortisol, glomerular filtration rate (by MDRD formula), and plasma fibrinogen levels did not differ between groups. Participants with follow-up Htn exhibited also higher baseline carotid intima-media thickness (IMT), left ventricular mass index (LVMI), age-normalized relative wall thickness (RWT), stroke index, cardiac index, with lower total peripheral resistance (Table). In multivariable analysis, adjusted for field center, family-relatedness and variables signifi- cantly different between groups in the exploratory statistics, Htn was pre- dicted by baseline systolic BP (OR = 1.08/mmHg, 95% CI: 1.06–1.10, diabetes (OR=2.78, 95% CI: 1.45–3.53), IMT (OR = 1.49/mm-10, 95% CI: 1.21–1.86) and LVM (OR=1.15±5 g/m², 95% CI: 1.10–1.30) or stroke index (OR=1.45±5 g/m², 95% CI: 1.02–1.70, all p<0.05), without significant impact for RWT.

Conclusions: In a population of young individuals with high prevalence of obesity, increased IMT and LVM precede clinical evidence of Htn, which is also indepen-dently predicted by diabetes and higher baseline systolic BP.

3231 | BEDSIDE
Longitudinal and orthostatic changes of blood pressure predict risk of dementia
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Background: The role of blood pressure (BP) variability in dementia is arguable. The aim of this study was to analyse how resting and orthostatic BP changes relate to incident dementia over a long-term follow-up.

Methods: In the prospective population-based Malmö Preventive Project, 18,240 study participants (mean age: 45±7 years, 63% male) were examined with resting BP and orthostatic BP measurement at baseline (1974–92) and re-examined after 23±4 years (mean age: 68±6 years with resting BP (2002–2006). A total of 428 participants (2.3%) were diagnosed with dementia through Dec 31, 2009. The association of resting and orthostatic BP changes with the risk of dementia was studied using multivariable-adjusted Cox regression models controlling for traditional risk factors.

Results: At baseline diastolic BP (DBP) decrease on standing was predictive of dementia (Hazard ratio (HR) per 10 mmHg: 1.22; 95% confidence interval (CI), 1.01–1.44, p=0.036). At re-examination, higher SBP and DBP lowered risk of dementia (HR 1.05 (95% CI: 1.05–1.16), p<0.001) compared with reference group (1st quartile); +15±7 mmHg); HR: 1.04 (0.98–1.10) 0.19

Conclusions: In this study there was no evidence that orthostatic BP changes relate to incident dementia over a long-term follow-up.

Table 1. Relationship between blood pressure levels at baseline and re-examination and dementia

Characteristic | HR, 95% CI* | p-value
--- | --- | ---
Baseline supine SBP | 1.04 (0.98–1.10) | 0.19
Baseline supine DBP | 1.05 (0.95–1.16) | 0.30
Mean orthostatic SBP reaction | 1.02 (0.89–1.15) | 0.74
Mean orthostatic DBP reaction | 1.22 (1.01–1.44) | 0.036
Re-examination supine SBP | 0.94 (0.89–0.99) | 0.011
Re-examination supine DBP | 0.87 (0.78–0.96) | 0.006
Supine SBP decrease between baseline and re-examination | 1.07 (1.03–1.12) | 0.002
Supine SBP decrease between baseline and re-examination | 1.16 (1.08–1.25) | < 0.001

Conclusions: Diastolic BP decrease on standing in the middle age, decline in BP between middle-and advanced age, and lower BP in advanced age are independent risk factors of developing dementia.

Acknowledgement/Funding: This study was supported by the Kockoska Foundation; Skåne University Hospital donation funds; the Medical Faculty of Lund University; the Crafoord Fou.
Upon reperfusion of occluded arteries, deleterious cellular mediators particularly located at the mitochondria level can be activated thus limiting the outcome in patients. This may lead to so-called ischaemia/reperfusion (I/R) injury. Calpains are cysteine proteases and mediators of caspase-independent cell death. They are cysteine proteases and mediators of caspase-independent cell death. They are associated with ischemia-reperfusion injury as well as pre- and post-conditioning. Exogenous S1P supplementation as well as the inhibition of its degradation by genetic or pharmacological means has been shown to decrease infarct size in mice with acute myocardial infarction (AMI). The impact of high endogenous S1P in cardiac remodeling and function after AMI over time has not been investigated. We hypothesized that inhibition of the S1P degrading enzyme S1P lyase improves cardiac remodeling after AMI independently of its effects on infarct size.

**Purpose:** To investigate the effect of pharmacological S1P lyase inhibition on cardiac remodeling after AMI in terms of ventricular geometry and left ventricular function by magnetic resonance imaging (MRI).

**Methods:** 12±2 week old C57BL/6 mice on standard rodent chow underwent AMI by ligation of the left anterior descending artery. The S1P lyase inhibitor 4-deoxygypenosidone orally was administrated and beginning 7 days prior to AMI. Effectiveness was monitored by determining peripheral CD4+ and CD8+ lymphocyte counts. Infarct size was measured 24 hours post AMI by late gadolinium enhancement, and cardiac remodeling and function evaluated at day 1 and 21 by magnetic resonance imaging. Data are mean ± standard deviation. P below 0.05 was considered significant.

**Results:** Infarct size did not differ between DOP-treated and control mice (27±9mg vs. 31±8mg, n.s.). In contrast, remodeling after AMI was improved by DOP. Stroke volume index improved in DOP treated mice (0.5±1.4 μl beating/beat body surface area [BSA] vs. 0.6±0.2 μl beating/BSA; p=0.01), while it did not improve in control mice (0.5±0.1 μl beating/BSA vs. 0.6±0.1 μl beating/BSA; n.s.). Stroke volume index at day 21 was higher in DOP treated mice as compared to control mice (0.8±0.2 μl beating/BSA vs. 0.6±0.1 μl beating/BSA; p=0.009).

**Conclusion:** Pharmacological inhibition of the S1P lyase improves cardiac remodeling after AMI in mice without affecting infarct size. This may be a promising approach to improve cardiac performance after AMI.

**GENETIC RISK SCORE IN CARDIOVASCULAR PREVENTION: DAWN OF A NEW ERA**

**2627 | BEDSIDE**

**Do metabolic risk factors mediate the genetic risk for coronary heart disease?**

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**Background:** Family history of coronary heart disease (CHD) as well as directly assessed genetic predisposition to CHD (genetic risk score, GRS) are strong predictors of CHD risk. It is, however, uncertain to what extent these risk predictors are mediated through the pathways of major metabolic risk factors. Some studies have shown that GRS and family history predict cardiovascular risk independently of classical CHD risk factors.

**Purpose:** We quantitatively assessed the fraction of family history and GRS mediated through established-cardio-metabolic risk pathways.

**Methods:** Statistical mediation analysis was used to estimate the total effects of family history and GRS on CHD and CHD risk factors. As indirect effects we assessed genetic predisposition to CHD (genetic risk score, GRS), as well as the effects mediated by apolipoprotein B (apoB), apolipoprotein A-1 (apoA-1), blood pressure, and diabetes mellitus (DM) on the incidence of CHD. Analyses were done in the Malmö Diet and Cancer study, a prospective, population-based study of 23,595 men and women aged 45–73 years recruited between 1991 and 1996. During a median follow-up of 14.4 years, 2,213 participants experienced a first CHD event.

**Results:** Family history and GRS50 (highest vs. lowest quintile) were associated with incident CHD, with hazard ratios of 1.52 (95% CI (confidence interval): 1.39 to 1.65) and 2.01 (95% CI: 1.76 to 2.30), respectively, after adjusting for age, sex, and smoking status. Small proportions of the family history effect were mediated by traditional risk factors: 8.3% (95% CI: 5.8% to 11.7%) through the apoB pathway, 1.7% (95% CI: 0.2% to 3.4%) through apoA-I, 8.5% (95% CI: 5.8% to 12.0%) through blood pressure, and 1.5% (95% CI: 0.8% to 2.8%) through DM. Similar, small proportions of GRS50 were mediated by traditional risk factor pathways: 6.0% (95% CI: 3.7% to 8.6%) of the effect was mediated through apoB, 1.1% (95% CI: -0.2% to 2.6%) through apoA-I, 3.5% (95% CI: 1.0% to 5.9%) through blood pressure, and 0.2% (95% CI: 1.1% to 2.7%) through DM. Total, 20.0% (95% CI: 14.8% to 26.4%) of the family history effect and 10.7% (95% CI: 5.8% to 16.0%) of GRS50 effect were mediated by these metabolic risk factors.

**Conclusions:** A fraction of the CHD risk associated with family history or with GRS50 is mediated through dyslipidemia and hypertension, but not through diabetes. However, a major part (>80%) of the genetic effect operates independently of established metabolic risk factor pathways. Therefore, family history and genetic disposition might warrant assessment in addition to established metabolic risk factors.
Genetic risk score in cardiovascular prevention: dawn of a new era / Atrial fibrillation ablation: novelties and advances

3269 | BEDSIDE
Genetic risk score, individual genetic variants and psychological stress as predictors of coronary artery disease, fatal myocardial infarction and cardiovascular death
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Background: Psychological stress is an independent risk factor for cardiovascular disease. Susceptibility to stress-mediated cardiovascular events differs between individuals, with genetic factors implied in both stress reactivity and cardiovascular reactivity.

Purpose: The aim of our study was to elucidate the association and interactions between a genetic risk score (GRS) consisting of 50 single nucleotide polymorphisms (SNP), individual genetic variants and psychological stress for three cardiovascular end points: coronary artery disease (CAD), fatal myocardial infarction (MI), and cardiovascular death.

Methods: A total of 18,559 participants from the Malmö Diet Cancer Study who had answered questions on stress, had provided complete genetic information, and without a history of prevalent CAD were included in the analyses. A composite categorical stress variable was constructed from 11 questions measuring job strain using the validated Swedish version of the Demand-Control Model, and one question assessing non-occupational stress.

Cox proportional hazards regression models were used and adjusted for a large number of known predictors of cardiovascular end points.

Results: Mean follow-up time was 14.6, 14.8, and 15.1 years for CAD (n=1938), fatal MI (n=436) and cardiovascular death (n=1071) respectively. Stress was not independently associated with any end point in the multivariable analyses whereas GRS was significantly associated with increased risks of CAD (top quartile hazard ratio [HR], 1.72; 95% confidence interval [CI], 1.51–1.96), fatal MI (top quartile HR, 1.62; 95% CI, 1.23–2.15), and cardiovascular death (top quartile HR, 1.29; 95% CI, 1.18–1.43).

One-by-one analysis of the 50 SNP’s indicated that four individual genetic variants interacted unfavourably with psychological stress. Post-hoc analyses showed that when constructing a stress-sensitive GRS comprised of these four SNPs, high psychological stress became significantly associated with fatal MI (HR, 2.47; 95% CI, 1.44–4.24) and cardiovascular death (HR, 1.77; 95% CI, 1.19–2.63) for individuals in the highest quartile of the stress-sensitive GRS.

Conclusion: A GRS composed of 50 SNPs and predictive of CAD was found for the first time to also strongly predict fatal MI and cardiovascular death. Our results point to a stress-sensitive component of the GRS which could be isolated based on individual genetic variants that interacted unfavourably with stress. Further research on stress-sensitive CAD genetic variants is warranted in order to understand stress-induced cardiovascular reactivity.

3293 | BEDSIDE
Impact of continuous monitoring of the pulmonary venous pressure on the acute results of cryoablation: A derivation and validation study
Background: In cryoablation of paroxysmal atrial fibrillation (PAF), pulmonary vein (PV) occlusion is essential for achieving antral contact and PV isolation, and is typically assessed by contrast injections. No studies have examined the utility of a continuous pressure monitoring of the PVs (CPM) during cryoablation.

Methods: The derivation cohort consisted of 20 consecutive patients (80 PVs) with PAF. In the validation cohort (n=36, 104 PVs), the patients were randomly divided into 2 groups according to the confirmation method of PV occlusion: CPM without contrast (group-1; n=19; 56PVs) or contrast injections (group-2; n=17; 48PVs). In the derivation cohort and group-1, PV occlusion was confirmed and monitored with a loss of a typical left atrial pressure waveform (Figure).

Results: In derivation cohort, in 76 (95%) of 80 PVs, complete PV occlusion by the cryoballoon was easily confirmed by CPM during the inflation, and the PVs were successfully isolated with the cryoballoon. In validation cohort, there was no difference in the procedure time or freezing time for isolating each PV or total procedure time to isolate all 4 PVs between the 2 groups. However, the total fluoroscopic dose and contrast volume to isolate all 4 PVs were less in group-1 than group-2 (both for p<0.05).

Complete PV isolation with cryoballoon was obtained in 63PVs (83%) in group-1 and 54 (84%) in group-2 (p=0.81). There were two potential complications including phrenic nerve palsy and periesophageal vagal nerve injury in group-2.

Conclusion: In cryoablation, complete PV isolations were easily confirmed by CPM. CPM was safe and could reduce the fluoroscopic dose and contrast volume during cryoablation.
3294 | BEDSIDE

Importance of non-pulmonary vein triggers in patients with high baseline fasting blood sugar undergoing catheter ablation for atrial fibrillation


Introduction: Diabetes is known to be an independent risk factor of atrial fibrillation (AF).

Purpose: This study investigated the impact of uncontrolled diabetes on the outcome of catheter ablation in AF patients.

Methods: Four hundred twelve patients with history of diabetes undergoing their first AF ablation at our center were included in this prospective analysis. Based on the baseline fasting blood sugar (FBS) level, participants were classified into 2 groups: 1) normal FBS (<110 mg/dL), 2) high FBS (>110 mg/dL). All patients underwent PV antrum and posterior wall isolation. Non-PV triggers (NPVTs) were elicited with isoproterenol challenge and were defined as ectopic triggers originating from sites such as left atrial appendage, coronary sinus, interatrial septum, superior vena cava, and crista terminals. Recurrence was acquired by event-recorders, EKG and series of quarterly 7-day Holter recordings during the 4-year follow-up.

Results: Baseline characteristics were not different between patients with normal FBS (n=97, age 66±9.1, 71% male, LVEF 56±13, 63% NPAF) and high FBS (n=315, age 66±8.7, 70% male, LVEF 57±10, 61% NPAF) (p<0.05). During the procedure, prevalence of NPVT were significantly higher in the high-FBS population [52 (53.6%) vs 208 (65%), p<0.025].

At the end of follow-up, 81 (83.5%) from normal-FBS group and 229 (72.7%) from high-FBS group remained arrhythmia-free (p=0.036) (figure). Forty (77%) of the 52 in normal-FBS group and 152/208 (73%) from high-FBS group with inducible NPVT received NPVT ablation based on the operator’s choice. At 4-years of follow-up, success rate was significantly higher with PVI +NPVT ablation in both groups [normal FBS gr: 34/40 (85%) vs 5/12 (41.7%), p<0.002; high FBS gr: 121/152 (79.6%) vs 26/56 (46.4%), p<0.001].

Presence of high FBS increased the risk of recurrence 1.76 times (p=0.038). Receiver operating characteristics (ROC) analysis revealed that cut-off of baseline FBS level at 110 mg/dL predicted recurrence with 86% sensitivity and 75% specificity (AUC-0.56).

Conclusion: Elevated baseline blood-sugar level was associated with higher incidence of non-PV triggers and reduced success rate after catheter ablation. Diabetes-related atrial substrate changes in the high-FBS group could be the underlying mechanism of poorer outcome in this subset of AF population. Elimination of non-PV triggers upon detection provided a significantly better long-term outcome.

Figure 1. Kaplan-Meier curve showing success rate of catheter ablation in normal- versus high-FBS group.

3295 | BEDSIDE

Durability of pulmonary vein isolation by various kind of ablation catheter

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Background: Pulmonary vein isolation (PVI) has been known as the cornerstone strategy for catheter ablation of atrial fibrillation (AF) and the durability of PVI is one of the crucial factors for the clinical recurrence. Recently emerged innovative technologies including cryoballon and contact force sensing catheter are expected to improve the durability of PVI in patients undergoing AF ablation. However, the durability of PVI depending on kind of catheters has not been fully elucidated.

Methods: Consecutive 1,116 patients undergoing catheter ablation for AF from 2008 to 2015 were enrolled. Patients were divided into 4 groups by the kind of ablation catheter in the first session: Convention group (n=500) including the patients ablated with 8mm non-irrigated tip radiofrequency catheter, Irrigation group (n=138) with irrigated tip radiofrequency energy (RF) catheter, CF group (n=258) with contact force sensing irrigated tip RF catheter, and Cryo group (n=220) with 28mm second generation cryoballon catheter. Ipsilateral extensive enucleating ablation using 3D navigation was performed in RF ablation groups and individual PVI in Cryo group. Completion of PVI was electrophysiologically confirmed by ring catheters. The durability of PVI in the second session was fully assessed with ring catheter in patients with clinical recurrence of AF.

Results: Baseline characteristics between the 4 groups were comparable except for smaller size of the left atrium and higher proportion of paroxysmal AF in Cryo group. All PVs were successfully isolated in the first session. The free rate from second session at one year were 82.2% for Convention group, 84.1% for Irrigation group, 84.5% for CF group, and 84.0% for Cryo group. The number of patients underwent second session was 190 (36.0%) during 51.6 months of follow-up period for Convention group, 40 (29.0%, 51.7months) for Irrigation group, 46 (17.8%, 23.9months) for CF group, and 20 (9.1%, 14.5months) for Cryo group (p<0.0001). Recurrence of PVI were observed 71.8% of the patients, 53.1% of the right sided PV and 49.7% of the left sided PV for Convention group, 67.5%, 55.0%, 42.5% for Irrigation group, 45.7%, 28.3%, 23.9% for CF group, and 36.8%, 10.5%, 31.6% for Cryo group (p<0.001, p<0.0001 and p<0.009, respectively).

Conclusions: The durability of PVI using cryoballon and contact force sensing catheter were higher than non-contact force sensing catheters.

3296 | BEDSIDE

Cryoballoon for persistent atrial fibrillation in comparison with non-irrigated radiofrequency technique: preliminary results of a randomised clinical trial

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Comparative data remain limited regarding cryoballon (CB) ablation verse radiofrequency (RF) techniques in ablation for atrial fibrillation (AF). Most published studies are non-randomised in mixed patient population including both paroxysmal and persistent AF (PsAF). This report aims to compare the two techniques used for AF ablation in relation to mid-term outcomes in patients with PsAF only.

Methods: Study patients who underwent their first left atrial ablation were prospectively recruited with written informed consent. Participants were randomised into 2 arms of CB or RF group in a 1:1 manner. For CB ablation, a single cryoballon (28mm, second generation) was used in each case conducted with local cryoablation catheters; no RF catheter was used in any case of CB group. Open-irrigated, non-force sensing RF ablation was applied in each case of the RF group with a 3D mapping system. Pulmonary vein (PV) isolation (PVI) and non-PV triggers were targeted in all cases. All procedures were performed by the same experienced operator who was blinded to the randomisation group before scrubbing. All participants were systematically followed up at Arrhythmia Clinics at 3, 6, and 12 months after the procedure with Holter monitoring ECGs.

Results: Of the first 90 participants, data from 82 patients (64±9 years, 82% male) who completed their 6-month follow-up were analysed in this report. There were 39 (63±9 years) in CB and 43 (64±10 years, p=ns) in RF group. Clinical characteristics were similar in both groups except that AF duration is rather longer in CB than RF groups (48±45 v 30±29 months, p<0.05). Acute PVI was achieved in 100% of cases of both groups. Significantly more patients in CB group was ablated to sinus rhythm (SR) by the end of the procedure compared to that in RF group (56% v 26%, p<0.01). Shorter procedure time was observed in CB than
Acknowledgement/Funding: National Natural Science Foundation of China (No.

Methods: Our study demonstrates that CB ablation leads to acute restoration of SR in more cases and associated with a higher rate of AF free at 6-month follow-up, and CB ablation in PsAF shortens overall procedure time compared with conventional RF ablation. More studies and longer follow-up are needed to confirm CB ablation can improve procedure efficiency and efficacy in PsAF.

Conclusion: We have –for the first time– proven that complete isolation of PV’s using a contactless externally applied energy source is a feasible procedure. The data shows plants is safe and feasible, and that long-term isolation of pulmonary veins can thus be accomplished.

3297 | BEDSIDE
Linear ablation following pulmonary vein isolation in patients with atrial fibrillation: a meta-analysis
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1 Second Hospital of Tianjin Medical University. Tianjin, China. People’s Republic of; 2 Evangelismos General Hospital of Athens, Second Department of Cardiology, Athens, Greece

Background: Previous studies have given conflicting data regarding the long-term adjunctive efficacy of linear lesions (LL) on top of pulmonary vein isolation (PVI) as an ablation strategy in patients with atrial fibrillation (AF).

Purpose: The aim of this meta-analysis was to provide a detailed analysis of the available randomized controlled trials (RCTs) regarding the efficacy of LL following PVI in AF patients.

Methods: Current databases were searched until October 2015. The primary outcome endpoint of the meta-analysis was recurrence of any symptomatic or documented episode of AF or atrial tachycardia after a single ablation procedure with or without the use of anti-arrhythmic drugs.

Results: Table 1 demonstrates a total of 1,144 patients were included in the meta-analysis. The pooled analysis of five trials concerning persistent AF (PeAF) patients (400 in PVI plus LL group and 182 in PVI alone group) suggested that the addition of LL following PVI does not lead to a significant reduction in the rate of recurrent late episodes of paroxysmal AF compared with PVI alone (RR = 0.97, 95% CI: 0.44–1.21, p = 0.22). Similarly, there was no incremental benefit of additional LL in patients (400 in PVI plus LL group and 182 in PVI alone group) assessed by a prior performed CT scan and a left atrial size <40cm² or ≤50mm. Patients are randomised to two times 1.2 or 3 minutes of cryoballoon applications per vein. Minutes of cryoballoon ablation are defined after reaching the maximum N20 cooling flow. PVI is checked using the Achieve mapping catheter directly after each application and at the end of the procedure, also using adenosine. During applications of the right PVs the PN is constantly stimulated and excursion of the diaphragm is monitored manually. If no ACh can be achieved with the assigned cryotherapy more and/or longer applications are applied until PVI is successful. This is classified as primary unsuccessful PVI. Patient follow up includes extensive rhythm registration 3, 6 and 12 months post PVI.

Conclusion: To the best of our knowledge this is the first meta-analysis to assess the optimal application duration using the second generation cryoballoon for PVI.

Abstract 3298 – Table 1. Periprocedural results

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**3200 | BEDSIDE**

Prevalence of triggers from left atrial appendage and coronary sinus in patients with history of coronary artery bypass grafting or maze procedure undergoing catheter ablation for atrial fibrillation

S. Mohanty1, P. Mohanty1, C. Trivedi1, C. Gianni1, J.D. Burkhart1, J. Sanchez1, G.J. Gallighouse1, A. Al-Ahmad2, R. Horton2, D.J. Lakireddy1, R. Hongo3, C.A. Froehle1, J.R. Anderson3, J. DiBiase1, A. Natale3, S. St. David’s Medical Center, Texas Cardiothoracic Arrhythmia Institute, Austin, United States of America; 2University of Kansas Medical Center, Kansas City, United States of America; 3California Pacific Medical Center, San Francisco, United States of America

**Introduction:** Atrial fibrillation (AF), new-onset or recurrent, is seen in 5–40% of patients following coronary artery bypass graft (CABG) surgery and 5–25% of post-MEZE cases. Untreated or de novo non-pulmonary vein (NPV) triggers have been reported to be possible source of arrhythmia in this population.

**Purpose:** We sought to assess the prevalence of NPV triggers and their impact on ablation outcome in post-CABG/MAZE patients undergoing AF ablation.

**Methods:** Four-hundred one (267 post-CABG and 134 post-MAZE) patients undergoing AF ablation were included in this analysis. All patients underwent PV antrum and posterior wall isolation. NPV triggers were elicited with isoproterenol challenge. Those were defined as ectopic triggers originating from sites such as left atrial appendage (LAA), coronary sinus (CS), interatrial septum, superior vena cava, and crista terminals. All patients were followed up for at least 2 years with event recorders, ECG and holter monitoring.

**Results:** During 44 NPV triggers were detected in 243 (91%) post-CABG and 124 (92.5%) post-MAZE patients. The triggers were most commonly mapped to CS (65%) and LAA (74%). NPV triggers at all locations were targeted for ablation in 179 (group 1), all locations except CS and LAA in 63 (group 2) and no NPV triggers in 99 (group 3) patients. At median (range) 33 months follow-up after single procedure, 124 (69%) from group 1, 25 (44%) from group 2 and 49 (39%) from group 3 remained arrhythmia-free off anti-arrhythmic drugs (log rank p < 0.001); success rate in group 1 was significantly higher than group 2 and 3 (p < 0.001).

**Conclusion:** Our results, for the first time, demonstrate that in post-CABG/MAZE patients experiencing AF, CS and LAA are the most prevalent sources of ectopic triggers and ablation of those triggers results in significantly better long-term outcome.

**3301 | BEDSIDE**

Outcome of conservative management with stents and clips in esophageal fistula and perforation following catheter ablation for atrial fibrillation: multi-center experience and literature review

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**Introduction:** Esophageal perforation, atrio-esophageal (AEF) and esophago-pericardial fistula (EPF) are rare but serious complications of atrial fibrillation (AF).

**Methods and results:** A total of 23 cases of esophageal complications following catheter ablation for AF were included in this analysis. Of the 11 patients receiving stent for AEF, 9 (81.8%) died and 2 patients survived after undergoing emergency surgical repair because of stent migration. The 5 patients with EPF and 1 with fistula connecting esophagus to coronary sinus (100%) recovered completely with stent placement. Two reported cases of esophageal perforation survived (100%) with successful resolution of the injury with fully-covered stents which were removed after 3–4 weeks. Endoscopic clip was utilized in 4 unpublished cases of which 3 achieved complete resolution of the lesion.

**Conclusion:** Esophageal stenting is an effective treatment strategy only for esophageo-pericardial fistula and esophageal perforation but not for atrio-esophageal fistula due to very poor outcome. Additionally, in case of perforation identified by absence of inflammatory changes during endoscopy, clipping is safe and effective in resolving the lesion completely. However, it should not be considered in the presence of mucosal ulceration or inflammation.
presentation (AMI versus Non-AMI) and the effect of SAPT relative to DAPT (P interaction=0.56).

Conclusions: Short DAPT <2-month after BMS implantation was as safe as prolonged DAPT ≥2-month in both AMI and Non-AMI patients.

Acknowledgement/Funding: Pharmaceuticals and Medical Devices Agency (PMDA) in Japan.

3304 | BEDSIDE
Clinical implications of low-dose aspirin in vasospastic angina: the 3-year prognosis
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Introduction: It is well established that high dose aspirin usage is associated with an aggravation of coronary artery spasm. However, there are inadequate data about the long term clinical implications of low-dose aspirin in chest pain patients who underwent provocation provocation test.

Objectives: This study was an observational, multicenter registry to determine clinical outcome and 3-year prognosis of low-dose aspirin usage in patients with chest pain who underwent intracoronary ergonovine provocation test. Patients who have intermediate and significant stenosis lesions on the baseline coronary angiograms are excluded.

Methods: A total of 2751 patients in the VA-KOREA (Vassospastic Angina in Korea) registry were classified into positive (n=570), intermediate (n=1049), and negative (n=1140) groups by intracoronary ergonovine provocation test. The positive & intermediate group result (n=1619) was reclassified into low-dose aspirin used (LAS) (n=709), and Aspirin not-used (control) (n=910) group. The 3-year incidences of adverse cardiac events (cardiac death, new-onset arrhythmia, and acute coronary syndrome) were determined (mean 486.8±292.2 days).

Results: Of the patients with positive and intermediate results, the prevalence of older age over 65 along with hypertension, Diabetes history, male and current smoking were higher in the LAS group compared to control group at baseline. The propensity score matching was used to randomly compare two groups. Cumulative composite MACE in the matched-pair cohort (n=1118) was 4.1% during 3 years. There was no significant difference in adverse cardiac events for LAS group vs control group (Hazard ratio [HR] 0.91; 95% confidence interval [CI] 0.56 to 1.48, P=0.71). In the adjusted multivariable Cox regression analysis, low dose Aspirin-usage was not an independent predictor for the primary endpoint ([HR] 1.06; 95% CI] 0.62–1.84, P=0.82).

Regarding prespecified subgroups, interaction analysis of MACE showed that the association of usage of aspirin with MACE was not modified by baseline age over 65 years and current smoking (P=0.01 for each). Even for the matched patients who have minimal organic stenosis on coronary angiography (n=409), Early use of aspirin did not make significant improvement of the primary end point (HRH 0.769; 95% CI] 0.325-1.82, P=0.55).

Conclusions: Low dose aspirin could not protect the cardiac events in vasospastic angina patients regardless of minimal coronary artery stenosis lesion.

3305 | BEDSIDE
Validation of the DAPT score in the all-comer PRODIGY trial
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Background: Prolonged dual antiplatelet therapy (DAPT) has been associated to a reduction of non-fatal ischemic endpoints but it is invariably associated to higher bleeding risk. The DAPT risk score has been recently introduced as a tool to simultaneously assess both the bleeding and ischemic risk, identifying patients who are more likely to derive harm (DAPT score <2) or benefit (DAPT score ≥2) from prolonged DAPT after percutaneous coronary intervention (PCI). An external validation of the DAPT score in the setting of a randomized study testing a differential DAPT duration is lacking.

Methods: We tested the DAPT score in the Doping Dual Antiplatelet Therapy After Grading Stented-Induced Intramural Hyperplasia Study (PRODIGY) trial, which enrolled all-comers patients undergoing PCI and randomized to up to 6 months vs. 24 months DAPT therapy.

Results: Of 1,970 patients, 739 (38%) had a DAPT score <2 and 1231 (62%) had a DAPT score ≥2. The incidence of the primary endpoint of death, MI or cerebrovascular accident (CVA) was not significantly different between patients with DAPT score ≥2 and those with DAPT score <2 (HR 0.80, 95% CI 0.59–1.07; P=0.14). The main safety endpoint of BARC 2,3,5 bleeding (HR 0.44, 95% CI 0.22–0.85, P<0.01) were significantly lower in patients with a DAPT score ≥2. The relative and absolute risk for the primary ischemic endpoint was similar in those with DAPT score ≥2 vs. <2, regardless DAPT duration, Figure 1. In the 6 month DAPT regimen group, the relative and absolute risk of the key safety endpoint of BARC 2,3,5 bleeding was similar between patients with a DAPT ≥2 vs. <2, regardless DAPT duration, while in the 24 month DAPT regimen group, both the relative and absolute risk of BARC 2,3,5 bleeding were significantly increased for patients with a DAPT score <2 compared to those with DAPT ≥2, Figure 1. These findings were confirmed at the landmark analysis from 6 to 24 months for both the primary ischemic (Pint for risk difference 0.13) and key safety endpoint (Pint for risk difference 0.02).

Conclusion: When applied in an all-comer population underwent PCI the DAPT score identified patients who were likely to be harmed by prolonged DAPT due to an excess of bleeding, whereas in our dataset it failed to discriminate patients deriving ischemic benefit from prolonging versus a shortened DAPT duration.

3306 | BEDSIDE
Aspirin desensitization in patients with coronary artery disease: results of a multicenter registry
R. Rossini1, G. Musumeci2, R. Pozzi3, C. Letteri3, I. Bossi3, M. Bianco2, S. Leonardi5, A. Iorio1, E. Collaku1, P. Colombo4, P. Canova4, A. Anzullini5, L. Ottonra Visconti5, O. Valsecchi5, M. Senni1, 1Ospedale Papa Giovanni XXIII, Bergamo, Italy; 2San Luigi Gonzaga Hospital, Turin, Italy; 3Hospital Carlo Besta, Milan, Italy; 4Niguarda Ca' Granda Hospital, Milan, Italy; 5Polyclinic Foundation San Matteo IRCSS, Pavia, Italy; 6Clinical Institute Humanitas of Castellanza, Castellanza, Italy

Background: Aspirin therapy is the cornerstone of treatment in patients with coronary artery disease (CAD). Aspirin sensitivity not only limits patients to benefit from the long-term use of this antiplatelet agent but is also often an impediment for percutaneous coronary interventions with stent implantation. The present study aimed to assess safety and feasibility of a standard desensitization protocol in patients with aspirin sensitivity and CAD, undergoing coronary angiography and to identify those patients that at the highest risk of developing adverse reactions.

Methods: This is a prospective, multicenter, observational study. A total of 61 centers in Italy participated in this registry. Patients with a history of aspirin hypersensitivity, admitted with acute coronary syndrome or with stable known or suspected CAD, before coronary angiography were identified and submitted to the desensitization protocol. A history of aspirin sensitivity was reported in 303 patients (mean age 67±11 y, 78% presenting with acute coronary syndrome). The most common history of reaction to aspirin was urticaria (N=139, 52%), followed by anaphylactic reaction (N=13, 5%). Of note, among patients with urticarial angioedema 13 patients (4%) had a history of idiopathic chronic urticaria. All patients underwent the desensitization procedure: six sequential doses of aspirin (1, 5, 10, 20, 40, and 100 mg) administered orally at predefined intervals, with the procedure lasting 5.5 hours. None received pretreatment with antihistamines or corticosteroids. Blood pressure, pulse, cutaneous, nasopharyngeal, or pulmonary reactions were monitored until 4 hours after the procedure. Patients were followed-up for 24±11 months.

Results: The desensitization procedure was performed before cardiac catheterization in all patients, but 59 (21%) who presented ST-elevation myocardial infarctions and in whom risk urgent reperfusion was required. Drug eluting stents were implanted in 59% of patients. The desensitization procedure was successful in 287 pts (95%), and in all patients with a history of anaphylactic reaction. Out of he 13 patients with a history of idiopathic chronic urticaria, only in two patients the desensitization failed. No serious adverse reactions occurred in patients with a failure of the protocol: 7 patients developed cutaneous reactions, 3 had mucous reactions, and 5 had a asthma-reactions. All reactions were immediately resolved with corticosteroids and antihistamines. At long follow-up term, 43 (14%)

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of patients had aspirin discontinuation, which was never due to sensitivity reactions.

Conclusion: This standard desensitization protocol is safe and effective in patients with coronary artery disease, irrespective of the type of sensitivity.

3307 | BEDSIDE
Ticagrelor reduces the risk of ischemic stroke after acute myocardial infarction compared with clopidogrel

R. Henriksson, A. Ulvenstam, A. Graipe, T. Mooe. Umea University, Department of Public Health and Clinical Medicine, Umea, Sweden

Background: Ischemic stroke is a known complication after acute myocardial infarction (AMI). There is a gap of knowledge on the effect of ticagrelor regarding the risk of ischemic stroke after an AMI in an unselected patient population.

Methods: Data for unselected patients with AMI treated with either clopidogrel or ticagrelor was obtained from the Swedish Register of Information and Knowledge about Swedish Heart Intensive Care Admissions (RIKS-HIA). Ischemic stroke events and deaths were identified by merging the RIKS-HIA register with the National Patient Register and the Cause of Death Register.

The patients were divided into two cohorts based on two separate time periods of approximately two years each, using the first prescription of ticagrelor (20 Dec 2011) as a cut-off point thus creating an early cohort (n=23447) treated only with clopidogrel and a latter cohort (n=24227) treated with either clopidogrel (47.9%) or ticagrelor (52.1%). Kaplan-Meier analysis was used to assess the risk of ischemic stroke over time and Cox regression analysis was used to identify predictors of ischemic stroke.

Results: Out of 47674 patients, there were 1203 cases of ischemic stroke. Cumulative Kaplan-Meier incidence estimates of ischemic stroke after one year were 2.8% (n=561) in the early cohort versus 2.4% (n=493) in the latter (p=0.001). Older age, previous ischemic stroke, diabetes, signs of congestive heart failure during hospitalisation, atrial fibrillation, and coronary artery bypass graft surgery during hospitalisation were associated with an increased risk of ischemic stroke in a multivariate Cox model. The latter cohort had a 17.6% (p=0.001) decreased relative risk of ischemic stroke after adjustment.

Conclusions: The risk of ischemic stroke in an unselected AMI population has decreased since the introduction of ticagrelor.

Acknowledgement/Funding: The study received funding from the Research Development and Education Unit, Region Jämtland Härjedalen

3308 | BEDSIDE
Clinical outcomes of dual antiplatelet therapy after implantation of drug-eluting stents in patients with different cardiovascular risk factors


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Objectives: The optimal duration of dual antiplatelet therapy (DAPT) after drug-eluting stent (DES) implantation has not been established yet. The objectives of this study was to evaluate the optimal duration of DAPT after DES implantation.

Methods and results: From three randomized trials (the Real Safety and Efficiency of 3-month Dual Antiplatelet Therapy Following Endeavor Zorotalimus-Eluting Stent Implantation trial; the Efficacy of 3-month Dual Antiplatelet Therapy Following Endeavor Zorotalimus-Eluting Stent Implantation trial; the Efficacy of 3-month Dual Antiplatelet Therapy Following Endeavor Zorotalimus-Eluting Stent Implantation trial) with MACES 1 year after DES implantation (hazard ratio [HR] = 1.132, 95% confidence interval [CI]=0.823–1.558, p=0.445). Predictors for a MACE were old age (>75 years), hypertension, diabetes mellitus, renal dysfunction (serum creatinine >2.0mg/dL), acute coronary syndrome, multi-vessel disease, and DES length >28mm. In patients with low cardiovascular risk (≤3 predictors), the incidence of MACE was not different between short-term and standard DAPT (HR=0.735, 95% CI: 0.466–1.159, p=0.185). However, in patients with high cardiovascular risk (>4 predictors), short-term DAPT was associated with more MACES than standard DAPT (HR=1.751, 95% CI: 1.098–2.791, p=0.019).

Conclusions: Clinical outcomes of DAPT after DES implantation depended on the burden of cardiovascular risk.

3309 | BEDSIDE
Pharmacodynamics of Low and Standard Doses of Ticagrelor in Patients with End Stage Renal Disease on Hemodialysis

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Objective: The aim of this study was to assess the functional impact of low dose ticagrelor in end stage renal disease (ESRD) patients receiving maintenance hemodialysis (HD).

Background: Patients with ESRD on maintenance hemodialysis are poor responders to clopidogrel. Our previous study has been reported that ticagrelor has superiority on platelet inhibition in compared with clopidogrel in patients with ESRD on HD. However, the rate of bleeding and complication is more frequent in ticagrelor group with standard dose.

Methods: In a single-center, prospective, randomized, crossover study, 54 ESRD patients on HD were assigned to receive clopidogrel (300mg loading dose (LD), 75mg once daily), standard dose ticagrelor (180mg LD, 90mg twice daily) or low dose ticagrelor (90mg LD, 90mg once daily) for 14 days. Platelet function was evaluated before and after antiplatelet therapy via light transmission aggregometry (LTA) and VerifyNow(TM) P2Y12 assay.

Results: There were significant differences of ADP-induced maximal extent of platelet aggregation (Aggmax) between the low dose ticagrelor groups and clopidogrel groups (ANOVA, p=0.04 for 5 μmol/L ADP stimuli; p<0.01 for 20 μmol/L ADP stimuli). Significant differences of inhibition of platelet aggregation (IPA) could be observed in an order of clopidogrel, low and standard doses of ticagrelor groups using adjusted intergroup comparison analysis (ANOVA, p<0.04 for 5 μmol/L ADP stimuli; p<0.005 for 20 μmol/L ADP stimuli). Both standard and low doses of ticagrelor treatments have lower P2Y12 reaction units (PRUs) than patients with clopidogrel (p<0.001) at 1 and 48 hours and 14 days (Fig 1). As LTA data was shown, there was a significant sequential reduction of PRU values in the following order: clopidogrel, low and standard doses of ticagrelor (ANOVA, p<0.001).

There was no bleeding event in patients with low dose ticagrelor group.

Conclusions: Low dose ticagrelor achieved greater platelet inhibition than clopidogrel in ESRD patients on HD.

3310 | BEDSIDE
Potential role of ticagrelor in preventing venous and cardiac thrombosis: insights from PEGASUS-TIMI 54

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Background: Previous studies have demonstrated that aspirin monotherapy reduces the risk of venous thromboembolism (VTE) by 32%. It is unclear whether P2Y12 inhibition with ticagrelor further reduces the risk of thrombosis when added to aspirin.
Purpose: We hypothesized that ticagrelor added to low-dose aspirin would reduce the risk of venous and intracardiac thrombotic events compared with aspirin alone in stable patients with prior myocardial infarction.

Methods: Pre-specified venous/carotid thrombotic events including deep vein thrombosis (DVT), pulmonary embolism (PE) and intracardiac thrombus, were identified from study site reported safety events in PEGASUS-TIMI 54 (NCT01225562), a randomized trial of ticagrelor 90 mg bid, ticagrelor 60 mg bid or placebo added to aspirin in patients with prior myocardial infarction. Patients requiring anticoagulation were excluded. Three-year event rates were calculated with the Kaplan–Meier method by treatment arm and compared using Cox proportional-hazards models.

Results: During a median follow-up of 33 months 174 patients of 21,162 randomized had at least one venous or cardiac thrombotic event (KM rate at 3 years: 2.1, 1.9, 2.1%). The addition of ticagrelor to aspirin significantly reduced the risk of thrombotic events by 32% with the 60 mg bid dose (HR 0.68, 95% CI 0.47–0.99; P=0.04) and by 16% with the 90 mg bid dose (HR 0.84, 95% CI 0.59–1.19) (figure). When stratified by type, it appeared that the risk reduction with ticagrelor was consistent for DVT/PE/right-sided cardiac thrombus (HR 0.79, 95% CI 0.55–1.13), superficial thrombophlebitis (HR 0.81, 95% CI 0.34–1.96) and other thrombotic complications including left-sided intra-cardiac thrombus (HR 0.58, 95% CI 0.27–1.21).

Conclusion: The addition of ticagrelor to aspirin reduced the risk of venous and cardiac thrombotic events in a population of stable non-anticoagulated patients with prior myocardial infarction.

3311 | BEDSIDE
Randomized comparisons of the platelet inhibitory effect of clopidogrel and low dose of ticagrelor in patients receiving antithrombotic therapy after percutaneous coronary intervention

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Background: Ticagrelor have greater antiplatelet efficacy but may increase the risk of bleeding. Recent data suggests that lower dose of ticagrelor might be more appropriate in East Asian patients. Therefore, we sought to compare the platelet inhibitory efficacy between low dose ticagrelor 90mg once daily, 45mg twice a day and clopidogrel 75 mg once daily.

Method and results: This study was an open label, single-center, prospective randomized controlled trial. All patients have received open-label clopidogrel 75 mg taken daily with 100 mg aspirin for 12 months after percutaneous coronary intervention (PCI). They randomly assigned clopidogrel 75 mg, ticagrelor 90 mg once daily and 45 mg twice a day with aspirin for 28 days. Platelet function testing was performed at baseline and 28 days after receiving assigned drugs using VerifyNow P2Y12 point-of-care assay. The primary endpoint was the comparison of P2Y12 reaction units (PRU) determined by Verifynow P2Y12 at 28 days after receiving assigned drugs using VerifyNow P2Y12 point-of-care assay.

Results: A total of 69 patients were randomized, 62 patients were included in the final analysis. There were no differences in baseline PRU between three groups (clopidogrel 75 mg vs ticagrelor 90 mg qd vs ticagrelor 45mg bid; 215.8±50.7 vs. 193.1±31.4 vs. 215.8±50.7, p=0.168). The ticagrelor 90 mg once daily and 45 mg twice a day had significantly lower PRU compared with clopidogrel 75 mg at 28 days (clopidogrel vs ticagrelor 90 mg vs ticagrelor 45 mg bid; 221.2±50.1 vs. 196.6±53.4 vs. 215.8±50.7, p=0.001). Comparing ticagrelor 90 mg once daily and 45 mg twice a day, there was no significant difference in PRU (98.6±73.4 vs. 65.5±58.8, p=0.01). Including ticagrelor 90 mg taken daily with 100 mg aspirin for 12 months after percutaneous coronary intervention (PCI). The clinical implication of our data should be investigated in a future clinical trial.

Conclusion: Two different regimens of low dose ticagrelor, 90 mg qd once daily and 45 mg twice a day, have more potent platelet inhibitory effect than standard dose of clopidogrel in patients treated with PCI. The clinical implication of our data should be investigated in a future clinical trial.

BEST POSTERS SESSION 4
BEST POSTERS IN NEW OBSERVATIONS IN STRESS ECHOGRAPHY

P3313 | BEDSIDE
Prognostic value of exercise stress echocardiogram in the follow-up of patients after percutaneous coronary intervention with stent placement


Introduction: Stress echocardiogram is commonly used in patients with chronic ischemic heart disease (CHD) after revascularisation for the study of recurrent chest pain, as a guide for repeat revascularization or for prognostic purpose. However, limited data are available about its role in the evaluation of percutaneous revascularized patients in the advances in percutaneous coronary intervention (PCI) in the current period.

Purpose: Evaluate the prognostic ability of the exercise echocardiogram (EE) after PCI with stent placement.

Methods: We included 897 consecutive patients with previous PCI in which EE was performed between Jan 2004-Dec 2009. In the majority of cases (75%), the indication of the stress test was risk stratification in patients without angina-like symptoms. Clinical follow-up was carried out regarding mortality and soft events (readmissions for chest pain and new revascularization).

Results: During a median follow up of 53 months, the mortality was 8% (72 cases, 1.8%/year), and the most common documented cause was non-cardiac death (cancer 47%). Variables independently associated with mortality were age over 65 yo (OR 1.82 [IC95: 1.07–3.09], p=0.028), ejection fraction <50% (OR 2.03 [IC95: 1.10–3.76], p=0.024) and functional capacity <6 METs (OR 2.32 [IC95: 1.05–5.15], p=0.002). Myocardial ischemia (MI) detected either on electrocardiogram (OR 1.58 [IC95: 0.90–2.90], p=0.17) or echocardiography (OR 1.05 [IC95: 0.56–1.98], p=0.89), however, showed no prognostic value. 169 soft events (18.8%) were reported, including 91 readmissions for chest pain and 72 revascularizations. Variables independently associated with soft events were: angina during EE (OR 3.26 [IC95: 2.00–5.32], p<0.001), electrocardiographic MI (OR 1.92 [IC95: 1.11–3.33], p=0.020), echocardiographic MI (OR 3.16 [IC95: 1.96–5.11], p<0.001) and poor functional capacity (OR 1.91 [IC95: 1.19–3.04], p=0.007).

Multivariate analysis with Cox regression model is displayed in the figure. A new revascularization based on the results of the stress echocardiogram did not improve outcomes in our patients. The multiple use of stress tests (53%) or cardiac catheterization (26.4%) is frequent during the follow-up of patients revascularized with stents.

Figure 1. Cox models

Conclusions: Mortality rates in CHD tend to be low. In our cohort the detection of MI in EE in asymptomatic patients had no prognostic value in terms of survival and was only associated with the incidence of soft events. Some variables obtained from the EE such as functional capacity or ejection fraction should be considered for prognostic stratification beyond the detection of ischemia.
**P3314 | BEDSIDE**

Significant prognostic impact of the preload reserve and diastolic reserve during acute preload stress echocardiography using leg-positive pressure manoeuvre in patients with heart failure


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**Background:** Identification of subgroup of heart failure (HF) patients who are likely to suffer clinical deterioration has important implications in the choice of interventional strategies to prevent overt HF. Recently, leg-positive pressure (LPP) manoeuvre, using customized air-bags inflated around both lower limbs to maintain a constant loading pressure (90mmHg for 5 minutes), is reported to be able to apply acute preload stress non-invasively without significant increase in either heart rate or blood pressure.

**Hypothesis:** We hypothesized that the ability to utilize the Frank-Starling mechanism without significant increase in left ventricular (LV) filling pressure in response to preload-increasing intervention could provide important prognostic information for patients with chronic HF.

**Methods:** Ninety-two HF patients (mean ejection fraction of 35±9%, all <45%) and 20 age and gender matched normal controls were prospectively recruited for this study. LV stroke volume (SV) was assessed by means of pulsed-wave Doppler at the LV outflow tract. The pulsed-wave Doppler derived transmural flow velocity and tissue Doppler-derived mitral annular velocity (E) were obtained, and the E/E’ ratio was calculated to estimate LV filling pressure. These Doppler parameters were obtained both at rest and during LPP stress. Event-free survival was then tracked for 280 days.

**Results:** All subjects well tolerated LPP stress during echocardiographic examination. The LPP stress caused significant increase in forward SV (from 50±13 to 62±17 ml/m², p<0.001) without significant increase in LV filling pressure (E/E’; from 102±5 to 112±6, n.s.) in normal controls, while LPP stress only slightly increased SV (from 41±13 to 44±15 ml/m², p<0.001) at the expense of the elevated LV filling pressure (E/E’; from 15±9 to 18±10, p<0.001) in patients with HF. During the follow-up period, 11 patients developed adverse cardiac events. During acute preload stress, forward SV increased significantly (from 41±13 to 45±15 ml/m², p<0.001) along with the minimal change in LV filling pressure (E/E’; from 15±10 to 17±10, p<0.01) in patients without cardiac events. On the other hand, Frank-Starling mechanism was significantly impaired (SVI: from 37±11 to 36±13 ml/m², n.s.), and LV filling pressure dramatically increased to the critical level (E/E’; from 18±8 to 23±9, p<0.006) in patients with cardiac events. When patients were divided into two subgroups based on the changes in the forward SV (ΔSV) and E/E’ ratio (ΔE/E’ ratio) in response to LPP stress, patients without preload reserve (ΔSV)>0) showed significantly worse event rate than the others (log-rank p<0.01). Similarly, patients without diastolic reserve (ΔE/E’ ratio < -3) exhibited significantly worse event-free survival than the others (log-rank p<0.01).

**Conclusions:** Preload reserve as well as diastolic reserve during acute preload stress echocardiography was important determinants of cardiovascular outcome for patients with HF.

**P3316 | BENCH**

Left ventricular contractile reserve by stress echocardiography as a predictor of response to cardiac resynchronization therapy in heart failure: a meta-analysis

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**Background:** The presence of left ventricular contractile reserve (CR) during stress-echo (SE) may provide an appealing simple alternative to pathophysiologically attractive, technically demanding but clinically disappointing dysynchrony indices to predict favorable response to cardiac resynchronization therapy (CRT) in heart failure patients.

**Purpose:** To perform a meta-analysis of available SE data in this large and expanding set of patients.

**Methods:** All studies published in international peer-reviewed journals were included in the meta-analysis if they fulfilled the following criteria: 1- heart failure patients with NYHA class III and IV, depressed ejection fraction (EF <35%) and GRS duration >120 ms at study entry; 2- SE with assessment of CR; 3- Clinical and/or echocardiographic follow-up information after CRT. All studies were individually evaluated to avoid inclusion of redundant or inadequate data. Large part of CR during SE was identified as a reduction in wall motion score index < 0.20, and/or an increase in ejection fraction >5%. Responders to CRT were identified on the basis of symptomatic (NYHA class decrease) and/or functional (reduction in LV end-systolic volume >15%) improvement in the follow-up post-CRT.

**Results:** From Pubmed scan from 2006 to 2015, 13 studies with 1002 patients (mean age 67±3 years, 73% male, 54% with ischemic cardiomyopathy) were included in the meta-analysis. The type of stress was either exercise (n=2) or dobutamine (n=11), the latter with low dose (up to 10 mcg) in 2, intermediate dose (up to 20 mcg) in 7, and high dose (40 mcg) protocol in 2 studies; 609 patients (81%) showed CR and 444 (64%) were responders to CRT. Resting ejection fraction was 25±3%, QRS duration 157±12 ms, end-diastolic and end-systolic volumes were 202±41 ml and 150±32 ml, respectively. The overall odds ratio for CR to predict a favourable CRT response was 9.549 (95%, CI 6.864–13.285), with no detectable difference across different stressors, doses, and CR criteria (Figure).

**Conclusion:** The presence of CR during SE with either dobutamine or exercise is associated to greater chances of functional recovery after CRT. This parameter is now ready to be tested in a prospective multicenter trial to select patients more likely to benefit from CRT.
BEST POSTERS IN DRUG THERAPY AND BLOOD PRESSURE LOWERING

P3318 | BENCH
ZD100: a novel cyclic GMP activating ANP-based designer peptide in experimental hypertension with structural insights into its unique carboxy-terminus

Background: Innovative blood pressure (BP) lowering and multigain protective drugs are highly needed for hypertension (HTN). Thus, we engineered a Mayo Clinic-designed novel natriuretic peptide (ANP)-based drug, ZD100, which possesses a unique 12 amino acid (AA) carboxy-terminus (CT) extension. ZD100 is more potent than ANP in reducing BP, inducing natriuresis and inhibiting aldosterone via pGC-A receptor and its second messenger cGMP. Notably, ZD100 is currently in clinical trials for HTN.

Purpose: To date, the in vivo actions of ZD100 in a model of essential HTN are undefined. Further, the importance of specific AAs in the CT of ZD100 is unknown and is critical to define, in attempt to enhance or minimize pGC-A activation.

Methods: Spontaneously hypertensive rats (SHRs) received intravenous (IV) ZD100 (300 pmol/kg/min) or vehicle and measured intracranial cerebral perfusion pressure (CIP) generation.

Results: In SHRs, acute IV ZD100 reduced BP, induced natriuresis and increased plasma and urinary cGMP. Of the 6 variants, deletion of tryptophan (W) alone (V1) and/or with addition of serine (S) (V3) increased the ability of ZD100 to activate pGC-A/cGMP in vitro, while atropine-sensitive variant (V4) or serine (S) reduced pGC-A activation (V2 and V3). AA minimization with deletion of 3 CT AAs (V6) resulted in the preservation of pGC-A activation (Figure).

Conclusions: ZD100 infusion was able to activate systemic and renal pGC-A/cGMP reduce BP and induce natriuresis in SHRs. Importantly, enhanced pGC-A activation is possible with targeted AA deletion, while specific minimization preserves pGC-A activation. Together, these findings support the development of ZD100 as a novel therapeutic strategy for HTN and will help guide the development of best-in-class ZD100 analogues.

P3319 | BEDSIDE
Oral paricalcitol therapy reduces arterial stiffness in hypertensive patients with chronic kidney disease and secondary hyperparathyroidism: Data from a 1-year follow-up study

Background/Introduction: Arterial stiffness is linked to the progression of atherosclerosis, while activation of vitamin D receptor exerts favorable cardiovascular effects in patients with renal insufficiency.

Purpose: In this study we investigated the effects of oral treatment with paricalcitol, a potent vitamin D receptor activator on arterial stiffness and osteopontin, a marker of atherosclerosis, in hypertensive patients with chronic kidney disease (CKD) and secondary hyperparathyroidism.

Material and methods: We followed up 29 treated hypertensive patients (mean age 74±1 years, 19 men, office blood pressure=132/85mmHg) with CKD stages 3–5 [mean glomerular filtration rate (GFR)=19.4±1ml/min/1.73m²], who were on thiazide diuretics for hyperparathyroid for 1 year. All patients had baseline undetermined complete physical examination, while venous blood samples were drawn for estimation of metabolic profile, levels of intact parathormone, phosphorus and calcium and osteopontin. Arterial stiffness was estimated based on carotid-femoral pulse wave velocity (PWV) measured with an automated device.

Results: After 1 year of treatment with paricalcitol compared to baseline there was no statistical difference in levels of GFR (19.5±4.8 ml/min/1.73m² vs 18.0±2.3 ml/min/1.73m², p=0.318) and calcium (9.11±2.3 vs 8.98±2.2 mg/dl, p=0.344). Regarding the metabolic profile of patients, levels of glucose, lipids or uric acid did not differ, while the product of calcium x phosphorus exhibited no pathological values. Additionally, carotid-femoral PWV was reduced after 1 year treatment with paricalcitol from 11.8±2.6 to 11.2±2.4 m/sec (p<0.05), while blood pressure values and osteopontin levels 1 year after therapy compared to baseline values had no statistical difference (p=NS).

Conclusions: Treatment with oral paricalcitol in hypertensive subjects suffering from CKD stages 3–5 and secondary hyperparathyroidism is accompanied by amelioration of arterial stiffness as reflected by the reduction of carotid-femoral PWV. These findings suggest that paricalcitol exerts pleiotropic favorable effects on the vascular system, thus improving cardiovascular prognosis in high risk hypertensive patients.

P3320 | BEDSIDE
Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis

Background: The benefits of blood pressure lowering treatment for prevention of cardiovascular disease are well established. However, the extent to which these effects differ by baseline blood pressure, presence of comorbidities, or drug class remains unclear. We performed a systematic review and meta-analysis to clarify these differences.

Method: For this systematic review and meta-analysis, we searched MEDLINE for large-scale blood pressure lowering trials, published between 1 Jan 1966 and 7 July 2016. All randomised controlled trials were eligible for inclusion if they included a minimum of 1000 patient-years of follow-up in each study arm. No trials were excluded because of presence of baseline comorbidities, and trials of antihypertensive drugs for indications other than hypertension were eligible. We performed meta-analysis for major cardiovascular disease events, coronary heart disease, stroke, heart failure, renal failure, and all-cause mortality. We used inverse variance weighted fixed-effects meta-analyses to pool the estimates.

Results: We identified 123 studies with 613,815 participants for the tabular meta-analysis. Meta-regression analyses showed that every 10 mm Hg reduction in systolic blood pressure significantly reduced the risk of major cardiovascular disease events [relative risk (RR) 0.85, 95% CI 0.77–0.93], coronary heart disease (0.83, 0.75–0.92), stroke (0.72, 0.65–0.79), and heart failure (0.68, 0.58–0.82). Treatment with oral paricalcitol from 11.8±2.6 m/sec to 11.2±2.4 m/sec (p=0.05), while blood pressure lowering significantly reduces vascular risk across various baseline BP levels and comorbidities. Our results provide strong support for lowering systolic blood pressure to less than 130 mm Hg and providing blood pressure lowering treatment to individuals with a history of cardiovascular disease, coronary heart disease, stroke, diabetes, heart failure, and chronic kidney disease.

Acknowledgement/Funding: NIHR Oxford Biomedical Research Centre, NIHR Career Development Fellowship, Oxford Martin School

P3321 | BEDSIDE
Stress management techniques for the management of idiopathic hypertension
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Background/Introduction: Arterial stiffness is linked to the progression of atherosclerosis, while activation of vitamin D receptor exerts favorable cardiovascular effects in patients with renal insufficiency.

Purpose: In this study we investigated the effects of oral treatment with paricalcitol, a potent vitamin D receptor activator on arterial stiffness and osteopontin, a marker of atherosclerosis, in hypertensive patients with chronic kidney disease (CKD) and secondary hyperparathyroidism.

Material and methods: We followed up 29 treated hypertensive patients (mean age 74±1 years, 19 men, office blood pressure=132/85mmHg) with CKD stages 3–5 [mean glomerular filtration rate (GFR)=19.4±1ml/min/1.73m²], who were on thiazide diuretics for hyperparathyroid for 1 year. All patients had baseline undetermined complete physical examination, while venous blood samples were drawn for estimation of metabolic profile, levels of intact parathormone, phosphorus and calcium and osteopontin. Arterial stiffness was estimated based on carotid-femoral pulse wave velocity (PWV) measured with an automated device.

Results: After 1 year of treatment with paricalcitol compared to baseline there was no statistical difference in levels of GFR (19.5±4.8 ml/min/1.73m² vs 18.0±2.3 ml/min/1.73m², p=0.318) and calcium (9.11±2.3 vs 8.98±2.2 mg/dl, p=0.344). Regarding the metabolic profile of patients, levels of glucose, lipids or uric acid did not differ, while the product of calcium x phosphorus exhibited no pathological values. Additionally, carotid-femoral PWV was reduced after 1 year treatment with paricalcitol from 11.8±2.6 to 11.2±2.4 m/sec (p<0.05), while blood pressure values and osteopontin levels 1 year after therapy compared to baseline values had no statistical difference (p=NS).

Conclusions: Treatment with oral paricalcitol in hypertensive subjects suffering from CKD stages 3–5 and secondary hyperparathyroidism is accompanied by amelioration of arterial stiffness as reflected by the reduction of carotid-femoral PWV. These findings suggest that paricalcitol exerts pleiotropic favorable effects on the vascular system, thus improving cardiovascular prognosis in high risk hypertensive patients.
Control (HLC), the latter using a scale that investigates the individual's beliefs regarding who is responsible for his/her health issues. Specific scales were formulated to evaluate the compliance to the treatment instructions and the satisfaction with the intervention.

**Results:** Systolic blood pressure was significantly reduced within the intervention group (mean reduction -9.7mmHg, p<0.001) and between groups (-9.7mmHg vs. -1.6mmHg, p<0.001). Although, DBP was significantly reduced within the intervention group (-1.7mmHg, p=0.04), the change was not significant compared to the control group (-1.7mmHg vs. -0.8mmHg, p=0.4). After adjusting for baseline BP levels and age, patients in the intervention group had larger SBP and DBP reductions than the control group (p<0.01 for both). The DASS depression score (p=0.002), DASS anxiety (p=0.01) and DASS stress (p<0.001) showed a significant reduction in subjective depression, anxiety and stress perception in the treatment group as compared to the PSS and the HLC scores showed a significant improvement after using the stress management program.

**Conclusion:** Stress management techniques play a major role in the management of hypertension. Simple techniques, such as RB, PMR and GI, which are easy to apply are an effective, low cost, non-pharmacologic therapy in the treatment of mild essential hypertension.

**BEST POSTERS IN RESTENOSIS TREATMENT**

**P3323 | BEDSIDE**

Impact of diabetes on the severity of calcified neatherosclerosis in extremely late in-stent restenosis over 10 years after bare-metal stent implantation

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**Background:** In-stent neatherosclerosis is a major concern of late stent failure for both drug-eluting stent (DES) and bare-metal stent (BMS). The incidence of late target lesion revascularisation (TLR) after BMS implantation has increased steadily over time. The characteristics of lesions with extremely late in-stent restenosis (EL-ISR) after BMS implantation that occurred beyond 10 years remain unclear.

**Purpose:** We characterised the lesions with EL-ISR in patients who required late TLR over 10 years after BMS implantation.

**Methods:** From August to February 2016, a total of 44 lesions in 44 patients (69±8±7.8 y.o.; 82.5± male) who underwent TLR due to EL-ISR over 10 years after the initial BMS implantation were analysed with intravascular ultrasound (IVUS). We estimated the severity of calcification with the maximum arc, longitudinal length and the number of calcification in lesions with EL-ISR. Twenty-one patients (47.8%) with diabetes mellitus (DM) were defined as having a history of DM treatment or Hba1c >6.5%.

**Result:** Forty-four lesions underwent TLR due to EL-ISR at a mean interval of 12.7±2.6 years (range 10–17 years) after the index procedure. Of the 44 patients, 18 patients (40.9%) presented with acute coronary syndrome, including 4 (9%) ST elevation myocardial infarction, 15 (34.1%) stable angina and 11 (25%) silent angina.

**Conclusion:** Neatherosclerosis in stents aged over 10 years after the BMS implantation contained serious levels of calcification. In particular, DM exacerbated calcified neatherosclerosis. Therefore, attention should be paid to the treatment of EL-ISR, especially in cases of DM to avoid incomplete dilation due to the existence of extensive calcification.

**P3324 | BEDSIDE**

Vascular smooth muscle cell-related microRNAs are up-regulated in human venous intimal hyperplasia of dialysis patients

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**Background:** Venous intimal hyperplasia is a significant problem of vein grafts, especially vascular accesses of dialysis patients. High increased vascular smooth muscle cell (VSMC) proliferative activity was demonstrated in stenotic veins but the molecular mechanisms are poorly understood. Recent animal studies demonstrated that microRNAs (miRNAs) are involved in control of proliferation and vascular smooth muscle differentiation. Nonetheless, translational evidence supporting the role of VSMC-related miRNAs in human venous intimal hyperplasia is rare.

**Purpose:** To address the role of VSMC-related miRNAs in venous intimal hyperplasia of dialysis patients

**Method:** Vein grafts tissues were obtained from surgical revision of eight patients with failed dialysis accesses. Control veins were obtained from the same patients at new access creations. Six VSMC-related miRNAs, miR-21, 130a, 133, 214, 221, and 222 were selected according to previous studies in rat carotid arteries. Both quantitative analysis and in-situ hybridization were performed. To prospectively confirm the pathological findings, 15 patients with early restenosis (less than 3 months) and 15 with late restenosis (beyond 6 months) were invited as the validation cohort. Debris gathered during percutaneous transluminal angioplasty was obtained by Filter wire for quantitative miRNA analysis. Vascular events were prospectively followed for three months.

**Results:** In the derivation cohort, the expressions of miR-21, 130a and 221 in tissues of stenotic vein grafts were significantly upregulated. In situ hybridization showed that miR-21 was aberrantly localized in neointima of stenotic veins, less present in non-significantly stenotic veins and totally absent in control veins. The expression of miR-145 was on the contrary to that of miR-21, i.e., aberrantly localized in normal veins but nearly absent in stenotic veins. In the validation cohort of 30 patients with dysfunctional vascular accesses, the levels of miR-21, 130a and 221 measured in the embolic debris were significantly higher in the early restenosis group. Kaplan-Meier plots also showed better restenosis-free patency in patients with low miR-21 levels of embolic debris (p<0.04).

**Conclusion:** Our results provide the first translational evidence in human that VSMC-related miRNAs are up-regulated in venous intimal hyperplasia of dialysis patients.

**Acknowledgement/Funding:** HCH104-10 and NSC104-2314-B-002-206

**P3325 | BENCH**

Development of a PPAR-γ agonist-coated implant for restenosis treatment

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**Background:** Peroxisome proliferator-activated receptor-γ (PPAR-γ) agonists improve insulin resistance and showed antiproliferative effects on vessel wall cells. The aim of the study was to develop a novel stent eluting the PPAR-γ agonist ciglitazone by a new releasing strategy and to investigate its effect on restenotic lesions.

**Methods:** Cobalt-chrome specimens were coated with ciglitazone, polylactid (PLA) and cyclooctydines (CD) or with ciglitazone and PLA alone in various combinations. Specimens were incubated in physiologic salt solution and the ciglitazone release was measured by UV/VIS spectroscopy. After validation, the effect of these complexes on human endothelial (EC) and smooth muscle cells (SMC) was assessed by proliferation assay. Subsequently, bare metal stents were coated with ciglitazone and PLA alone or in complex with CD and implanted in an in vitro arterial vessel model mimicking neointimal hyperplasia. After 6 weeks stents were examined by histochemical (HE and EvG staining) characterization, and inhibition of EC and SMC proliferation in the vessel was measured.

**Results:** UV/VIS spectroscopy revealed a significant increase in ciglitazone release in complex with cyclooctydines. Furthermore, the ciglitazone release could be adjusted by varying the CD content. After incubation in cell culture for 48 h, the inhibition of EC and SMC proliferation was significantly more inhibited with the ciglitazone-CD-PLA complex, compared to ciglitazone and PLA alone. Six weeks after implantation, the vessels showed a significantly smaller proliferation area in case of ciglitazone in complex with CD and PLA (81±7.8%), compared to ciglitazone and PLA alone (34±11.6%) (Figure), whereas endothelialization was not affected.

**Conclusion:** The experimentally engineered drug delivery system proved significant anti-restenotic efficacy in this model and merits attention as a promising novel stent coating.
The development of in-stent restenosis (ISR), defined as narrowing of the stented segment. The pathophysiology is not fully understood, however a number of clinical risk factors have been identified, including renal disease. Cardiovascular mortality accounts for 50% of deaths in end-stage renal disease (ESRD). The mechanisms leading to accelerated atherogenesis is thought to be different in hemodialysis (HD) and peritoneal dialysis (PD). PD patients have higher rates of de novo coronary artery disease compared to HD. Given the different mechanisms leading to atherogenesis in HD and PD, rates of ISR could potentially be different in these patients.

Purpose: To compare the rates of ISR in HD versus PD ESRD patients in Manitoba.

Methods: A retrospective chart review was performed of ESRD patients who underwent PCI (2010–2014), at a single tertiary care center. Patients were cross-referenced with the Manitoba Renal Program Database. Basic demographics, past medical history and angiographic data were reviewed.

Results: A total of 1450 ESRD patients were screened: 1170 on HD (81%) and 280 on PD (19%). Mean age was 56 years in HD and 62 years in PD (p=0.16). Traditional cardiac risk factors were prevalent in these patients, however the rates were higher in HD compared to PD. Diabetes was the most common etiology of ESRD (88% HD vs 50% PD, p<0.0001).

Ten percent (n=148) had undergone PCI during the study period -118 HD and 30 PD. The rate of ISR was 14% in the HD group (n=16) and 27% in the PD group (n=8), which was statistically significant (p=0.035). Both groups were more likely to have DES in comparison to BMS (77% HD, 73% PD, p=0.62). HD were more likely to receive multiple stents/resolution (81%) compared to PD (63%, p=0.007). HD patients had a lower mean of stents/patient (1.93) than PD patients (2.75) although this was not statistically significant (p=0.18). Mean time to ISR was shorter in HD than PD lesions (26 months vs 18 months, p=0.29). The mean stent length did not differ between the two groups (20.9 mm in HD vs 20.4 mm in PD, p=0.12). Focal ISR was more common (58% HD vs 68% PD). Patients were more likely to have calcification (81% HD vs 41%, p<0.0001). The mortality rate was significantly higher (p<0.0001) in the PD (75%) compared to HD patients (44%).

Conclusions: This is the first study to examine ISR rates in HD in comparison to PD patients. Despite being younger and having less cardiac risk factors, PD patients had higher rates of ISR and mortality. Given the modest sample size of this retrospective study, a prospective study is needed. This study highlights the importance of cross-specialty collaboration (Cardiology, Cardiac Surgery, Nephrology and Allied Health) to provide optimal care to this unique patient population.

Best Posters in Cardiac Resynchronisation Therapy

P3328 | BEDSIDE
The concept of competing risks applied to a CRT-D population
B.A. Schaer1, D. Weber1, D. Theuns2, T. Reichlin1, M. Kuehne1, C. Sticherling1

Ten percent (n=148) had undergone PCI during the study period -118 HD and 30 PD. The rate of ISR was 14% in the HD group (n=16) and 27% in the PD group (n=8), which was statistically significant (p=0.035). Both groups were more likely to have DES in comparison to BMS (77% HD, 73% PD, p=0.62). HD were more likely to receive multiple stents/resolution (81%) compared to PD (63%, p=0.007). HD patients had a lower mean of stents/patient (1.93) than PD patients (2.75) although this was not statistically significant (p=0.18). Mean time to ISR was shorter in HD than PD lesions (26 months vs 18 months, p=0.29). The mean stent length did not differ between the two groups (20.9 mm in HD vs 20.4 mm in PD, p=0.12). Focal ISR was more common (58% HD vs 68% PD). Patients were more likely to have calcification (81% HD vs 41%, p<0.0001). The mortality rate was significantly higher (p<0.0001) in the PD (75%) compared to HD patients (44%).

Conclusions: This is the first study to examine ISR rates in HD in comparison to PD patients. Despite being younger and having less cardiac risk factors, PD patients had higher rates of ISR and mortality. Given the modest sample size of this retrospective study, a prospective study is needed. This study highlights the importance of cross-specialty collaboration (Cardiology, Cardiac Surgery, Nephrology and Allied Health) to provide optimal care to this unique patient population.

BEST POSTERS IN CARDIAC RESYNCHRONISATION THERAPY

P3329 | BEDSIDE
Anticoagulation therapy in patients with left ventricular endocardial stimulation for cardiac resynchronization therapy
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Background: The presence of a permanent electrode in the left ventricle (LV) and systemic arterial circulation potentially increases the risk of thromboembolic complications where there is no coronary sinus occlusion (CSO) (TC). Current guidelines recommend prolonged duration, modes of anticoagulation (AT) to prevent TC in patients with indications for permanent endocardial left ventricular stimulation (ELVS) for cardiac resynchronization therapy (CRT).

Aim of our study: To investigate early and late thromboembolic and hemorrhagic complications in patients with permanent ELVS and oral anticoagulation therapy with warfarin (W) and rivaroxaban (R).

Methods and results: 24 patients - 18 males, age 40–67 years, with indication for CRT were operated: 17 – using subclavian vein and puncture interventricular septum (IVS) and 7 – using thoracotomy and puncture the apex of left ventricle (LV). 21 of them (87.5%) had previously-failed transvenous attempts. Mean NYHA functional class was 3.1±0.5. Atrial Fibrillation had 20 pts (83.3%), persistent form - 17 of them (70.8%). CHA2DS2VASC score was 2.6±0.3. Patients were heparinized during the implantation of LV electrode: ACT level 250–300 sec. Continuous oral anticoagulation with W (22 pts) had been initiated on the next day after procedure, in addition using enoxaparin until targeted INR 2.5–3.5 reached. In follow up, oral AT was monitored in hospital and individually by patients using coagulometer Innova 2 PM Monitoring System, USA. Target therapeutic range of INR was 76% of test points. Two patients started (R) in the evening on the day of the procedure. During 17±5 months of follow-up there were no endpoints as strokes, transient ischemic attacks and systemic thromboembolism. Computer tomography imaging of the brain was performed before the procedure and 8 patients after (10 pts) didn’t reveal any silent ischemic strokes. No major bleeding occurred during follow-up. The absence of thromboembolic complications we explain the careful control of coagulation. Endothelization of the electrode which occurs after implantation and the use of anticoagulants reduces the risk of thrombocytopenia.
the determination of cardiac output in Tri-V or conventional biventricular pacing (Bi-V). The final mode (Tri-V vs Bi-V) was programmed according to the hemodynamic performance. Follow-up (FUP) assessment was performed at 6 and 12 months, and included clinical assessment with NYHA class determination, quality of life (QoL) assessment with the Minnesota QoL questionnaire, 6-minute walk test (6MWTT) and echocardiogram with determination of the ejection fraction (EF). Patients were classified as responders if NYHA class was reduced by at least one level and EF increase of ≥10%, and as super-responders if NYHA class at FUP was I and EF ≥50%. Survival rates and survival free of heart failure hospitalization were calculated. For statistical analysis we used the paired samples T test.

Results: We included 40 pts (93% male, mean age 72±10 years), 32 (80%) were programmed in Tri-V based on the hemodynamic test results. The following results pertain to this subgroup. At baseline, 58% of pts were in NYHA class III and 42% in NYHA class II, with a mean ejection fraction of 28% ± 5. After completion of 1 year of follow-up, mean QoL score more than halved (31±21 vs. 15±18; p=0.017 at 12 months), the 6MWTT distance was significantly improved in the responder group (416±104 m to 465±107 m, p=0.005 at 12 months) and the mean ejection fraction also increased (28.5 vs. 40.1; p=0.001 at 6 months and 28.5 vs. 41.10; p=0.001 at 12 months). The responder rate was 62% at 6 months and 76% at 12 months. The super-responder rate was 9% at 6 months and 25% at 12 months. 4 pts died. Survival free of heart failure hospitalization was 87.5%.

Conclusion: Tri-V CRT yielded a high response rate, and a much higher super-response rate. MR improvement was specified as a reduction of at least one grade in its severity. This was a clear improvement in functional capacity and QoL, as well as positive reverse remodeling. These results may warrant considering Tri-V as a first line therapy for CRT.

P333 | BEDSIDE Improvement of mitral regurgitation predicts response to cardiac resynchronization therapy
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Background: Cardiac resynchronization therapy (CRT) is a proven treatment in chronic heart failure (CHF). However, despite updating guidelines, proportion of non-responders remains high. Factors predicting CRT response are subject of many studies, but not all of them have been clearly identified so far.

Aim: To assess prevalence of mitral regurgitation (MR) in CRT recipients and evaluate its significance for CRT response and clinical outcome.

Methods: a) Follow-up CRT recipients (male 76%, mean age 60.36±8.8 years, ischemic etiology 46.8%, mean left ventricle ejection fraction (EF) 24.3%±5.7) underwent standard echocardiography 1 day before the implantation and after 6 months. MR grade was quantified by effective regurgitant orifice area (EROA) as: mild (0–0.19), moderate (0.2-0.39) or severe (≥0.4) and measured as ≥0.2 in ischemic etiology recipients and ≥0.1 in non-ischemic etiology recipients. A reduction of at least one grade in its severity was defined as a CRT response. b) Among 197 patients who reached 6 months follow-up, 118 (59.8%) responded to CRT (responders vs non-responders: EF 34.85±8.12 vs 27.86±7.94 p=0.001, EROA 0.17±0.10 vs 0.11±0.10 p=0.001, persistent severe MR 4.27% vs 18.98% p=0.002).

Multivariate logistic regression showed, that MR improvement of at least one grade is one of the strongest predictors of CRT response (OR 4.09; ±95% CI 1.91–8.75 p=0.001), while others are right ventricle systolic pressure (RVPV) <50mmHg (OR 10.14; ±95% CI 2.53–40.6 p=0.0009), non-ischemic CHF etiology (OR 2.75; ±95% CI 1.37–5.50 p=0.003), transverse arch stenosity ≥60m (OR 2.35; ±95% CI 1.17–4.72 p=0.01), avoidance of digoxin uptake (OR 0.14; ±95% CI 0.03–0.67 p=0.01) and no history of hyperthyreosis (OR 0.27; ±95% CI 0.07–0.85 p=0.10).

5 year follow-up revealed, that CRT response comes with favourable clinical outcome: NYHA I or II class (58.4% vs 24.5% p=0.0001), lower rate of cardiovascular hospitalizations (36.5% vs 58% p=0.001), and all-cause (16.8% vs 48.5% p=0.000) as well as cardiovascular mortality (13.9% vs 36.7% p=0.0001).

Conclusion: Mitral regurgitation is a common finding in patients with chronic heart failure. As MR improvement is a strong predictor of reverse remodeling and CRT response, assessment of MR grade at baseline might be useful while selecting potential CRT recipients.

P3333 | BENCH Deletion of hypoxia-inducible factor 1 alpha in myeloid lineage exaggerates angiotensin ii-induced abdominal aortic aneurysm via downregulation of tissue inhibitor of metalloproteinase 1 (TIMP-1)
Y. Takahara, T. Tokunou, H. Kojima, Y. Hirooka, T. Ichiki. Kyoto University Graduate School of Medical Sciences, Cardiology, Fukuoka, Japan

Background: Hypoxia-inducible factor (HIF) 1α is a transcription factor that regulates various genes reacting hypoxic conditions. In atherosclerotic lesion, HIF-1α is thought to be regulating inflammatory responses. We previously reported that myeloid-specific activation of HIF1α had protective effects on hypertensive cardiac remodeling in mice. In this study, we investigated the role of HIF1α in myeloid lineage in the formation of abdominal aortic aneurysma (AAA).

Methods and results: Myeloid-specific HIF-1α knockout (MyHIFKO) mice were created using Cre-lox recombination system in the background of apolipoprotein E-deficient mice (ApoeKO). MyHIFKO (n=18) and control (n=11) mice were fed a high-fat diet (HFD) and infused with Angiotensin II (All 1800 ng/kg/min) by an osmotic pump for 4 weeks to promote AAA formation. The experiments and analysis were performed in an operator-blinded fashion regarding genotype of mice. Deletion of HIF1α increased AAA formation rate (94.4%, vs. 81.8% in control) and aortic diameter (2.47±0.21 mm, vs. 1.80±0.28 mm in control, p=0.037). Elastic lamina degradation grade determined by Elastica van Gieson staining was deteriorated in MyHIFKO mice (3.91±0.08, vs. 3.25±0.31 in control, p=0.013). The number of infiltrated macrophages into abdominal aorta was increased in MyHIFKO mice (565±110.3 cells/section, vs. 390±51.96 cells/section in control, p=0.031). Real-time PCR and gelatin zymography of the AAA tissue revealed that there were no significant difference in the expression level of matrix metalloproteinase (MMP)-2 and MMP-9 between control and MyHIFKO mice. mRNA expression level of metalloelastase in aortas was significantly lower in MyHIFKO mice (n=4) vs control (n=4) biopsies of AS patients after MACS isolation (CD31) and measured CILP transcript levels in the presence of TGF-β2 at 48h. CILP expression was very low to undetectable in baseline aortas, but it was significantly upregulated in MyHIFKO mice (18.98% p=0.002) compared to control mice (3.3% p<0.001).

Conclusion: HIF1α in myeloid lineage cells plays a protective role against AAA formation induced by All and a HFD in ApoeKO mice possibly through upregulation of TIMP-1.

P3334 | BENCH Deletion of hypoxia-inducible factor 1 alpha in myeloid lineage exacerbates angiotensin ii-induced abdominal aortic aneurysm via downregulation of tissue inhibitor of metalloproteinase 1 (TIMP-1). Deletion of hypoxia-inducible factor 1 alpha in myeloid lineage exacerbates angiotensin ii-induced abdominal aortic aneurysm via downregulation of tissue inhibitor of metalloproteinase 1 (TIMP-1)
**P3335 | BENCH**

**Absence of transforming growth factor-beta1 in murine platelets reduces neointima formation without affecting thrombosis**

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**Background:** Activation of platelets at sites of vascular injury results in the release of their granule contents, which may affect the vascular wound healing response to injury. Transforming growth factor (TGF)-β is a major component of platelet α-granules and also expressed by activated smooth muscle cells and macrophages. By binding to receptors expressed on cells within the vascular wall, TGF-β may act to promote smooth muscle cell (SMC) proliferation, myofibroblast transdifferentiation and fibrosis.

**Methods:** Mice with platelet-specific deletion of TGFβ1 were generated by crossing mice expressing Cre recombinase under the megakaryocyte-specific PF4 promoter with mice carrying floxed (fl/fl) TGFβ1 alleles. Arterial thrombosis and neointima formation were induced using the ferric chloride model.

**Results:** Whole blood count analysis revealed a normal platelet number and mean platelet volume, and examination of mice using the tail cut assay excluded major bleeding defects. Platelet releases of PF4.Cre tg x TGFβ1fl/fl (Plt.TGFβ-KO) mice contained lower amounts of total TGFβ1 (2.18±0.17 ng/million Plt.TGF-β-WT controls) compared to controls. TGFβ1 KO mice showed that targeting TGFβ1 produced by platelets resulted in a marked reduction in neointima formation, as shown by a lower neointima area (P<0.01), intima-to-media ratio (P<0.001) and lumen stenosis (P<0.001 in Plt.TGFβ-KO compared to Plt.TGFβ-WT mice). On the other hand, the media area (P>0.05) and total vessel area (P>0.05) were found to be increased in Plt.TGFβ-KO mice. Notably, medial SMCs in Plt.TGFβ-KO mice exhibited a de-differentiated phenotype and were highly positive for the mesenchymal markers fibroblast-specific protein 1 (FSP1) and actin, and low positive for the myoblast receptor–β, whereas the amount of α-smooth muscle actin-positive cells was found to be reduced. On the other hand, Sirius staining revealed similar amounts of interstitial collagen, and no differences in Mac2-immunopositive macrophages were detected between both genotypes.

**Conclusion:** Our findings demonstrate an essential role for platelet-derived TGFβ1 in chronic vascular remodelling processes involving SMCs and suggest that targeting TGFβ1 may improve postthrombotic wound healing without affecting haemostasis.

**BEST POSTERS IN DIAGNOSIS IN HEART FAILURE**

**P3338 | BEDSIDE**

**Discrimination of body mass index and dual X-ray absorptiometry in classification of adiposity status of men with chronic heart failure**

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**Introduction:** High adiposity is regarded as a key factor for morbidity and mortality worldwide. Body-mass index (BMI) has been regarded as the standard modality to define weight status. However, BMI is a measure of weight adjusted for height and does not measure body composition directly. Unfortunately, the index is an indirect surrogate of body fat, which is not able to distinguish lean body mass from fat mass. Dual-energy X-ray absorptiometry (DXA) is often recommended to be used as a gold standard for assessing body composition. In heart failure (HF) actual BMI is a net result of catabolic and anabolic processes with consequent changes in body composition, which may be highly variable. DXA can estimate adiposity with high accuracy.

**Aim:** We aimed at analyzing the discordance between BMI and DXA in assessing adiposity status in patients with chronic heart failure.

**Material and methods:** We enrolled 675 men (Age 54±8 years; LVEF 25±5%; ischemic etiology 58%) with stable, eudema-free HF (NYHA class < IV) treated according to current guidelines. In each patient we calculated BMI, measured body composition by DXA and classified them into adiposity categories defined by BMI as underweight (<18.5), normal (18.5–25.9), overweight (26.0–29.9) and obese (>30.0), and percentage of body fat (%BF) as normal adiposity (%BF<25%) and obesity (%BF>25%). We calculated rates of misclassifications to adiposity categories according BMI and %BF.

**Results:** Median BMI was 26.3 and median %BF was 27.8. There was a strong positive correlation between %BF and weight (Spearman R = 0.57; P<0.001) and between BMI and %BF (Spearman R = 0.62; P<0.01). Nevertheless, we observed a high rate of misclassification of adiposity status according to BMI and DXA, especially in the normal weight and obesity subgroups. BMI tended to overclassify patients as normal weight and underclassify patients as obese compared to DXA. Figure 1 demonstrates the magnitude of discordance in the classification of adiposity status by BMI and %BF. ROC curve analysis identified a cut-off value for BMI of ≤27.2 for the best prediction of obesity defined by %BF. Multivariate logistic regression identified independent predictors of underestimation of adiposity status by BMI: total lean mass (per 100 g increment) OR 1.19 95% CI: 1.07–1.31; LVEF (per 1%) OR 1.39 95% CI: 1.25–1.55; and sodium level (per 1 mmol/L increment) OR 1.04 95% CI: 1.00–1.07; and oxygen level (per 1 mmol/L increment) OR 1.31 95% CI: 1.17–1.47.

**Conclusions:** The accuracy of BMI in predicting adiposity status by %BF in HF is poor. The spectrum of independent predictors for under- and overestimation of adiposity by BMI suggests the possible contribution of HF pathophysiology-related factors.
The use of lung ultrasound in addition to physical examination during outpatient visit reduces the hospitalizations for acute decompensated heart failure in chronic heart failure patients.

**Methods:** This is a multicenter prospective randomized study. Chronic HF patients were enrolled according to the following criteria: (1) History of HF for at least 6 months, (2) Left ventricular ejection fraction <45% measured by transthoracic echocardiography, (3) Optimal medical therapy for HF for at least 2 months. Patients were randomized in two groups: group A, patients undergoing LUS; and group B, patients undergoing only physical examination. Diuretic therapy was modified according to the presence and severity of B-lines in group A and physical examination in group B. The ultrasound examination was performed by a trained echocardiography. Patients were evaluated at baseline and after 3 months of follow-up. The primary end-point was a significant reduction of hospitalizations for acute decompensated heart failure (ADHF) in group A during follow-up period. Secondary endpoints included changes of NT-proBNP values and quality of life (QLT) scores and cardiac mortality.

**Results:** We enrolled 144 patients (mean age 75.2±11.6 years, 96 males): 75 in group A and 69 in group B. The hospitalization rate for ADHF in group B during 3 months was 12% in group A and 26% in group B (OR: 2.1; 95% CI: 1.04–4.5; p=0.03). In group A, the NT-proBNP value was reduced after 3 months (2859.57±3429.12 pg/ml vs. 1849.21±2837.77 pg/ml; p=0.01), while in group B there was a non-significant increase (2454.37±2499.38 pg/ml vs. 2531.67±3153.48 pg/ml; p=0.8). No differences in mortality rate was observed between the two groups after 3 months (2.6% in group A vs. 2.6% in group B; OR: 1.0; 95% CI: 0.15–7.5; p=0.9). The NYHA class improved significantly in group A (2.38±0.56 vs 2.21±0.47; p=0.04), whereas it was unchanged in group B (2.27±0.59 vs 2.38±0.62; p=0.09).

**Conclusions:** The identification of B-lines by LUS is a useful tool in addition to physical examination for the outpatient management of chronic HF patients. This approach can potentially aid the physician in optimizing diuretic therapy and consequently reducing the rate of hospitalizations for ADHF.
the method of Kaplan–Meier. Multivariate Cox regression was applied to study the association of (complete) CR with mortality, adjusted for baseline characteristics.

Results: Mean age was 58.8 years and 77% were men. Propensity matching was successful, as there were no differences in clinical characteristics between CR participants and controls. During a median (25th - 75th percentile) follow-up of 10 years (range 4–12) a total of 335 patients had died. Throughout the entire follow-up period, mortality was lowest in patients who completed CR (figure). Patients with complete CR had 47% lower mortality than non-CR controls (10-year mortality 13.6% vs. 23.5%, adjusted hazard ratio [aHR] 0.53 and 95% confidence interval [CI] 0.42–0.68), whereas patients with incomplete CR had 25% lower mortality (10-year mortality 18.9%; aHR 0.75; 95% CI 0.52–1.78).

Conclusions: Patients who underwent pPCI for MI, and who participated in a CR program had lower mortality then their non-CR counterparts. Mortality was particularly low in patients who completed the program.

P3344 | BEDSIDE
Challenges and opportunities for cardiac rehabilitation: a meta-analysis of hard outcomes from recent randomised trials 2010-2015
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Background: Meta-analyses of cardiac rehabilitation trials up to 2010 showed a significant reduction in all-cause mortality but many of these trials were conducted before the modern management of acute coronary syndromes.

Purpose: We undertook a meta-analysis of contemporary randomised controlled trials published in the period 2010 to 2015, including patients with other forms of atherosclerotic cardiovascular disease, to investigate the impact of secondary prevention and exercise rehabilitation on all hard outcomes including survival.

Methods: Medline and Embase were searched using the same search strategy as the most recent Cochrane analysis for cardiac rehabilitation.

Results: 18 trials randomising 7,691 patients to secondary prevention and rehabilitation or usual care were selected. All-cause mortality was not reduced (RR 1.00, 95% CI 0.88 to 1.14), but cardiovascular mortality was by 58% (95% CI 0.21, 0.88). Myocardial infarction was also reduced by 30% (95% CI 0.54, 0.91) and cerebrovascular events by 60% (95% CI 0.52, 0.74). The number needed to treat was 45 for MI and 82 for cerebrovascular events. Comprehensive programmes managing six or more risk factors reduced all-cause mortality in a subgroup analysis (RR 0.63, 95% CI 0.43, 0.93) but those managing less did not.

In the three programmes that prescribed and monitored cardioprotective medications for blood pressure and lipids all-cause mortality was also reduced (RR 0.35, 95% CI 0.18, 0.70).

Conclusions: The challenge for cardiac rehabilitation is that all-cause mortality is no longer reduced in the era of acute revascularisation and cardioprotective medications. However, cardiovascular mortality, MI, and for the first time, cerebrovascular events, were all reduced across a broader spectrum of patients with coronary and other atherosclerotic disease. Only comprehensive programmes managing six or more risk factors, and those prescribing and monitoring medications within the programme to lower blood pressure and lipids, were effective in reducing all-cause mortality. Cardiac rehabilitation should take the opportunity to evolve into truly comprehensive programmes addressing all aspects of lifestyle, risk factor management and adherence with cardioprotective medications in order to reduce cardiovascular deaths and events, including stroke, and also increase the quality of life.

Acknowledgement/Funding: Dutch Heart Foundation

P3345 | BEDSIDE
The prognostic effect of cardiac rehabilitation in the era of acute revascularisation and statin utilization: the cardiac rehabilitation outcome study (CROS)
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Background: Despite having over sixty clinical trials and numerous meta-analyses the prognostic effect of multi-component cardiac rehabilitation (CR), in the modern era, remains a matter of debate. The purpose of this systematic review and meta-analysis was to evaluate the effect of strictly defined CR on total mortality specifically in patients with coronary artery disease (CAD) in the era of statins and acute coronary revascularization.

Methods: Randomized controlled trials (RCT) and controlled retrospective and prospective cohort studies (rCSS, pCSS) evaluating CR in patients either after an acute coronary syndrome (ACS), coronary artery bypass grafting (CABG) or in a mixed population with the index event ≥1995 and a follow-up of at least 6 months were included. Databases used were PubMed, Embase, Cochrane Central, CIAHL, LILACS, CIRIEC, and ICTRP without language restriction, and searches were performed from ≥1995 until December 22nd, 2015. CR was defined as a structured, exercise based multi-component programme including supervised exercise training at least twice a week plus components like education, motivation and psychosocial support. Statistical analyses were done separately with regard to study designs and predefined populations.

Results: 25 studies were identified (RCT n=1; pCSS n=7; rCSS n=17) including 219,702 participants (ACS: n=46,338 CABG: n=14,583, mixed population: n=158,781; male: 74.9%; mean age: 60.8 years, mean follow up: 40.35 months), and total mortality was evaluated in 23 studies. Apart from different designs the studies showed heterogeneity in biometrical assessment of results and potential confounders. CCS evaluating ACS patients showed a significantly reduced mortality for CR-participants [pCCS (HR 0.37, 95% CI 0.20–0.69), rCCS (HR 0.64, 95% CI 0.49–0.93)] and CABG patients [pCCS (HR 0.28, 95% CI 0.15–0.52), rCCS (HR 0.67, 95% CI 0.53–0.83)]. The only RCT included showed a neutral result [HR 1.01; 95% CI 0.85–1.21]. Participation in CR was also associated with a reduced mortality in the CABG [CCS (HR 0.13; 95% CI 0.03–0.72), rCCS (HR 0.63; 95% CI 0.55–0.73), and the mixed CAD population [pCCS (HR 0.57; 95% CI 0.48–0.72), rCCS (HR 0.65; 95% CI 0.54–0.75) and OR 0.57; 95% CI 0.28–1.18].

Conclusions: Using data from the modern era of CAD treatment and applying quality methods to study inclusion we conclude that exercise based multi-component CR is strongly associated with reduced total mortality. The lack of RCTs in the CROS study, compared to previous meta-analyses, is a consequence of our CAD-ACS focus and strict criteria about the timing and content of CR. Heterogeneity of the evaluated studies highlight the need of further investigations and minimal standards in performing and presenting CR outcome studies in future.

Acknowledgement/Funding: Grants from German Heart Foundation, German Society of Prevention & Cardiac Rehabilitation, Pfizer Switzerland

P3346 | BEDSIDE
The prognostic significance of improvement in exercise capacity in heart failure patients who participate in cardiac rehabilitation program A. Sabbag, I. Mazin, D. Rott, I. Hay, N. Gang, B. Tzur, I. Goldenberg, A. Israel, R. Klempfer. Sheba Medical Center, Heart Institute, Ramat Gan, Israel

Introduction: Cardiac rehabilitation (CR) was shown to reduce morbidity and mortality in several patient populations, including heart failure (HF) patients. However, there are limited contemporary data regarding the association between improvement in cardiovascular fitness in HF patients who participate in a CR program and the risk for subsequent hospitalizations.

Methods: The present study population comprised 409 patients with HF that participated in our CR program between the years 2000–2015. All were evaluated by a standard exercise stress test (EST) before initiation, and underwent a second EST upon completion at least 3 months of training. Participants were dichotomized according to fitness level at baseline, according to percent of pre-
dicted age and sex norms achieved. Each group was further divided according to its degree of functional improvement, between the baseline and the follow-up EST test. Major improvement was defined as improvement above median value in each group. The combined primary end point was all-cause hospitalization or all-cause mortality.

Results: A total of 205 (50%) had low baseline fitness (<75% for age and sex predicted value). Compared to patients with higher fitness, those with a low baseline fitness were more commonly smokers, hypertensive, diabetic and obese (p-value <0.05 for all). The median improvement in fitness between the stress tests was significantly higher in patients with low baseline fitness (21.7% vs. 3.5%, p <0.001). The cumulative survival free of the primary endpoint at 2.5 years was highest in patients with high baseline fitness and a major improvement, intermediate in patients with high baseline fitness and minor improvement or low baseline fitness with a major improvement, and lowest in patients with poor baseline fitness and minor improvement in follow up (log rank p-value <0.001, Figure). Multivariate Cox proportional hazard regression analysis showed that independently of baseline capacity, age, and other established predictors of clinical outcomes, improvement of 1% of predicted fitness was associated with a 1.1% decreased risk for the primary endpoint (HR 0.988, p =0.001, 95% CI [0.982–0.994]).

Conclusion: In heart failure patients participating in CR program, Improvement in cardiovascular fitness is associated with reduced risk of mortality or hospitalization during long-term follow-up, independently of baseline fitness.

BEST POSTERS IN CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION

P3348 | BEDSIDE
Pulmonary artery denervation for improving outcome in patients with residual pulmonary hypertension after pulmonary thromboendarterectomy: early experience
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Aim: To evaluate safety and efficacy of pulmonary artery radiofrequency denervation (PADN) for pulmonary artery (PA) pressure decrease in patients with residual pulmonary hypertension after pulmonary thromboendarterectomy. Methods: PADN was performed in 14 patients with residual pulmonary hypertension after pulmonary thromboendarterectomy. Indication for PADN was mean PA pressure level >25 mm Hg with absence of proximal PA lesion according to CT scan. For PADN efficacy assessment with V/Q-scanning, echocardiography, right heart catheterization and 6-minute walking distance test were performed. During preoperative evaluation subsegmental PA perfusion defects were revealed in all patients. PADN was performed using nonfluorescent 3-D navigation system with standard catheter for radiofrequency ablation. Swan-Ganz catheter was used for intraoperative hemodynamic measurements. All patients were followed up during 30 days after procedure.

Results: There were no complications or death during the procedure and before discharge. Mean procedure time was 105 [93; 120] min. After PADN the mean PA pressure decreased from 37.3 mm Hg [29; 38] to 24.6 [17; 30] mm Hg (p=0.011) and pulmonary vascular resistance from 672 [387; 556] dyn sec cm⁻⁵ to 386 [153; 449] dyn sec cm⁻⁵ (p=0.017). There were no significant increase of cardiac output and 6-minute walking distance test compared to baseline data (3.4 [3.2; 3.4] l/min vs 3.5 [3.2; 4.0] l/min; p=0.412 and 427 meters [352; 510] vs 447 m [370; 525]; p=0.161, respectively). All patients noticed reduction of dyspnea and improving exercise tolerance.

Conclusion: Our initial experience demonstrated that PADN in patients with residual pulmonary hypertension after pulmonary thromboendarterectomy is safe and effective it terms of pulmonary PA decrease. Long-term follow up and further studies are needed to assess the role of PADN in the treatment of these category of patients.

P3349 | BEDSIDE
Optical frequency domain imaging has a potential to refine balloon pulmonary angioplasty procedure for the patients with chronic thromboembolic pulmonary hypertension
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Background: Balloon pulmonary angioplasty (BPA) in patients with chronic thromboembolic pulmonary hypertension (CTEPH) is an emerging therapy. High-resolution imaging is useful to visualize the complex structures of the pulmonary arteries of CTEPH. The use of intravascular ultrasound (IVUS) during BPA has resulted complications. Optical frequency domain imaging (OFDI) has been suggested to be a promising alternative to IVUS for the visualization of coronary arteries.

Purpose: The aim of this study is to evaluate quality of OFDI images and safety of OFDI guided BPA.

Methods: Consecutive 193 OFDI pull back of pulmonary arteries were evaluated and stratified to "Fair", "Possible" and "Poor" by experienced interventionalists. All complications related with BPA procedures in consecutive 279 lesions (OFDI guided 176 lesions and IVUS guided 103 lesions) were recorded. The risk of complications was compared between OFDI guided BPA and IVUS guided BPA.

Results: Qualities of obtained OFDI images were Fair 48%, Possible 31% and Poor 21% (Figure). Obtained OFDI images were obviously high-resolution compared to IVUS images. Angiography and computed tomographies revealed 27 pulmonary bleedings (include micro wire perforation) and 10 pulmonary artery dissections. There was no significant difference in occurrence of complications between OFDI guided and IVUS guided BPA (10% vs. 17%, p=0.13).

Conclusions: OFDI system provided usable high resolution images to BPA in 79% of lesions. The safety of OFDI guided BPA was similar to IVUS guided BPA. OFDI has a potential to refine BPA procedures.

P3350 | BEDSIDE
Changing of the balloon pulmonary angioplasty strategy resulted in reduced complication ratio and mortality
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Purpose: The purpose of this study was to assess safety and benefits of refined pulmonary angioplasty procedure for the patients with chronic pulmonary hypertension (CTEPH).

Methods: We qualified into BPA program only patients diagnosed with CTEPH, who were disqualified from pulmonary endarterectomy (PEA). From June 2013 to January 2016 a 107 procedures of BPA have been performed in 37 patients (aged 64±14; 19 females) with very severe baseline haemodynamic (mPAP: ≥55±10 mmHg) and functional capacity (NYHA 4–31%; NYHA 3–69%). The first 49 (group A) procedures were focused on recanalization of chronic occlusions, aggressive wiring and anticoagulation. The strategy of another consecutive 58 (group B) procedures was focused on using reduced tip load microguidewires, dilatation mainly lesions of types “webs” and “rings” and less aggressive anticoagulation in perioperative period. For each patient, a right heart catheterization (RHC) was performed directly before and after each BPA procedure. Overall re-
sults from RHC performed at baseline and after at least 3rd BPA are presented. Baseline and follow-up functional capacity (NYHA class) was analysed. Complications were noticed during the in-hospital stay in every patient.

Results: Table 1 presents reduction in mortality and complication ratio in group B vs. group A. Significant reduction of PVR (10.9±4.1 vs 6.1±2.5 Wood units; p<0.001) and (52±10 mm Hg vs 40±8 mm Hg; p=0.001) and improvement of NYHA functional class (54% pts; p<0.005, Wilcoxon test) was observed in patients undergoing at least 3 BPA.

Conclusions: Changing of BPA strategy reduces mortality and the impact of complications. BPA provides significant improvement of functional NYHA class and hemodynamics.

P3351 | BEDSIDE
Importance of Angiopoietin-2 (Ang-2) for the transition from acute pulmonary embolism (PE) to chronic thromboembolic pulmonary hypertension (CTEPH)
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Background: Incomplete thrombus resolution followed by vascular remodeling is considered the critical mechanism for the development of CTEPH after acute PE. Predictors suggest that Ang-2, an antagonist of the Tie2 receptor, may lead to dysregulated thrombus resolution. Own previous data demonstrated that in patients with acute PE plasma concentrations of Ang-2 ≥5.5 ng/ml on admission were associated with a 93-fold elevated risk for the diagnosis of CTEPH during follow-up. Therefore, we aim to investigate the role of Ang-2 in patients with CTEPH.

Results: First, we studied 57 patients (47.8% women; median age, 65 [IQR, 40–73] years) with confirmed CTEPH scheduled for pulmonary endarterectomy (PEA) (median pulmonary capillary wedge pressure [PCWP], 10.0 [9.6–13.0] mmHg; median pulmonary arterial pressure [mPAP], 43.0 [33–55] mmHg; pulmonary vascular resistance [PVR] 6.0 [4.4–10.5] WU) at an international large referral center for CTEPH surgery. Ang-2 plasma levels (median, 3.6 [2.1–7.6] ng/ml) correlated with haemodynamic status and parameters indicating RV dysfunction (mPAP [r=0.60; p=0.001] and mPAP [r=0.47; p=0.002]). Of note, Ang-2 plasma levels in CTEPH patients were higher compared to patients with acute PE (median, 2.5 [1.6–4.4] ng/ml) and a healthy reference population (median, 1.8 [1.1–3.4] ng/ml).

Second, CTEPH tissue specimens obtained during PEA were histomorphologically classified as fresh thrombus, early- and late-organized thrombus, myofibroblast-rich or vessel-rich regions, and fibrosis. Quantitative analyses showed Ang-2 positive cells in all areas of interest, with pronounced Ang-2 presence in early-organized thrombi (median, 5.3 [2.6–6.1] %), late-organized thrombi (median, 7.7 [4.4–10.3] %) and vessel-rich regions (median, 7.5 [3.4–11.8] %), as opposed to fresh thrombi (median, 0.6 [0.2–1.5] %) and fibrosis (median, 1.4 [0.5–2.7] %; p<0.05 each).

Finally, cells involved in the Ang-Tie2 pathway were immunohistologically detected and quantitative analyses demonstrated phosphorylated Tie2 receptor and VEGF in all areas, especially in late-organized thrombi (median, 2.6 [1.7–4.3] % and 2.4 [1.2–6.5] %) and vessel-rich regions (median, 3.4 [1.6–4.3] % and 2.6 [1.5–4.4] %), in contrast to early-organized thrombi (median, 0.2 [0.1–0.3] % and 0.6 [0.0–1.1] %), fresh-thrombi (median, 0.1 [0.1–6.4] % and 0.2 [0.1–0.3] %), myofibroblast-rich regions (median, 0.0 [0.0–0.3] % and 0.4 [0.1–1.0] %) and fibrosis (median, 0.2 [0.0–0.5] % and 0.4 [0.1–1.9] %; p<0.05 each).

Conclusion: Circulating Ang-2 is associated with right ventricular compromise in patients with CTEPH. Moreover, the analysis of CTEPH tissue specimens illustrated a potential role for Ang-2 in early stages of thrombus resolution as well as scarlessly available angiogenic activity at myofibroblast and fibrotic areas, supporting the hypothesis that defective angiogenesis is a key mechanism of misguided thrombus resolution and contributes the transition from PE to CTEPH.

Acknowledgement/Funding: German Federal Ministry of Education and Research (BMBF 01EO1003 and BMBF 01EO1503)

P3353 | BEDSIDE
Treatment strategy and long-term outcomes of patients with prior stroke presenting with non-ST-segment elevation acute coronary syndromes
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Introduction: Atherosclerosis in peripheral arteries is an independent risk factor of coronary artery disease development. However, data for management and long-term outcomes in patients with Prior Stroke (PS) and Non-ST-segment Elevation Acute Coronary Syndromes (NSTEMI-ACS) are limited.

Aim: The aim of the present study was to evaluate the effect of history of PS in patients presenting with NSTEMI-ACS on treatment strategy and 12-month prognosis, and influence of the invasive treatment (PCI) on long-term outcomes in PS group.

Methods: Single-center data of consecutive 2,355 patients hospitalized for NSTEMI-ACS between 2006 and 2012 were included. Patients were divided into two groups according to a history of PS. The comparison of the two groups was performed for Composite Endpoint defined as (1) All-cause Death, (2) Non-fatal Myocardial Infarction (MI) and (3) ACS-driven Revascularization during 12-month observation period. The post-hospitalization data, available for 99.8% of the included patients, were obtained from the official National Health Fund records.

Results: PS occurred in 124 patients (5.3%) of study population. There were significant differences in the baseline characteristics between both analyzed groups, inter alia patients with PS was older (69.1±10.8 vs 64.4±10.0 years; P<0.0001) and with higher risk in GRACE score (118.6±28.6 vs 108.1±28.7 points; P=0.0003). The percentage of PCI was 66.1% in PS, and 77.0% in non-PS group. After adjusting for both baseline and angiographic characteristics, PS reduced the likelihood of PCI (odds ratio [OR]: 0.53; 95% confidence interval [CI]: 0.31:0.92; P=0.022). At 12 month, PS was independently associated with higher rates of Composite Endpoint (30.6 vs 19.9%; HR: 1.50; 95% CI: 1.09,2.07; P=0.012), which was mainly driven by higher percentage of All-cause Mortality (17.7 vs 7.7%; HR: 1.59; 95% CI: 1.01,2.31; P=0.0198).

Conclusion: PS is an independent factor of worse long-term prognosis. PS group is less often treated with PCI irrespective of angiographic status. Moreover, in this population PCI in acute phase is not associated independently with 12-month prognosis.

P3354 | BEDSIDE
Impact of central sleep apnea on infarct size and changes of left ventricular systolic function in patients with acute myocardial infarction
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Background: Adverse effects of central sleep apnea (CSA) are characterized by frequent hypoxia and reoxygenation and increased sympathetic nerve activity. The purpose of this study was to evaluate the effect of CSA on infarct size and changes of left ventricular systolic function in patients with acute myocardial infarction (STEMI).

Methods: This study included 313 patients with STEMI who underwent primary percutaneous coronary intervention (PCI) within 12 h of symptom onset. Infarct size was estimated from the peak creatine kinase (CK) level. Changes in LV ejection fraction (LVEF) and LV end-diastolic volume index (LVEDVI) were measured using left ventriculograms immediately after PCI and after 12 days. All patients were treated with PCI irrespective of angiographic status before discharge. CSA was defined as apnea–hypopnea index (AHI) of ≥ 15 events/h with central-type dominance.

Results: Fifty patients fulfilled CSA criteria. Peak CK level was higher in patients with CSA than in control patients (2673 [1189–6081] IU/L vs. 1777 [841–4084] IU/L; P<0.002). Predictors for peak CK and delta LVEF

Peak CK

Dependent variable

Predictors for peak CK and delta LVEF

Best Poster in Treatment of Multimorbid Acute Coronary Syndrome Patients

BEST POSTERS IN TREATMENT OF MULTIMORBID ACUTE CORONARY SYNDROME PATIENTS
SHyper during STEMI attack was associated with a greater degree of myocardial injury. SHyper may be a stress response to STEMI. Further studies need to be conducted to verify the specific mechanisms of this response, also to understand whether SHyper reflects a protective change or a maladaptive process during ischemic stress.

P3355 | BEDSIDE
Effect of body mass index on bleeding and long-term mortality in patients admitted for primary percutaneous coronary intervention


Background: Prior studies reported more favorable clinical outcome in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention (PCI) and high body mass index (BMI).

Methods: 4441 patients from the years 2009–2013 of an electronic, prospective primary PCI-registry of a high volume catheterization laboratory were included in the study. The BMI, patient’s age, sex, body mass index, glucose, lipid, medical therapy, and angiography data were collected. Association between SHyper during STEMI attack and the degree of myocardial injury was assessed. Thyroid hormone tests were finished within 24 hours after admission. Association between SHyper and bleeding in the lowest BMI quartile (n=326). Bleeding rates were inversely proportional to BMI, with the highest rate of bleeding in the lowest BMI quartile (in Q1 8.9%, in Q2 7.5%, in Q3 7.4% and in Q4 5.6%; p<0.03). When adjusted for other known bleeding predictors including age, sex, renal failure and left ventricular dysfunction BMI remained independently associated with BARC ≥ 2 bleeding (p=0.04).

Conclusions: The present study has shown that the incidence of bleeding in the lowest BMI quartile is higher compared to the other BMI quartiles. The interaction of BMI with SHyper was not a significant predictor of bleeding in that patient subset.

P3356 | BEDSIDE
Subclinical hyperthyroidism indicates the greater degree of myocardial injury in STEMI patients

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Background: Critical illness like ST elevation myocardial infarction (STEMI) is often associated with thyroid hormonal abnormalities. The association between subclinical hyperthyroidism (SHyper) and coronary heart diseases has been observed in several studies. However, very few studies have focused on the STEMI population. The aim of this study was to evaluate the potential association between SHyper during STEMI attack and the degree of myocardial injury.

Methods: A total of 391 STEMI patients without previous intrinsic thyroid diseases admitted within 12 hours of symptom onset were enrolled. All patients underwent primary percutaneous coronary intervention. The baseline characteristics, including clinical and laboratory parameters were collected retrospectively. The peak values of thyroid stimulating hormone (TSH) and high-sensitivity C-reactive protein (hsCRP), after adjusting for CK-MB or cTnI.

Results: Of the 391 patients, 14.1% had high-sensitivity C-reactive protein (hsCRP) levels >2 mg/L. TSH and hsCRP, after adjusting for CK-MB or cTnI (r = 0.3, p<0.001), cTnI (r = –0.3, P = 0.001), and hsCRP (r = –0.18, P = 0.005). After adjusting for hsCRP, TSH, and cTnI, the association was not statistically significant between these two groups. Furthermore, TSH showed significantly negative correlations with CK-MB (r = 0.34, p<0.001) in women with STEMI. TSH levels were significantly higher in women with STEMI (p<0.05) and were associated with a greater degree of myocardial injury. SHyper may be a stress response to STEMI. Further studies need to be conducted to verify the specific mechanisms of this response, also to understand whether SHyper reflects a protective change or a maladaptive process during ischemic stress.
out significant differences between males and females (C-index 0.93 vs 0.87 respectively, p=NS).

FEMALE PATIENTS

MALE PATIENTS

Conclusion: Dobutamine stress contrast echo is a strong predictor of end points in women with known or suspected CAD, regardless patient gender. This makes DSCE an attractive screening option for women, in whom CAD assessment can be challenging.

P3359 | BEDSIDE
Impact of negative inotropic drugs on echocardiographic evaluation of left ventricular filling pressure in patients with normal left ventricular ejection fraction during exercise stress test

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Background: The ratio of early diastolic transmitral flow velocity to tissue Doppler mitral annular early diastolic velocity, E/e’, and left ventricular end-diastolic pressure (LVEDP) have been shown to be correlated. Use of positive inotropic drugs has recently been shown to impair this correlation and data concerning the influence of a physiological exercise stress on this correlation are scarce. We investigated the impact of negative inotropic drugs (NID) on the accuracy of E/e’ ratio as a surrogate for LVEDP in patients with normal LV ejection fraction (LVEF) before and after a low-charge exercise test.

Methods and results: A 50 watts exercise cardiac invasive hemodynamic monitoring and a 50 watts exercise echocardiographic examination were collected prospectively within the same day from 60 patients (77% male, 62±9.8 years) with normal LVEF and no history of cardiac failure. Before exercise, these patients had scattered LVEDP (13.7±5.7 mmHg) and septal E/e’ (8.8±2.9). Half of the remnant were on NID: 29 on beta-blocker and one on verapamil. The correlation between septal E/e’ and LVEDP was moderate for examinations performed at rest (r=0.35, p=0.01) with no significant impact of NID use. For examinations performed at 50 Watts, presence of NID had a significant impact on the association of septal E/e’50watts and LVEDP50watts (r=0.28, p=0.03, ANCOVA analysis).

P3360 | BEDSIDE
Exercise-induced pulmonary hypertension affects exercise capacity in patients with hypertrophic cardiomyopathy

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Background: Exercise-induced pulmonary hypertension (PH) has been suggested as an early and clinically relevant phase of PH and may attribute to poor prognosis. Clinical outcome of exercise-induced PH in patients with hypertrophic cardiomyopathy (HCM) remains unclear. Here, this study aimed to clarify our hypothesis whether the indices during exercise assessed by exercise echocardiography would be associated with exercise capacity in patients with HCM.

Methods: This study included sixty-five patients with HCM who underwent symptom-limited exercise echocardiography with supine bicycle. Conventional echocardiographic parameters, including systolic pulmonary artery pressure (SPAP), were recorded at rest and during exercise. The symptom-limited cardiopulmonary exercise testing using a cycle ergometer was also performed for the measurement of peak oxygen consumption (peak VO2).

Results: No significant correlations were found between the resting echocardiographic parameters, including SPAP at rest and peak VO2, although, SPAP during exercise was well correlated with peak VO2 (r=0.53, p<0.05). Based on the exercise capacity, all patients were stratified into the Group 1 (maintained exercise capacity, % predicted peak VO2 >80%, n=29, 46.2%) or Group 2 (reduced exercise capacity, % predicted peak VO2 <80%, n=36, 70.8%). No differences in left ventricular volume, ejection fraction or mass were found between the two groups; however, Group 2 revealed higher SPAP during exercise (56.3±12.3 vs. 47.8±14.7 mmHg, p<0.05) and greater left atrial dimension (41.2±4.8 vs. 38.1±1.7 mm, p<0.05) than Group 1. The multivariate analysis demonstrated that SPAP during exercise was an independent predictor of peak VO2 (odds ratio 1.05, 95% confidence interval 1.01–1.10; p=0.05). The receiver operating characteristic analysis indicated that SPAP during exercise with the cut-off value of ≥53.8 mmHg, could predict reduced exercise capacity with sensitivity of 69.7% and specificity of 67.8% (Figure).

Conclusions: SPAP during exercise was independently associated with exercise capacity. Exercise echocardiography may be helpful to understand the mechanism of reduced exercise capacity in patients with HCM.

P3361 | BEDSIDE
Exercise echocardiography results and outcome in patients with suspicion of heart failure with preserved ejection fraction

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The role of exercise echocardiography (ExE) for the assessment of patients with suspected heart failure with preserved ejection fraction (HFrEF) is promising.
We aimed to review the clinical characteristics and outcome of patients with this condition referred for ExE to our center.

**Methods:** Consecutive patients referred for evaluation of dyspnea from outcients were considered. After exclusion of those with myocardiopathies, moderate or severe valvulopathies, congenital heart disease, and LV systolic dysfunction as defined by a LV ejection fraction ≤ 45%, 420 patients were included. Mitral regurgitation, the ratio of early LV inflow wave to early diastolic annulus wave (E/e’), and wall motion abnormalities (WMAs) were measured, both at rest and at exercise. An E/e’ value >13 was considered abnormal. Functional capacity was assessed by testing the better of two, achieved predicted Metabolic Equivalents (METs) estimated by age and sex. Ischemia was defined as the development of new or worsening WMAs with exercise.

**Results:** Mean age was 66±12 years and 243 patients (58%) were women. Ischemia was present in 79 patients (19%), whereas WMAs were already present at rest in 44 patients (10.5%). Mean achieved METs were 8.2±2.8. A percent achieved of predicted METs > 100% was found for most of the patients (69%). Also, most patients had normal E/e’ values at rest and at exercise (n=275, 66%), whereas elevated values in both conditions were seen in 62 (15%). In 40 patients (10%) E/e’ values increased exclusively with exercise, and in 38 (9%) increased E/e’ values were observed only at rest. The worse survival was seen in patients with increased E/e’ values in both conditions (85.5%), in comparison with patients with increased E/e’ values only at rest (95%), only at exercise (97.4%), or without increase (98.2%, Log Rank test =14.9, p=0.002). During follow-up of 1.15±1.69 years, 17 patients died (annualized mortality rate 3.5%). Independent predictors of overall mortality were age (Hazard Ratio [HR]=1.07, 95% Confidence Interval [CI]=1.01–1.14, p=0.03), male gender (HR = 6.74, 95% CI: 2.02–22.02, p=0.002), and E/e’ value at rest (HR=1.05, 95% CI: 1.03–1.08), and presence of resting WMAs (HR= 4.21, 95% CI: 1.45–12.22, p=0.008).

**Conclusions:** Despite of favorable ExE results, overall mortality remains high among patients with suspicious of HFpEF referred for ExE.

P3362 | BEDSIDE

Rest and stress coronary diastolic perfusion time in patients with stable coronary artery disease treated with ivabradine or carvedilol: new insights into their mechanism of actions

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**Background:** We have already demonstrated that ivabradine has a better effect in improving coronary flow velocity reserve (CFVR) compared with bisoprolol, in patients with stable coronary artery disease (CAD), despite a similar heart rate reduction. It is clear that also diastolic coronary perfusion time mainly affects subendocardial blood flow. The aim of the study was to compare, for the first time in humans, differences between ivabradine and carvedilol on coronary diastolic perfusion time, assessed by transthoracic Doppler echocardiography, both at rest and after stress tests, in patients with stable CAD.

**Methods:** 78 patients (48 M, 30 F; mean age 72±7 years) with stable CAD were enrolled in the study. Then baseline data were collected and all patients underwent stress echocardiography, using dipyrindamole (0.4 mg/kg). Coronary flow was assessed in the left anterior descending coronary artery (LAD). Coronary diastolic perfusion time (CDPT) and diastolic perfusion time to RR interval ratio (CDPT/RR) were calculated at baseline and after stress test. CFVR were determined as the ratio of hyperemic to baseline diastolic peak coronary flow velocity. Patients were randomly assigned to carvedilol and ivabradine for one month (after titration phase). Stress echocardiography was performed again at the end of treatment period.

**Results:** There were no significant differences in baseline characteristics between ivabradine and carvedilol group. CFVR was successfully performed in all patients. At baseline, both CDPT and CDPT/RR significantly increased after therapy with carvedilol (486.4±52.1 ms vs. 411.3±49.3 ms; p=0.006 vs. 0.49±0.05 - p=0.01) and with ivabradine (541.1±62 ms vs. 408.6±50.3; p=0.003 vs 0.48±0.02 - p=0.01), but they were significantly higher in ivabradine group, despite a similar lowering of heart rate. After stress echocardiography, CFVR reduced in both carvedilol and ivabradine group, but it remained significantly higher in ivabradine group (446.5±57 ms vs. 415.2±49.5 - p=0.01). CDPT/RR increased to a greater extent in ivabradine group, compared with carvedilol (0.62±0.05 vs 0.57±0.03 - p=0.01). CFVR increased in both groups but it was significantly better in ivabradine group compared with carvedilol group (3.44±0.41 vs. 3.15±0.55 - p=0.01).

**Conclusions:** Ivabradine is able to improve coronary flow, by increasing coronary perfusion time, better than carvedilol, in patients with stable CAD. This effect occurs both at rest and after stress test, with a mechanism that is at least partially independent from heart rate reduction. Our data also confirm a significant improvement in CFVR with ivabradine, compared with beta-blockers. These data show that ivabradine has a different effect on pathophysiology of coronary circulation, compared with beta-blockers.

P3363 | BEDSIDE

Prognostic usefulness of stress echocardiography in patients with left bundle branch block and impact of contrast use on stress echocardiography in improving prediction of outcome

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**Introduction:** Stress echocardiography (SE) is a useful tool for the non-invasive diagnosis of ischaemic heart disease (IHD) and the determination of patients’ prognosis. However in left bundle branch block (LBBB) the SE interpretation may be challenging in view of the abnormal septal motion, which could influence the test’s prognostic value.

**Purpose:** We aimed to assess the prognostic value of SE in LBBB patients and examine techniques that could improve its ability to predict outcome.

**Methods:** We retrospectively studied 190 consecutive SEs (exercise and dobutamine) in patients with LBBB and symptoms suggestive of IHD over a six-year period. The wall thickening score index (WTSI) at rest, intermediate and peak stage was calculated with the 16-segment model and score proposed by the American Society of Echocardiography. Fourteen tests were inconclusive and excluded from the study. Cox regression analysis was performed to assess predictors of all-cause mortality.

**Results:** The mean patient age was 70±11.5 years and mean baseline left ventricular ejection fraction (LVEF) 50.1±10%. LVEF<50% was present in 38.6% of patients. Contrast was used in 132 (75%) patients. Exercise SE was performed in 49 (27.8%) patients and dobutamine in 128 (71.6%). Only six out of the 14 inconclusive tests were due to interpretation difficulties (3.3%). Inducible ischaemia was present in 27 (15.3%) patients, whereas mean WTSI at peak stress (WT-Speak) was 1.13±0.3. During the mean follow-up (35.4±20.2 months) there were 32 deaths (18%). Independent predictors of mortality were age (HR 1.1, 95% CI 1.04–1.15, p=0.01) and WTSIpeak (HR=4.65, 95% CI: 1.67–12.9, p=0.003). WTS-Speak and measure of combined LV function and extent of inducible ischaemia at peak stress.

**Conclusion:** Stress echocardiography in patients with LBBB is feasible providing a diagnosis in 97% of the cases in patients with suspected myocardial ischaemia. WTSpeak, which is a measure of combined LV function and extent of inducible ischaemia at peak stress was an independent predictor of mortality. The use of contrast is associated with detection of prognostically significant WTSpeak. Thus SE is feasible and provides important prognostic information in patients with LBBB and suspected angina. Contrast improves the prediction of outcome in SE.
**P3365 | BEDSIDE**

Female false positive exercise ECG testing - fact versus fiction

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**Background/Purpose:** Exercise stress testing is a well validated method for assessing cardiovascular status and disease. Accuracy for the test has been documented at about 60%. False positive ECGs (diagnostic ECG changes on testing with non-obstructive disease on anatomical testing) are common, especially in women. Females have a higher incidence of false positive ECG tests, limiting the effectiveness of ETTs in women. This research was conducted to investigate this proposition in a large cohort and in a contemporary setting.

**Methods:** "Open access" stress echocardiography was performed using the Bruce protocol for patients with suspected myocardial ischemia. All consecutive stress echocardiograms performed at HeartCare Partners clinical testing facilities were initially included. The only exclusions were true positive stress echocardiograms and patients requiring dobutamine stress echocardiography. False positive ECG stress test results were then systematically reviewed. The definition of false positive ECGs is diagnostic ECG changes on testing without pain and with the stress echocardiogram not suggesting myocardial ischemia. Data was collected prospectively. Potential and predictable causes for a false positive ECG stress test were recorded before the test.

**Results:** A total of 2927 consecutive negative stress echocardiograms were analysed. There were 1014 females (35%) and 1913 males (65%). Mean age was 60.5 years. The baseline characteristics of the patients were similar in both groups. False positive ECG ETTS were recorded in 542 tests (18.5%). There were 188 female false positive ECG ETTS recorded (18.5%). False positive ECG ETTS were found in 354 male tests (18.5%, p=ns for the difference). Potential causes for false positive ECG tests were recorded before the stress echocardiogram in 44 (23.4%) of the female false positive ECG tests and 276 (78.0%) of the male false positive ECG tests (p=0.0001 for the difference). Potential causes for false positive ECG stress tests included hypertension, left ventricular hypertrophy, known coronary artery disease, arrhythmia, diabetes mellitus, valvular heart disease, resting ECG changes.

**Conclusions:** These data suggest that false positive ECG stress tests are equally common in women and men, occurring in almost one in five tests. Most false positive stress ECG tests in men can be predicted by patient history, while most in women cannot. As such, being female is a risk factor for a false positive ETT. These data reinforce the incremental accuracy and specificity of stress echocardiography, particularly in women.

**P3367 | BEDSIDE**

Detection of left main/ostial left coronary artery and ostial circumflex stenosis in patients with air lead ST-segment elevation during the exercise stress test

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**Background:** ST-segment elevation in lead aVR is an important predictor of death in left main (LM) coronary artery obstruction, but its predictive value in a setting of exercise treadmill testing is still unclear.

**Purpose:** The aims of our study were to assess the incidence and predictors of LM/ostial left anterior descending (LAD) coronary artery and/or ostial circum-

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**P3366 | BEDSIDE**

Artificial neural network based model can better risk stratify patients undergoing stress echocardiography or nuclear stress test and reduce studies by >50%

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**Introduction:** Coronary Artery Disease (CAD) accounts for more than half of all cardiovascular events. Stress testing remains the cornerstone for noninvasive assessment of patients with possible or known coronary artery disease (CAD). Clinical utilization reviews show that most patients who present for evaluation of stable CAD by stress testing are categorized as low risk prior to the test. Attempts to better risk stratify individuals being sent for stress testing seems to be more in need today.

**Purpose:** The aim of the present study was to compare Artificial Neural Networks (ANN) based prediction models to the other risk models being used in practice (the Diamond-Forrester and the Morise models).

**Methods:** We prospectively recruited patients older than 19 years old, who were being evaluated for coronary artery disease through nuclear Stress Test or treadmill Stress Echocardiography. Inclusion criteria were: patients who were presenting with symptoms suggestive for stable angina, as well as those with features of unstable angina with normal ECG and negative cardiac biomarkers (2 sets of troponin). We excluded patients with Non-ST elevation Myocardial Infarction (NSTEMI), ST Elevation Myocardial Infarction (STEMI) as well as those with Unstable Angina or EH. The changes. We recruited 486 patients presenting for evaluation of chest pain at our institution (American University of Beirut Medical Center), of whom 89 underwent nuclear Stress Test and 397 underwent Stress Echocardiography.

**Results:** In 486 patients included, we demonstrated higher discriminatory power of ANN (DP=1.61; good) based model compared to Morise (DP=0.45; poor) and Diamond-Forrester (DP=0.64; poor) scores. This ANN model has a negative predictive value of 98%, Sensitivity 91% [81% - 97%], Specificity 65% [60%-79%] and a positive predictive value 26% while reducing non-invasive studies by 59% (Table 1).

**Conclusion:** We showed that ANN model has a higher discriminatory power than Diamond-Forrester and Morise risk models in predicting ischemia with stress echo or nuclear stress test. This ANN model can significantly decrease downstream testing by 59%.

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**Echo contrast / Stress / Novel techniques 651**

Performance of Diamond-Forrester, Morise scores and ANN models to assess for reversible ischemia by stress imaging

<table>
<thead>
<tr>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>LR+ (%)</th>
<th>LR- (%)</th>
<th>DP</th>
<th>Stress imaging avoided (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morise 69 [49–79]</td>
<td>55 [51–59]</td>
<td>9.2</td>
<td>96</td>
<td>1.44</td>
<td>0.63</td>
<td>0.45</td>
<td>54%</td>
</tr>
<tr>
<td>DF 69 [53–83]</td>
<td>59 [55–62]</td>
<td>9.5</td>
<td>96</td>
<td>1.68</td>
<td>0.52</td>
<td>0.64</td>
<td>57%</td>
</tr>
<tr>
<td>ANN 91 [81–97]</td>
<td>85 [80–90]</td>
<td>26</td>
<td>98</td>
<td>2.6</td>
<td>1.4</td>
<td>1.61</td>
<td>59%</td>
</tr>
</tbody>
</table>
Table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Non-ischaemic</th>
<th>Ischaemic</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radial strain (peak-basal)</td>
<td>5.8</td>
<td>-14.15</td>
<td>0.004</td>
</tr>
<tr>
<td>Circumferential strain (p-b)</td>
<td>4.20</td>
<td>-3.84</td>
<td>0.003</td>
</tr>
<tr>
<td>3D strain (p-b)</td>
<td>4.75</td>
<td>-10.70</td>
<td>0.011</td>
</tr>
<tr>
<td>Longitudinal strain (p-b)</td>
<td>-0.90</td>
<td>-1.61</td>
<td>NS</td>
</tr>
<tr>
<td>Area tracking (p-b)</td>
<td>4.02</td>
<td>-5.75</td>
<td>0.019</td>
</tr>
<tr>
<td>End diastolic volume (p-b)</td>
<td>-15.59</td>
<td>6.1</td>
<td>NS</td>
</tr>
<tr>
<td>End systolic volume (p-b)</td>
<td>-9.91</td>
<td>0.29</td>
<td>NS</td>
</tr>
<tr>
<td>LVEF (p-b)</td>
<td>6.46</td>
<td>-2.62</td>
<td>0.027</td>
</tr>
</tbody>
</table>

Conclusions: The improvement in myocardial function observed after dobutamine stress in non-ischaemic patients seems to mainly depend on circumferential strain. However, the presence of ischaemia has deep impact on most 3DST global parameters. This finding could be useful to improve the detection of ischaemia in addition to regional contractility assessment. Further investigations are needed.

P3368 | BEDSIDE

Behavior of 3D-speckle-tracking parameters during stress echocardiography


Background: 3D Speckle tracking 3DD (3DST) segmental values could be useful to quantify the regional contractility in response to stress. Nonetheless, nor global values performance is well known in this context, neither their utility to quantify the regional contractility in response to stress. Nonetheless, nor global ejection fraction (LVEF) (basal 61.31, peak 65.87; p=0.03).

Methods: We performed both basal and stress ST3D ETT to 35 consecutive patients. From those, we discarded 5 cases because of insufficient imaging quality. We finally selected 30 cases, mean age of 63.57 (±10.43) and 28.1% of women. The modality of stress was dobutamine in 78.1% of the cases, dipyridamole in 9.4%, exercise in 12.5%. 32% of the patients (32/100) showed trend to more severe wall motion abnormalities with exercise (delta WMSI ≥0.2). Patients with aVR lead ST-elevation were 10.35% during exercise, while significant right coronary artery stenosis was determined in 11% of patients and Cx in 7%. Normal angiogram was found in 12% of patients. There were no statistically significant differences in majority of baseline clinical characteristics and hemodynamic response between patients with and without significant LM/ostial LAD or ostial Cx stenosis. However, patients with LM/ostial LAD and ostial Cx stenosis were older (64±7 vs years and 59±8 years, p=0.049), with a lower Duke treadmill score (-8.6 vs -34, p<0.005) in comparison to those without significant LM/ostial LAD or ostial Cx stenosis, and they showed trend to more severe wall motion abnormalities with exercise (delta WMSI 0.6±0.3 vs 0.42±0.3, p=0.085). Sensitivity of Duke score ≤5 in detection of significant LM/ostial LAD or ostial Cx stenosis was 70%, with specificity of 67% (AUC 0.75). Patients with aVR lead elevation accompanied by horizontal ST-segment depression in leads V3–6, are most likely to have significant LM/ostial LAD or ostial Cx stenosis (p<0.03).

Conclusions: ST-segment elevation in lead aVR has limited sensitivity in detecting LM/ostial LAD or ostial Cx stenosis. Nevertheless, if ST-segment elevation is accompanied by ST-segment depression in leads V3–V6, patients are most likely to have significant LM/ostial LAD or ostial Cx stenosis. Additionally, the Duke treadmill score can be calculated to help identify this subset of patients.

P3369 | BEDSIDE

Diagnostic accuracy of stress echocardiography compared with invasive coronary angiography with fractional flow reserve

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Introduction: Haemodynamically significant coronary artery disease (CAD) is an important indication for revascularisation. Wall motion analysis during stress echocardiography (SE) is a noninvasive alternative to invasive fractional flow reserve (FFR) for evaluating haemodynamically significant CAD. We sought to determine the diagnostic accuracy of SE compared with invasive coronary angiography with FFR for the diagnosis of haemodynamically significant CAD.

Methods and results: Between January 2008 and April 2015, all patients who underwent clinically indicated FFR measurements during invasive angiography and SE in close succession were analysed. Patients were excluded if tests were not done within 6 months of each other, or an intervening percutaneous coronary procedure or acute coronary syndrome occurred. 184 patients (mean age 66.5yrs, 59 (32%) female) were identified. The majority of patients underwent coronary angiography following SE. The prevalence of diabetes, known CAD and non obstructive coronary artery disease were 43%, 46% and 13% respectively, and 14% (26) of patient had previous coronary artery bypass surgery. Exercise SE was performed in 84 (46%) patients and Dobutamine SE in 100 (54%) patients. Contrast was used in 158 patients (86%). In 108 patients (59%), the SE was positive for in-deniable ischaemia. From 217 vessels analysed, the Left Anterior Descending Artery, Right Coronary Artery, Left Circumflex Artery and Left Main Coronary artery were involved in 120 (55%), 47 (22%), 30 (14%), 18 (8%) respectively, with 2 vessels being grafts. 46 FFR measurements were positive (21%) and 17 were negative (79%), using a cut off of ≤0.80. At the vessel level, the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of SE for identifying significant disease as assessed by FFR was 70%, 77%, 45% and 90% respectively. In 73 patients, there was single vessel disease on angiography. At the vessel level, the sensitivity, specificity, PPV and NPV were 85%, 68%, 37% and 95%.

Conclusion: To date this is the largest study comparing SE and FFR for the assessment of the physiological significance of a coronary lesion, and reflects real world diagnostic experience. SE demonstrates good diagnostic accuracy and excellent NPV for excluding flow-limiting disease. The low PPV is likely to represent the commencement of medical therapy following a positive SE, as well as referral bias (since only patients with positive SE underwent angiography) as well as the low prevalence of positive FFR measurements in this population. The presence of a haemodynamically significant stenosis can be accurately ruled out with SE.

P3370 | BEDSIDE

Comparison of mitral valve repair versus replacement for hemodynamics during exercise in patients with primary mitral regurgitation: An exercise echocardiography study

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Purpose: Mitral valve repair, rather than replacement, is the criterion standard treatment for primary mitral regurgitation (MR). Only a few recent studies have demonstrated that functional mitral stenosis (MS) after mitral valve repair may occur; however, the comparison between mitral valve repair and replacement have not been performed.

Methods: This study prospectively included 50 patients who underwent mitral valve repair (n=38, 76%) or replacement (n=12, 24%) for primary MR. All patients underwent symptom limited semi-supine bicycle exercise echocardiography.

Results: No differences in systolic or diastolic blood pressure were found between the two groups. Although no differences in mean pressure gradient (MPG) and gradient on the area (EVAR) between the two groups at rest, the repair group had lower MPG (9.7±5.0 vs. 13.0±5.2mmHg) and larger EOA (1.7±0.5 vs. 1.5±0.5cm², both P<0.05) during exercise than the replacement group. The prevalence of functional MS (EOA<1.5cm²) was lower in the repair group than the replacement group (45 vs. 75%, P<0.05), whereas severe functional MS (EOA<1.0 cm²) was observed in 3 patients in replacement group.

Conclusions: Mitral valve repair had more advantages in exercise hemodynamics than replacement. However, a small number of patients with mitral valve repair revealed very severe functional MS. These results suggest that we should give careful consideration to the type of mitral valve surgery.
P3371 | BEDSIDE
The diagnostic utility and prognostic value of stress echocardiography in octogenarians over clinical variables for predicting hard events
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Introduction: The prevalence and severity of Coronary Artery Disease (CAD) increases markedly with age, and a disproportionate number of both Myocardial Infarction (MI) and MI fatalities occur in octogenarians. Although stress echocardiography (SE) is invaluable in younger populations, its prognostic value may be attenuated in the elderly due to shorter life expectancy and the frequent presence of severe co-morbidities. This study sought to evaluate the clinical effectiveness of stress echocardiography, particularly its prognostic value over clinical variables, including recognized prognostic markers not previously evaluated in this setting, in predicting hard events.

Methods and results: From 2007–12, 337 consecutive octogenarians who underwent clinically indicated SE were analysed. The mean age was 83.5 years and 182 (54%) were female. 310 (92%) patients had dobutamine and the remaining underwent exercise stress echocardiography. Contrast was used in 206 (61%) patients. There were no major complications during any of the tests, and a diagnostic test was achieved in 325/337 patients (96%). 42 patients (12%) had inducible ischaemia demonstrated on SE, of which 26 (62%) proceeded to angiography. Flow limiting disease was present in 20 (77%) patients. During a mean follow up of 4.1 years there were 124 deaths from all causes and 34 non-fatal Myocardial Infarction (NFMI). The annualized event rates in patients with a normal SE and patients with inducible ischaemia were 4.3% and 7.1% respectively. On unadjusted analysis age, prior MI, chronic kidney disease (CKD), Atrial Fibrillation (AF), Peripheral vascular disease (PVD), left ventricular dysfunction and the presence of inducible ischaemia all predicted all-cause mortality. However on multivariate analysis, after censoring patients that underwent revascularization, predictors of hard outcomes were age (HR 1.11 95% CI (1.05–1.18) p=0.001), CKD (HR 2.64 95% CI (1.78–3.92) p=0.001) and AF (HR 1.58 95% CI (1.05–2.38) p=0.03). Predictors of NFMI on multivariate analysis were prior MI (HR 3.98 95% CI 1.46–10.87 p<0.005), PVD (HR 5.31 95% CI 1.91–14.76 p<0.004), and inducible ischaemia (HR 4.29 95% CI 1.55–11.90 p<0.011). The larger the extent of ischaemia, the greater the incidence of MI (Figure).

Results: The rest velocity in LAD was 31.9±8.3 cm/s, at the peak of exercise 77.4±15.3 cm/s, ΔV 45.3±13.4 cm/s, and CFVR 2.51±0.59. There was not a significant difference in the subgroups of different ages. Women had a lower CFVR in comparison with men (2.32±0.55 vs. 2.63±0.58; p<0.02).

Conclusion: Values of Doppler coronary artery velocity of the healthy subjects for exercise tests were obtained. The study does not demonstrate the impact of age on CFVR. Women have a lower CFVR during exercise tests.

P3373 | BEDSIDE
Reduced cardiopulmonary exercise capacity in subjects without structural heart disease: is it possible to find an echocardiographic predictor?

Background: Left atrium (LA) function is an important contributor to cardiac performance. Two-dimensional speckle-tracking echocardiography (2D-STE) has been applied to the study of the LA mechanics.

Purpose: We aimed to evaluate the association of echocardiographic parameters with the functional capacity in apparently healthy subjects.

Methods: Voluntary subjects were prospectively recruited, with the following inclusion criteria: sinus rhythm, normal left ventricle (LV) and right ventricle size and systolic function. Subjects with moderate-to-severe valve disease, signs of heart failure or with known pulmonary disease were excluded. We performed a transthoracic echocardiogram (TTE) and assessed the LV (16 segment model) and LA mechanics (P-wave timed, 12 segment model) with 2D-STE. Immediately after the TTE, each subject underwent a treadmill cardiopulmonary exercise testing using Bruce protocol. Participants were encouraged to reach a maximal effort by monitoring the respiratory exchange ratio (~1.15). Peak VO2 was used as a measure of functional capacity and VE/VCO2 slope as a surrogate of ventilation/perfusion mismatch.

Results: Twenty subjects were included with a mean age 51±14 years and male gender predominance (65%). Peak VO2 was strongly correlated with age (r=0.83, P<0.01), with the E/e’ ratio (r=0.72, P<0.01) and with the LA reservoir and conduit phase mechanics – r total/reservoir (r=0.55, P<0.01), r positive/conduit (r=0.58, P<0.01) and strain rate (SR) early negative/conduit (r=0.82, P<0.01) – Figure 1. LA stiffness (E/e’ to 86965 reservoir ratio) was also significantly correlated (r=0.72, P<0.01). There was no correlations between peak VO2 with LV mechanics. A similar pattern of associations was identified for the VE/VCO2 slope.

Conclusions: In healthy subjects, LA conduit phase SR was significantly associated with the peak VO2, supporting the use of LA mechanics as a surrogate echocardiographic marker of the functional capacity.

P3372 | BEDSIDE
Normal values of coronary flow velocity parameters measured non-invasively by Doppler methods during exercise
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Background: Assessment of coronary flow is used during pharmacological tests. Several recent studies showed the application of coronary flow assessments during supine bicycle exercise. Nevertheless, there is a lack of information about coronary artery flow velocity parameters in healthy subjects during exercise tests.

Aims: Define 1) coronary artery flow velocity values in a healthy group at rest and during exercise tests; 2) differences in these values within age and sex groups.

Methods and methods: There is a single center study of 145 consecutive healthy patients who underwent a bicycle exercise echocardiography with the analysis of coronary artery flow velocities in the left anterior coronary artery (LAD). Coronary flow velocities were measured before and at the peak of exercise at the medium segment of the LAD. In addition, the coronary flow velocity reserves (CFVR) and difference between peak and rest velocities (ΔV) were calculated.

Results: The rest velocity in LAD was 31.9±8.3 cm/s, at the peak of exercise 77.4±15.3 cm/s, ΔV 45.3±13.4 cm/s, and CFVR 2.51±0.59. There was not a significant difference in the subgroups of different ages. Women had a lower CFVR in comparison with men (2.32±0.55 vs. 2.63±0.58; p<0.02).

Conclusion: Values of Doppler coronary artery velocity of the healthy subjects for exercise tests were obtained. The study does not demonstrate the impact of age on CFVR. Women have a lower CFVR during exercise tests.

Figure 1. LA stiffness (E/e’ to 86965 reservoir ratio) was also significantly correlated for the VE/VCO2 slope.
Circulating CD14+ and CD14-highCD16- classical monocytes are reduced in patients with signs of plaque neovascularization in the carotid artery

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Background: There is experimental evidence that monocytes play a key role in the initiation and progression of atherosclerosis and contribute to plaque destabilization through the generation of signals promoting inflammation and neointima-giogenesis. Studies correlating the features of circulating monocytes of advanced atherosclerotic lesions in humans are lacking.

Purpose: To investigate the relation between ultrasonographic and contrast-enhanced ultrasound (CEUS) characteristics of carotid artery plaques and the concentration of selected circulating monocytes sub-populations in patients with asymptomatic carotid artery stenosis of intermediate severity without indication for carotid revascularization.

Methods: Maximal stenosis in common carotid artery, carotid bulb and internal carotid artery, overall disease burden as estimated with total plaque area (TPA), greyscale and plaque neovascularization were evaluated in 244 advanced carotid plaques of 55 consecutive patients (mean age 69 years, 56% males) with intermediate asymptomatic carotid stenosis (40–70% in diameter). Absolute circulatory counts of CD14+ monocytes, of classical (CD14highCD16-), intermediate (CD14highCD16+) and non-classical (CD14lowCD16+) monocytes and of their HLA-DR+ activated subsets were evaluated with flow cytometry.

Results: No relationship was found between monocytes and overall atherosclerotic burden, nor with markers of systemic inflammation such as high sensitivity C-reactive protein (hsCRP). In contrast, plaque signs of neovascularization was associated with significantly lower counts of CD14+ monocytes (297 versus 350 cells/mm², p = 0.039) and of classical monocytes (255 versus 310 cells/mm², p = 0.029).

Conclusions: Neovascularized atherosclerotic lesions selectively associate with lower blood concentrations of CD14+ and CD14-highCD16- monocytes despite low systemic proinflammatory activity, as indicated by normal hsCRP levels. Whether the reduction of circulating CD14+ and CD14-highCD16- monocytes is due to a potential redistribution of these cell types into active lesions remains to be explored.

Acknowledgement/Funding: Giovane Ricercatore 2009 Grant from Italian Health Ministry (project code GR-2009-1608780).

Impact of Experience

Conclusion: The use of GLS in clinical trials is dependent on the consistency of measurement after training. These results show that after initial quality control and training, GLS continues to have better precision between core laboratory and international sites’ readers than does EF. The robustness of GLS suggests its superiority as a marker of cardiac function.

Acknowledgement/Funding: General Electric Medial Systems

How experiences affect the precision of strain measurement?


Methods: Fifty-eight readers from North America, Europe, Asia and Oceania measured GLS of 4 cases with adequate measurement quality. Readers were divided by experience into 4 groups: no experience (n=13, 0 cases experience, Group “No”), less experienced (n=12, 1–20 cases, Group “Limited”), intermediate (n=10, 21–100 cases, Group “Intermed”), and experienced (n=23, experience with >100 cases, Group “High”). Averaged GLSs from 5 highly experienced readers with >1000 cases experience were used as a reference and compared with those from the 4 groups. Vendor-dependent speckle tracking software was used. Mean difference between the reference and values from each group (MD), standard deviation (SD), coefficient of variation (CV), and Intraclass correlation coefficients (ICCs) were used to determine concordance.

Results: Although ICC of Group “No” was very good (0.975 [0.912, 0.988], that of Group “High” was even better (0.996 [0.988, 1.000], p<0.0002). Along with the accumulation of GLS experience, MD, SD, and CV became significantly less variable (Figure). Post-hoc comparison between the groups showed that the MD of Group “High” was significantly smaller than that of Group “No”: MD (0.885±0.46% vs. 1.675±0.77%, p=0.001), with the same for SD (0.610±0.44% vs. 1.330±0.86%, p<0.003), and CV (3.3±2.5% vs. 7.6±5.4%, p=0.003). In addition, the CV of Group “Intermed” was significantly smaller than Group “No” (3.5±1.5% vs. 7.6±5.4%, p=0.04).

Acknowledgement/Funding: General Electric Medial Systems

Echo contrast / Stress / Novel techniques

How experiences affect the precision of strain measurement?


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Acknowledgement/Funding: General Electric Medial Systems
P3377 | BEDSIDE
The long-term CRT outcome correlates with the degree of re-alignment of hemodynamic forces
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Background: We hypothesize that the misalignments of pressure gradients of left intra-ventricular vortex flow, reflects progressive impairment of left ventricu-
lar volumetric remodelling in non responders pts post cardiac resynchronization therapy (CRT).

Aim: To investigate the incremental role of echocardiographic-contrast particle image velocimetry (Echo-PIV) in patients with HF-LBBB analyzing the directional
distribution of hemodynamics forces during the whole heart cycle; in particular we evaluated if these hemodynamics vectors are aligned along the left ventricu-
lar chamber, in compliance with the emptying-filling process, or they deviate
by developing non-physiological transversal components as changes in electri-
cal activation alter the orientation of blood flow momentum post implant. For this
purpose, a single flow angle parameter, flow-momentum (LV-phi) indicating the
dominant orientation the hemodynamics forces, is evaluated pre implant and at f.t. (6m).

Methods: We analysed 10 consecutive non ischaemic patients (mean age 57±4
years; 2 female) with a mean EF 25±8%. 2D B-mode apical 3-chambers view with
infusion of contrast agent was recorded for the evaluation of intra-cavity LV blood
motion.

Results: In all patients, quantitative LV vortex flow analysis was feasible: a signifi-
cant correlation was found between LV-phi post implant and volumetric reductions
(deltaEDV: r 0.52; deltaESV: r 0.72). We found a significant difference of LV-phi (45.2±5° vs 34.2±4.8°, respectively; p<0.0001) pre and post CRT. Relevant in-
crease of the LV-phi (>-40°) was observed in non responders pts (2/10).

Conclusions: Echo-PIV offers a new method to obtain additional information on
LV hemodynamic. Changes in electrical activation alter the orientation of blood
flow momentum. The long-term CRT outcome correlates with the degree of re-
alignment of hemodynamic forces. These preliminary results suggest that flow
orientation could be used for optimizing the biventricular pacing setting.

P3379 | BEDSIDE
Differentiation between benign and malignant cardiac tumors. The significance of contrast enhancement using the technique of bolus vs continuous injection of contrast

Contrast hyperenhancement of cardiac tumors suggests a highly vascular or ma-
lignant cardiac tumor (MCTs). Conversely, benign cardiac tumors (BCTs) have
usually a poor blood supply and appear hypoenhanced.

Methods: We used the technique of bolus injection in comparison to continuous
injection of contrast on the same patient to study 5 MCTs and 9 BCTs. The as-
essment of contrast enhancement (CE) in either real-time or a triggered mode
was assessed using dedicated software.

Results: Our study showed as expected hyperenhancement of MCTs compared
to the surrounding myocardium with both techniques while BCTs showed hypoen-
hancement. Mass contrast enhancement —MaCE— of MCTs in the case of bolus
injection persisted several minutes after the disappearance of myocardial contrast
elevation (MCE, Figure 1, panels 1–3 and Figure 2). On the contrary using the
same technique MaCE of BCTs disappeared before MCE.

Conclusions: Texture analysis with advanced computational tools applied to
echocardiograms recorded 7 days after reperfused S-T elevation MI can predict
cardiac function and remodeling after one year. Performance of SVM and MLP
as well as native vs CPS images was similar. Best accuracy was obtained for
WMSI improvement (77–79%).
increase of LA global strain (pre-ablation: -21 ± (3.2) % vs. post-ablation: -34.5 (2.9) %, p<0.001) as well as in LV global strain (pre-ablation: -14.4 (2.3) % vs. post-ablation: -28.7 (2.4), p<0.001). LA volume index was significantly reduced (pre-ablation: 44.5 (2.6) ml/m² vs. post-ablation: 31.8 (4.5) ml/m², p<0.005). LV remodelling as measured with 3D volumes, EF and mass was similar in both groups. The rate of AF recurrence was strongly associated with increased LA volume index (r=0.9, p<0.05) Interestingly, only LA early and late diastolic peak strain rate were increased post PAF ablation (p<0.01 respectively)

Conclusion: Early PAF ablation benefits atrial and ventricular function by increasing regional strain and strain rate and leading to reverse atrial remodelling.

P3381 | BEDSIDE
Contrast-enhanced echocardiography in 3D strain measurement
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Background: Three-dimensional (3D) myocardial deformation analysis (strain) is an emerging clinical tool for assessing subtle cardiac dysfunction. The use of contrast-enhanced 3D strain measurement has not been assessed. In this study, we aimed to assess the feasibility and the accuracy of contrast-enhanced 3D strain in echocardiography.

Methods: We obtained two independent 3D dataset materials. One material consisted of healthy hearts with good image quality and normal ejection fraction, no wall motion abnormalities and normal 2D strain (n=14). The second consisted of 26 consecutive research patients over 10 weeks. We used 0.2–0.5 ml of contrast agent as intravenous bolus injection. All recordings were assessed for 2D and 3D strain measurements. The global longitudinal strain (GLS) and the average segmental GLS were compared between 2D measurements and the two different 3D images by using paired sample’s T-test.

Results: In both materials, the GLS from contrast-enhanced 3D data was comparable with 2D GLS (mean difference -0.6% and -0.4% in good-quality data and in consecutive data, respectively, Table 1). The 3D non-contrast enhanced native GLS was significantly smaller than 2D data in the healthy hearts and borderline smaller in the larger material (Table 1). When the average segmental longitudinal strain was assessed, the differences were even more pronounced (Table 1). The correlation was not significant for any of the studied pairs, only borderline

Table 1. Global longitudinal strain (GLS)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean (SD)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>2D GLS</td>
<td>21.08 (1.70)</td>
<td>reference</td>
</tr>
<tr>
<td>3D contrast GLS</td>
<td>21.68 (3.06)</td>
<td>0.60</td>
</tr>
<tr>
<td>3D native GLS</td>
<td>18.96 (1.68)</td>
<td>2.39</td>
</tr>
</tbody>
</table>

Conclusions: Contrast-enhanced 3D imaging is feasible and accurate. It may even be more accurate than the native 3D strain echocardiography. Acknowledgement/Funding: Paavo Nurmi Foundation

BIG DATA ANALYSIS IN CARDIOLOGY, REGISTRIES AND DATABASES

P3382 | BEDSIDE
Programmed parameters significantly change implantable cardioverter-defibrillator longevity
M. Bennett1, A. Patel2, L. Sheresse3, T. Brown, F. Liu, J. Andrade1, A. Krahm1, N. Hawkins1, 1University of British Columbia, Heart Rhythm Vancouver, Vancouver, Canada; 2Medtronic, Mounds View, United States of America

Background: Although ICD parameters (e.g. pacing rate/mode/output, threshold and type of anti-tachycardia therapy) are primarily changed to optimize patient outcomes, adjustment may also increase the maximum device longevity. This may decrease generator changes and their associated morbidity (primarily infection) and health care costs.

Methods: We evaluated the relative impact of adjustable programming parameters on ICD longevity in a large cohort.

Results: Of the entire cohort of over 300,000 pts, 5669 were assessed (75% male; mean age 61 yrs) with implant dates ranging from 1/2006 to 01/2011. Only 35 patients (0.6%) had parameter changes following initial programming. On the remaining 5664 pts, 7 of 17 parameters had statistically significant differences in device longevity associated with their programmed values (Table 1); specifically, devices having EGM pre-storage Off and pacing mode Rate Response Off throughout usage had significantly longer device longevity.

Abstract P3382 – Effect of parameters on longevity

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Setting (if of patients, observed ERI rate at 7 years</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EGM pre-storage</td>
<td>Off (3054, 11.1%)</td>
<td>On continuous (1716,19.3%)</td>
</tr>
<tr>
<td>Pacing mode</td>
<td>Off (440, 18.6%)</td>
<td>VVI (497, 27.3%)</td>
</tr>
<tr>
<td>Activity acceleration/deceleration</td>
<td>Both off (5164, 13.9%)</td>
<td>One or both on (497, 27.3%)</td>
</tr>
<tr>
<td>Upper sensor rate (bpm)</td>
<td>VVI (5164, 13.9%)</td>
<td>90–120 (250, 29.5%)</td>
</tr>
<tr>
<td>Lower current (mA)</td>
<td>30–40 (448, 13.6%)</td>
<td>45–60 (973, 16.6%)</td>
</tr>
<tr>
<td>Monitor zone</td>
<td>On (5050, 13.4%)</td>
<td>Off (2134, 16.7%)</td>
</tr>
<tr>
<td>Ventricular pulse width (msec)</td>
<td>0.03–0.3 (76, 12.2%)</td>
<td>0.6 (709, 15.0%)</td>
</tr>
<tr>
<td>VF Initial NID, (VT) Stability, Onset, Wavelet, VT Detection, VT Therapies, ATP (while Charging), Deliver ATP if last 8 R-R ≥, SVT V Limit, Ventricular Amplitude</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

Conclusions: In a large single-chamber ICD population, EGM pre-storage, rate response, ventricular pulse width and lower rate programming significantly impact ICD longevity.

P3383 | BEDSIDE
Superior survival of women versus men following initial high power device implant
J. Sims, S. Chartton, A. Patel, S. Liu. Medtronic, Inc, Moundsview, United States of America

Introduction: Long-term survival of implantable cardioverter-defibrillator (ICD) and cardiac resynchronization therapy-defibrillator (CRT-D) patients in...
widespread practice has not been broadly studied. Moreover, women have been historically underrepresented in landmark clinical trials. We sought to understand survival in women versus men in a large, unselected patient cohort.

Methods: Deidentified data for ICD and CRT-D device patients in the United States enrolled in a large remote monitoring database since 2002 were retrospectively analyzed. Patients were excluded if an initial device implant date was unknown. Mortality data was obtained from the company device registration database and cross-referenced with the U.S. Social Security Death Index. Data for active patients were censored as of Nov 5, 2013. A Kaplan-Meier survival analysis was conducted to evaluate patient survival after their initial device implant.

Results: 329,455 patients were identified with an initial implant of an ICD or CRT-D device between January 1998 and November 2013 (mean age 64±13 years, 73.5% male; 70.6% ICD). The figure depicts survival of women versus men following their initial high power device implant. The 10 year survival of women was 66.9% compared to 61.7% for men (HR 1.18, 95% CI (1.16–1.20), p<0.0001). The survival rates for these patients, irrespective of gender, were higher than previously reported in landmark clinical trials.

Patient longevity after initial high power device implant

Conclusion: In this retrospective analysis of a large unselected population of patients with various device indications and co-morbidities, survival following initial ICD or CRT-D implant is higher than in previously reported clinical trials. Moreover, survival in women is higher than that of men. The data indicate that despite initial risks and economic factors associated with device implantation, better long-term survival of these patients in a real world setting suggests that device therapy is a beneficial therapeutic option, especially in women.

P3384 | BEDSIDE

Usefulness of neural network model for prediction and prognosis of myocardial infarction in patients with previous revascularization; 2-year experience

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The purpose of this study was to assess the usefulness and accuracy of artificial neural network in the prediction and prognosis of acute myocardial infarction (AMI) in patients with previous coronary artery bypass grafting (CABG).

Materials and results: From April 1988 to January 2016, the baseline characteristics and clinical data were recorded in 4380 consecutive patients. The data set contains 13 predictor variables per patient. It was first randomly split into training (2190 cases) and test sets (2190 cases). Artificial neural network performance was evaluated using the original data set for each network, as well as its complementary test data set, containing patient data not used for training the network. The program compared actual with predict outcome for each patient, generating a file of comparative results. At the end, results from this file were analyzed and compared, on the basis of receiver operating characteristics (ROC) areas. Logistic regression analysis, as one of standard prediction models, was not efficient for prediction and prognosis of acute myocardial infarction in patients with prior CABG. The results show that a traditional statistical model is not able to perform class separation in multidimensional space and that a non-linear approach is necessary.

Conclusions: In this clinical situation, artificial intelligence appears to be superior to traditional method for prediction and prognosis of AMI in patients with previous CABG.

Acknowledgement/Funding: The Belgrade Cardiology Club, Belgrade

P3385 | BENCH

Endothelial dysfunction in children with white coat hypertension and in essential systemic hypertension

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Introduction: White coat hypertension (WCH) is defined as the observation of high blood pressure (BP) levels in the doctor's office and normal BP during ambulatory monitoring. Endothelial dysfunction is considered to be an early indicator of atherosclerotic changes preceding the morphological alterations, commonly associated with elevated blood pressure. Several studies have demonstrated endothelial dysfunction in patients with essential hypertension. However, the presence of endothelial dysfunction in children with WCH has not been studied. Therefore, we aimed to study the endothelial function in children with WCH and essential hypertension using a novel method based on assessment of flow mediated dilation (FMD).

Methods: One hundred thirty eight children – 46 (23 boys) children suffering from WCH, 46 (23 boys) patients with essential hypertension and 46 age/gender matched healthy controls - were examined under standard conditions. The age period of all children ranged from 14 to 18 years. Vascular ultrasound scans were performed with a Prosound F75 Aloka ultrasound machine. Flow increase was induced by inflation of a pneumatic tourniquet to 200 mm Hg for 5 minutes. Diameter of right brachial artery was measured basally and 60 seconds after cuff deflation. Diameter changes were expressed as the percentage change relative to the average baseline scan. Diameter changes <5% at 60 seconds were considered as a deficient FMD.

Results: Statistical analysis revealed significant differences in the FMD between the both hypertensive groups (WCH, EH) and control group (9% vs 13%; p<0.01). Although the fact that deficient FMD was found in both hypertensive groups (WCH, EH), no significant differences were found between both WCH and essential hypertensive groups. None of the patients in the control group had deficient FMD.

Conclusions: The presence of endothelial dysfunction in children suffering from white coat and essential hypertension suggests that hypertensive children have early atherosclerosis associated with increased cardiovascular risk. Importantly, WCH should not be considered a harmless trait and has common features with essential hypertension.

P3386 | BEDSIDE

Effects of cigarette tobacco exposure on heart rate variability in patients scheduled for elective surgery

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Background/Introduction: Complex dynamic cardio circulatory regulatory system in humans is reflected in heart cycle variations. Tobacco consumption has been associated with specific alterations of heart rate variability parameters with increasing k sympathetic and decreasing parasympathetic measures of the overall measures of cardiac autonomic nervous system tone.

Purpose: The aim of the trial is to assess if there are significant differences in parameters of heart rate variability in subjects who have habit of consumption of tobacco cigarettes versus subjects who do not consume tobacco cigarettes.

Methods: Subjects of ASA II class with mild arterial hypertension using a new method based on assessment of flow mediated dilation (FMD) were included in the trial. Twenty-two subjects with the history of smoking twenty or more cigarettes per day for several years are allocated to group I, and twenty-three subjects without history of consuming smoking cigarettes are allocated to group II. Electrocardiogram was recorded by holter device in order to assess short-term heart rate variability (five minutes periods) during preoperative period. Linear measures of time domain (SDNN-standard deviation of NN intervals, mean RR interval, mean heart rate) and frequency domain measures (low frequency (LF), high frequency (HF), and LF/HF ratio) were analyzed.

Results: Baseline measures of mean RR interval and standard deviation of normal to normal interval (NN) have shown slightly lower values in subjects who were consuming nicotine by cigarette smoking in regard to nonsmokers but without significant difference (640±15ms vs 675±8ms, p<0.01, 45.1±3.4ms vs 51±4.3 ms, p<0.08, respectively). Frequency domain parameters (LF/HF and LF/HF ratio) have shown variations between two groups but without significant differences.

Conclusion: In this trial with small groups of subjects who participated no significant difference could be shown between subjects who are exposed to tobacco ingredients by cigarette smoking in regard to subjects who are not exposed to tobacco smoking.
P3387 | BEDSIDE
Myocardial electric instability markers in patients with chronic obstructive pulmonary disease and connective tissue dysplasia
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Background: The results of Copenhagen City Heart Study demonstrated a high incidence of life-threatening arrhythmias of multifactor nature in patients with chronic obstructive pulmonary disease (COPD). Connective tissue dysplasia (CTD) is an additional arrhythmogenic factor. CTD contributes to the formation of myocardial electric instability through the structural changes of the heart.

Purpose: To study the electrocardiographic markers of myocardial electric instability in patients with COPD and CTD syndromes.

Methods: 49 patients with COPD diagnosed in accordance with the recommendations COLD 2011 were examined. All the subjects were split into 2 groups according to the presence and prevalence of CTD markers: group 1–23 subjects (10 men and 13 women) with no CTD signs (average age 59±8.1±9, group 2–26 subjects (12 men and 14 women) with signs of undifferentiated CTD (average age 62±2±1,8). All groups were comparable in age and gender (p>0.05). All the patients underwent 24-hour Hofer ECG monitoring in three orthogonal leads according to Simpson on hardware-software complex “Kardiotekhnika-04-AD-3” (Russia, 2007). Statistical data processing has been done by means of STATISTICA 6.1.

Results: The average corrected QT-interval per day, during daytime and nighttime reached 414.5 ms, 410.0 ms and 415.5 ms in group 1, and 409,0 409.0 ms and 409.0 ms in group 2, respectively. QT dispersion was found in 14.8% of subjects in group 1 and 16.0% of subjects in group 2, respectively (p=0.048). The dependence between the values of the corrected QT interval, QT dispersion and T-wave microalternations and the frequency of occurrence of various cardiovascular arrhythmias was revealed in group 2. Atrial and ventricular late potentials (ALP and VLP) settings were captured only in group 2 (34.4% and 31.4%, respectively).

Conclusion: The main markers of myocardial instability that increase the risk of life-threatening arrhythmias in patients with COPD and CTD are: corrected QT-interval, QT dispersion, T-wave microalternations, and the parameters of ALP and VLP.

P3388 | BEDSIDE
Prevalence of patients with familial hypercholesterolemia (FH) in the German cardiology office-based setting
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Introduction: Patients with an autosomal-dominant familial hypercholesterolemia (FH) are exposed to high low density-lipoprotein (LDL)-cholesterol (C) levels from birth and therefore at very high risk for premature cardiovascular events (CVE). Germany specific data on prevalence of FH is scarce.

Purpose: This large cross-sectional registry aimed to evaluate the prevalence of FH according to the Dutch Lipid Clinic Network (DLCN) criteria in patients presenting in the cardiology office-based setting in Germany.

Methods: This cross-sectional registry was conducted on 5 days in December 2014 in 32 cardiology practices (including 49 physicians) in Germany. 1000 consecutive patients with the following inclusion criteria were enrolled: history of CVEs and/or diagnosis of hypercholesterolemia, age ≥18 years of age and availability of laboratory parameters at day of enrollment.

Results: A total of 723 males and 277 females with a mean age of 69.5±10.4 (SD) years were included. Of those, 90.4% were diagnosed with hypercholesterolemia and 87.2% were secondary prevention patients. More than half (59.2%) have been diagnosed with coronary artery disease and 31.7% had a history of myocardial infarction. Over one third (33%) of patients exhibited >1 CV-related co-morbidity, with 26% reporting type-2 diabetes. With a mean body mass index of 28.6 the majority of patients were overweight. The mean LDL-C was 109.12 mg/dl ± 36.4 (SD), high-density lipoprotein-cholesterol was 51.32mg/dl ± 15.2 (SD) and triglycerides were 160.17mg/dl or 101.2 (SD). Most patients (85.8%) were on statins (of any dose) but only 4.5% received combination treatment with ezetimibe. Fibrates were used in 7 patients, bile acid sequestrates in none. Only 45.8% of patients reached the ESC/EAS/DGK treatment goals of LDL-C <100mg/dl and few (9.9%) achieved an LDL-C <70mg/dl.

Conclusion: In this large patient population Registry at high CV-risk enrolled in cardiologist’s offices across Germany (on a consulting basis), 54% and 90% of the patients did not reach LDL-C-level <100mg/dl and <70mg/dl, respectively. Combination therapy was used in less than 5% of the patients despite additional co-morbidities in more than half of them. To be able to achieve the recommended treatment targets (LDL-C <100mg/dl or <70mg/dl), both specialists and general practitioners would benefit from continuous and complete information sharing around LDL-C goals. These data suggest a pronounced need for guidelines and implementation of more effective LDL-C lowering treatments as mono- or combination therapy.

Acknowledgement/Funding: Amgen GmbH

P3390 | BEDSIDE
Association between hyperuricemia and risk of deep vein thrombosis - a nationwide population-based cohort study
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Background: Although the association of hyperuricemia and cardiovascular diseases is well established by previous research studies, the relationship between hyperuricemia and deep vein thrombosis (DVT) remains unclear. We conducted a nationwide longitudinal cohort study to investigate the relationship between hyperuricemia and DVT.

Methods: We used the Taiwan National Health Insurance Research Database to identify patients with hyperuricemia diagnosed in Taiwan during 2000–2011, and we followed up these patients to determine the incidence of DVT among them.

Hyperuricemia was defined as having at least one episode of gout attack requiring long-term treatment with uric acid-lowering agents. The association between hyperuricemia and DVT was analyzed by cox proportional hazard model.
Results: The study cohort included 35,959 patients with hyperuricemia and 35,959 matched controls without hyperuricemia. The prevalence of comorbidities such as cardiovascular risk factors and risk factors for DVT were similar between the hyperuricemia and control groups. During the median follow-up of 7.5±3.6 years, the incidence rate of DVT was significantly higher in patients with hyperuricemia than in control group (13.48 versus 9.77 per 104 person-years, \( p < 0.001 \)). Kaplan-Meier analysis revealed a tendency toward DVT development in hyperuricemia patients (log rank test, \( p < 0.001 \)). In a Cox model, patients with hyperuricemia were found to have a 1.38-fold (95% confidence interval [CI], 1.18 to 1.62, \( p < 0.001 \)) higher risk of developing DVT.

Risk of DVT among two matched cohort

### Table 1. Odds for drug initiation

<table>
<thead>
<tr>
<th>Odds ratios (95% CI)</th>
<th>Statin initiation</th>
<th>Beta-blocker initiation</th>
<th>Aspirin initiation</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCA vs EST</td>
<td>2.30 (2.15–2.46)</td>
<td>0.95 (0.88–1.03)</td>
<td>1.94 (1.81–2.09)</td>
</tr>
<tr>
<td>CCTA vs EST</td>
<td>2.13 (1.96–2.31)</td>
<td>2.02 (1.85–2.20)</td>
<td>1.38 (1.24–1.55)</td>
</tr>
<tr>
<td>Age (5 year increase)</td>
<td>1.26 (1.25–1.28)</td>
<td>1.19 (1.17–1.21)</td>
<td>1.29 (1.27–1.31)</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>1.57 (1.47–1.67)</td>
<td>1.25 (1.16–1.34)</td>
<td>1.54 (1.44–1.65)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.32 (1.22–1.42)</td>
<td>1.26 (1.16–1.37)</td>
<td>1.19 (1.10–1.29)</td>
</tr>
<tr>
<td>Nitrates</td>
<td>1.38 (1.10–1.72)</td>
<td>0.95 (0.77–1.19)</td>
<td>1.30 (1.06–1.59)</td>
</tr>
</tbody>
</table>

Conclusion: Anatomic testing with CCTA was more likely to lead to initiation of coronary angiography than EST or MPS.

Acknowledgement/Funding: The Lundbeck Foundation Clinical Research Fellowship. The Danish Council for Strategic Research.

P3393 | BEDSIDE

The influence of air pollution on the occurrence and decompensation of cardiovascular diseases, and mortality in the population of highly polluted agglomerations

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Introduction: There are data on higher incidence of cardiovascular diseases (CVD) connected with higher pollution of air agglomerations. The aim of the study was to determine the impact of air quality factors on frequency of hospitalizations caused by acute cardiovascular events, reporting to primary care clinics (PC) and mortality in patients with CVD living in the highly urbanized agglomeration.

Material and methods: Information on patients’ hospitalizations and clinic visits in 2006–2014 were obtained from the database, based on data from the National Health Fund. Data on all-cause and cardiovascular mortality in general population were obtained from the National Institute of Public Health – National Institute of Hygiene database. The values of the quantitative analysis of air were obtained from the Regional Inspectorate for Environmental Protection. Further analysis included concentrations of sulphur dioxide (SO2), nitric monoxide (NOx).
Conclusions: The study performed on large population of patients living in highly urbanized region confirms the influence of air quality on incidence of adverse events and CVD exacerbations.

HYPERTENSION, OTHER

P3396 | BEDSIDE
The T-α (rs11646213) gene polymorphism of cadherin-13 (CDH13) gene is associated with risk of developing hypertension in Mexican population.

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1Instituto Nacional de Cardiología Ignacio Chavez, Mexico City, Mexico; 2Hospital Infantil de Mexico Federico Gomez, Department of Research in Community Health, Mexico City, Mexico; 3Instituto Nacional de Medicina Genomica, Laboratory of Genomics of Bone Metabolism, Mexico City, Mexico

Background: Hypertension (HTN) is the major public health problem, and it is a common disease affecting about 30% of the adult population that is associated with an increased risk of morbidity and cardiovascular disease. Recent reports have shown that the T-cadherin receptor characteristically expressed on endothelial and vascular smooth muscle cells, is involved in hypertension.

Purpose: The aim of the present study was to evaluate the role of cadherin-13 (CDH13) gene polymorphisms as susceptibility markers for hypertension in the Mexican population.

Methods: Six CDH13 polymorphisms (rs11646213, rs11646411, rs6563943, rs3096277, rs3784990 and rs254340) were genotyped by 5′ exonuclease TaqMan assays in a group of 644 hypertensive and 765 non-hypertensive individuals.

Results: Under co-dominant, dominant, and additive models, the CDH13 A-T (rs11646213) polymorphism was associated with increased risk of developing hypertension when compared to non-hypertensive individuals (OR=1.83, 95% CI: 1.31–2.37, P<0.01; OR=1.59, 95% CI: 1.15–2.19, P=0.005; OR=1.63, 95% CI: 1.09–2.45, P<0.01) respectively. Results were adjusted for gender, age, body mass index (BMI), type II diabetes mellitus, alcohol consumption, dyslipidemia and smoking habit. Linkage disequilibrium analysis showed two haplotypes (ACGCAG, and TCTAGG) with increased frequency in hypertensive patients when compared to non-hypertensive individuals (OR=3.50, 95% CI: 1.64–7.46, P=0.001, OR=3.06, 95% CI: 1.24–7.56, P=0.016, respectively).

Conclusion: In summary, our data suggest that the CDH13 A-T (rs11646213) polymorphism play an important role in the development of hypertension in Mexican patients. In addition, it was possible to distinguish one protective and two risk haplotypes for development of hypertension.

Acknowledgement/Funding: This work was supported in part by grants from the Consejo Nacional de Ciencia y Tecnología (Project number 233277), Mexico City, Mexico.

P3397 | BEDSIDE
Calcium metabolism and bone mineral density in patients with arterial hypertension and osteoarthritis

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Introduction: Bone and cartilage diseases often go with arterial hypertension (AH), especially in older people. These disorders have the same pathophysiology aspects. Increased renal calcium excretion in AH activates production of parathyroid hormone that affects bone tissue. Osteoporotic changes in subchondral bone of OA can contribute to progression of cartilage damage in patients with osteoarthritis (OA).

Aim: To evaluate calcium metabolism and bone mineral density in patients with AH and OA.

and dioxide (NO2), carbon monoxide (CO), ozone (O3), particulate matter with aerodynamic diameter less than 10 μm (PM10) or less than 2.5 μm (PM2.5), values of temperature (T), humidity (H), wind speed (WS) and atmospheric pressure (AP). The Smog Alert (SA) was defined as PM10 air concentration more than informing threshold of 200 μg/m³. Mentioned parameters were compared with the number of hospitalization with the diagnosis of myocardial infarction (MI), stroke, pulmonary thrombosis (PT), FA, PCC visits and mortality. The relationship between the parameters was determined with a generalized linear model with logarithmic joining function, and assumed Poisson distribution for the dependent variable.

Results: 24,249 cases of MI, 25,123 stroke, 4,260 PT, 32,788 FA, 14,016,058 PCC visits and 176,620 all-cause deaths including 74,052 cardiovascular deaths were analyzed. The significant relationships between air quality parameters and adverse events are shown on the table.

<table>
<thead>
<tr>
<th>SMOG</th>
<th>NO</th>
<th>NO2</th>
<th>O3</th>
<th>PM10</th>
<th>PM2.5</th>
<th>SA</th>
<th>AP</th>
<th>WS</th>
<th>H</th>
<th>MI</th>
<th>Stroke</th>
<th>PT</th>
<th>CV death</th>
<th>Total death</th>
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<tr>
<td>0.395</td>
<td>1</td>
<td>3.445</td>
<td>7.054</td>
<td>21.30</td>
<td>17.782</td>
<td>1.388</td>
<td>1.293</td>
<td>1.397</td>
<td>1</td>
<td>1.192</td>
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</tbody>
</table>

Conclusions: This study performed on large population of patients living in highly urbanized region confirms the influence of air quality on incidence of adverse events and CVD exacerbations.
Materials and methods: Oral calcium load test (0.25 mmol calcium lactate per kg) for 240 minutes was administered to 64 patients with AH (age range 42–76 years) and 103 patients with AH and OA (age range 41–74 years) to assess calcium intestinal absorption and calcium renal excretion. 30 volunteers (age range 40–55 years) were recruited to serve as controls for patient groups. Calcium level in blood and urine was assessed by spectrophotometry. All the patients underwent x-ray spine densitometry (“Lunar DPX”).

Results: In patients with AH average increase of calcium blood level in 120 minutes after oral calcium intake was lower (+0.33±0.02 mmol/l; p<0.05) in comparison with control group (+0.42±0.03 mmol/l). In patients with AH and OA increase rate of calcium blood level in 120 minutes was lower than in patients with AH (+0.23±0.02 mmol/l; p<0.05), that can testify about low calcium absorption in such patients. In 240 minutes after calcium overload general calcium blood level was +2.56±0.03 mmol/l in patients with AH and OA. For the period 0–120 minutes of calcium load test renal calcium excretion increased from 2.32±0.39 to 4.59±0.48 mmol/min in patients with AH and from 2.13±0.33 to 4.21±0.42 mmol/min (p<0.001) in patients with AH and OA. Calcium excretion index increased in 2 times in patients with AH (p<0.05) and in 1.8 times in patients with AH and OA (p<0.05). In 240 minutes after calcium overload renal calcium excretion index was 4.72±0.45% in patients with AH and 4.86±0.39% in patients with AH and OA, that was higher than in control (2.99±0.20%; p<0.05). Mineral bone density matched age standards in a half of patients with AH and OA, osteoporosis was detected in 26 patients (6 patients with AH) and osteoporosis (OA patients) were detected more often (p<0.05). Average bone mineral density level in group with AH was 1.03±0.01 g/cm², in group with AH and OA 0.93±0.02 g/cm² (p<0.05). Bone mineral density level correlated with rate of elimination or calcium overload (r=+0.51; p<0.05) in patients with AH and OA, in group with AH correlation connection was not so strong (r=+0.42; p<0.05).

Conclusion: This study demonstrated that in patients with AH and OA there were calcium metabolic disorders - low calcium absorption and increased renal calcium excretion, that can lead to decrease of bone mineral density and future progression of cartilage damage.

P3398 | BEDSIDE
Apelin and Visfatin plasma levels in healthy individuals with high normal blood pressure

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Background: High normal blood pressure (BP) (130–139/85–89 mmHg) seems to be related with increased cardiovascular risk compared to normal BP (<120/80 mmHg) or optimal BP (<120/80 mmHg). Low plasma apelin levels have been associated with arterial hypertension and atherosclerosis while high visfatin plasma levels may promote vascular inflammation and atherosclerotic plaque destabilization and have been evaluated as a marker for identifying stages of essential hypertension. We sought to compare the apelin and visfatin plasma levels between subjects with high normal BP and subjects with normal or optimal BP matched for age, gender, smoking, and body mass index (BMI).

Methods: Twenty-five subjects with high normal BP (office BP 136±3/88±2 mmHg and 57±7 years), 76% males, 32% smokers, BMI 24.0±1.7 kg/m² and 35 subjects with normal or optimal BP (office BP 118±2/78±2 mmHg, age 55±7 years, 63% males, 29% smokers, BMI 23.2±1.4 kg/m²) were studied. The apelin and visfatin plasma levels were determined with the enzyme-linked immunosorbent assay.

Results: Compared to normal or optimal BP subjects, apelin levels were significantly lower (205±108 vs. 325±152 pg/ml, p<0.001) and visfatin levels significantly higher (11.0±2.0 vs. 7.2±0.9 ng/ml, p<0.002) in high normal BP subjects. No significant differences were found between the 2 groups (p>NS) regarding the basic clinical characteristics, the glycemic/lipid profile and the renal function parameters.

Conclusions: The emerging, from the present study, lower apelin and higher visfatin plasma levels in high normal BP subjects compared to normal or optimal BP individuals may partially explain the higher cardiovascular risk of the high normal BP group.

P3399 | BEDSIDE
P wave dispersion and its association with hypertension


Hypertension and obesity in adults have been associated with increased P wave dispersion. This is postulated from correlation of hypertension with diastolic function and atrial function. Various atrial conduction due to atrial enlargement could be identified by variation in P wave duration between differently oriented surface electrocardiogram (ECG) leads. Interlead variation in P wave duration is called P wave dispersion (PWD).

Purpose: We aim to assess PWD and its association with hypertension in the CRIsPs Malaysia population.

Methods: CRIsP study is a community-based study conducted between the year 2007 and 2014. Participants were required to complete questionnaires on cardio-vascular risk factors, medical history, physical examinations, blood tests, ECG and echocardiography examinations. P wave dispersions were measured by calculating a minimum of nine leads of P wave duration on the 12 leads ECG. PWD is defined by maximum P wave duration – minimum P wave duration. Exclusion criteria include previous myocardial infarction, thyroid dysfunction, diabetes mellitus, valvular heart disease, cardiomyopathy, electrolyte imbalance, alcoholism and medications that affect atrial conduction. 125 participants with hypertension are randomly selected and their PWD are compared to 125 randomly selected healthy subjects.

Results: A total of 10, 805 subjects participated in the CRIsPs. The mean age was 52.6 years (±11.6) with 56% of females. 25.4% of subjects have a diagnosis of hypertension, 4.4% ischaemic heart disease, 1.3% previous stroke and 11.7% with diabetes mellitus.

Maximum P wave duration is significantly increased in the hypertensive cohort with 116.8±17.7 ms compared to 103.2±22.0 ms in the control group (P<0.001). There is also a significant increase in minimum P wave duration in hypertensive subjects at 53.7±11.8 ms compared to control group with 48.6±15.7 ms (P<0.004). There is a significant increase in the P wave dispersion in hypertensive group at 63.0±18.2 ms compared to control (54.6±21.9 ms) with P<0.001.

Conclusion: P wave dispersion is significantly increased in hypertension. P wave dispersion could be a simple, non invasive method of predicting risk of hypertensive cardiomyopathy in prehypertensive and hypertensive patients.

P3400 | BEDSIDE
The relationship between left atrial area and left ventricular properties in hypertensive and three-dimensional speckle tracking echocardiography study

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Purpose: Left atrial (LA) volume (LAV) and function are strong predictors of cardiovascular outcome. The properties of the LA are very complex due to the close coupling between the LA and left ventricle (LV). The aim of this study was to use speckle tracking echocardiography (STE) to evaluate LA properties including LA deformation parameters and to examine the relationship between LA and LV properties in hypertension (HTN) and hypertensive heart failure (HHF).

Methods: We used 2D-STE and 3D-STE with high volume rates to measure phasic LA emptying function (LAEF), LAV index, LA strain and strain rate (SR) in 53 controls (67±10 years), 105 patients with HTN (69±11 years) and 48 patients with HHF (71±11 years). LAV was measured during the isovolumetric relaxation period and time intervals included previous myocardial infarction, thyroid dysfunction, diabetes mellitus, valvular heart disease, cardiomyopathy, electrolyte imbalance, alcoholism and medications that affect atrial conduction. Echocardiography examinations. P wave dispersions were calculated by measuring LV ejection fraction (LVEF), LV ejection fraction (LVEF), and estimated LV stiffness, systolic and diastolic stress and pulmonary capillary wedge pressure (ePCWP), as we reported previously. ePCWP was calculated as 10.8–2.4 x (active LAEF/minimum LAV). LV stress was calculated as LV diastolic stress thickness. LV stiffness was calculated as LV stress/LV strain by 3D-STE. LA stiffness was estimated as ePCWP/LA strain.

Results: LVEF in HTN was similar to control, but LVEF in HHF was decreased, and this was associated with increased LV systolic stress (LVEF: control 57±5, HTN 55±10, HHF 40±12%2; p<0.05 vs control; LV systolic stress: 62±19, 85±22, 85±40) dynes/cm², respectively). LV and LA stiffness in HHF were increased (LV stiffness: control 0.26±0.09, LV systolic stress: 0.68±0.44; LA stiffness: 0.23±0.19, 0.28±0.30, 1.21±1.1; respectively), and this was associated with increased ePCWP and LV diastolic stress (ePCWP: 7.3±3.4, 15.5±5.5 mmHg; LV diastolic stress: 10.4±3.4, 18.9±5.2 dynes/cm², respectively). Total, passive and active LAEF and LA strain in HTN were similar to control, whereas those parameters were reduced in HHF (total LAEF: control 54±8, HTN 51±12, HHF 36±12%; p<0.05 vs control; LV systolic stress: 62±19, 85±22, 85±40). There was a significant increase in maximum LAV in HHF compared to control (maximum LAV: 42±15, 48±20, 66±21 ml/m² respectively).

Conclusions: LA function including reservoir, conduit and pump function was decreased and LA phasic volume was increased in HHF, and this was associated with increased ePCWP LA strain and LV stiffness, and LV strain. The relationships between LA and LV properties in HTN and HHF were noninvasively assessed by STE.
P3401 | BEDSIDE

Biomarkers of kidney injury and fibrosis in patients with different severity of hypertension

Background: Hypertension is a known risk factor promoting kidney dysfunction, fibrosis resulting in end-stage renal disease. The early timely detection of kidney injury may have an impact on treatment strategy and patient’s prognosis.

Purpose: The aim of the present study was to compare conventional and some new potentially more early and sensitive investigational biomarkers (urine and ultrasound) of kidney injury in patients with different severity of hypertension.

Methods: Urine levels of neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule-1 (KIM-1), liver fatty-acid binding protein (L-FABP) and serum levels of Cystatin C and creatinine were measured by quantitative enzyme immunoassay in 92 hypertensive patients, divided into four age and sex-matched groups according to severity of hypertension: 1 degree (n=24), 2 degree (n=26), 3 degree (n=17) and resistant hypertension (n=25). Glomerular filtration rate (GFR) was estimated by MDRD and CKD-EPI formulas. Instrumental examination was performed after 5 days of discontinuation of antihypertensive medications and included Doppler ultrasonography with assessment of intraparenchymal renal arterial resistance indices - RI and PI (Vivid 7 dimension) and ambulatory blood pressure monitoring (ABPM, Space Labs 9207).

Results: Patients with 1, 2, 3 degrees of hypertension had no differences in Cystatin C, L-FABP, NGAL, KIM-1, creatinine levels, eGFR and ultrasound RI and PI. Patients with resistant hypertension were characterized by higher Cystatin C (0.97±0.18 pg/mL; p<0.01) and L-FABP (9270.2±3094.5 pg/mL; p<0.05) levels, associated with mean 24-hours systolic blood pressure (BP) level (r=0.246, p=0.03 and r=0.339, p=0.006 respectively) and higher RI in right and left arcuate arteries (0.61±0.07; 0.61±0.07; p=0.04), PI in right and left arcuate arteries (1.06±0.23; 1.08±0.25; p=0.03), higher RI in right and left intralobular arteries (0.62±0.09; 0.64±0.08; p=0.04) and PI in right and left intralobular arteries (1.07±0.29; 1.16±0.29; p=0.02). Also in hypertensive patients mean 24-hours BP levels were associated with PI in right and left arcuate arteries (r=0.309, p<0.02 and r=0.369, p=0.008, respectively), RI in right and left intralobular arteries (r=0.295, p<0.03 and r=0.346, p=0.01, respectively), PI in right and left intralobular arteries (r=0.309, p<0.02 and r=0.391, p<0.006, respectively). In addition in hypertensive patients Cystatin C were associated with RI in right and left intralobular arteries (r=0.257, p=0.04 and r=0.402, p=0.001, respectively), PI in right and left intralobular arteries (r=0.267, p=0.04 and r=0.419, p=0.001, respectively).

Conclusions: Cystatin C, L-FABP and intraparenchymal renal arterial resistance indices seem to be potentially more sensitive biomarkers of kidney injury and fibrosis than conventional biomarkers, and their levels increase with the severity of hypertension.

P3402 | BENCH

Apelin and relaxin levels as a cardiometabolic risk factor in young healthy offspring of hypertensive patients
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Background: Healthy offspring of hypertensive patients exhibit several features of metabolic syndrome. Adipocytokines are implicated in metabolic syndrome by affecting insulin sensitivity, glucose and lipids metabolism. The exact role of apelin and relaxin adipocytokines in the development of a variety cardiovascular diseases is still under research.

Purpose: We aimed to determine apelin and relaxin levels in healthy offspring of hypertensive patients.

Methods: Forty-six healthy offspring of hypertensive patients, (Group A), and 50 healthy offspring of normotensive parents (Group B), matched by gender, age, and body mass index (BMI) were studied. The apelin and relaxin plasma levels were calculated by enzyme-linked immunosorbent assay (ELISA) method.

Results: Group A showed significantly lower plasma apelin and relaxin levels compared with group B (Table 1).

Table 1

<table>
<thead>
<tr>
<th></th>
<th>Group A (n=46)</th>
<th>Group B (n=50)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>18±3</td>
<td>18±3</td>
<td>NS</td>
</tr>
<tr>
<td>Male gender</td>
<td>24</td>
<td>28</td>
<td>NS</td>
</tr>
<tr>
<td>Body mass index (BMI, kg/m²)</td>
<td>22±1.4</td>
<td>22±1.7</td>
<td>NS</td>
</tr>
<tr>
<td>Apelin (pg/mL)</td>
<td>6±3</td>
<td>105</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Relaxin (pg/mL)</td>
<td>0.07±0.07</td>
<td>0.01±0.01</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Conclusion: Our findings suggest that healthy offspring of hypertensive patients have significantly lower plasma apelin and relaxin levels than those with normotensive parents, indicating a potential cardiometabolic risk factor. Further studies will warrant this implication.

P3403 | BENCH

ANP-aldosterone imbalance in human hypertension in the general community
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Background: Higher plasma aldosterone (ALDO) and lower natriuretic peptides levels, especially atrial natriuretic peptide (ANP) which is an inhibitor of ALDO synthesis, may play a causal role in hypertension (HTN) and a pathological imbalance in the ANP/ALDO axis may exist.

Purpose: Investigate the role of ALDO, ANP and their interrelationship in human HTN.

Methods: We stratified a cohort from the general community living in Olmsted County, based on the presence (n=477) or absence (n=1073) of a diagnosis (Dx) of HTN. We analyzed plasma ALDO and ANP levels according to the number of antihypertensives taken. We then compared subjects with Dx of HTN (treated and non-treated) to subjects with elevated blood pressure (BP) but treatment free at the study visit, and to subjects taking cardiovascular drugs, including antihypertensives, without Dx of HTN.

Results: Subjects with Dx of HTN had higher ALDO and ANP levels, greater BMI and prevalence of diabetes. Subjects with Dx of HTN taking 3 or more antihypertensives showed an inverse relationship between ALDO (higher) and ANP (lower). Interestingly, subjects with elevated BP but treatment free at the study visit had lower ANP levels, and subjects taking antihypertensives for non-HTN indications had higher plasma ANP and greater prevalence of cardiac disease.

Conclusions: Our results extend the concept that higher plasma ALDO and lower ANP may contribute to the pathogenesis of HTN. Further studies are needed for a tailored treatment with ALDO antagonists and/or ANP-like drugs to compensate for ALDO excess and ANP deficiency in human HTN.

P3404 | BEDSIDE

Chronic depression symptoms and salivary NOx are associated with retinal vascular dysregulation: the SABPA study
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Background: Depression has been associated with impaired nitric oxide (NO)-mediated vasodilation and vascular dysregulation (VD). Whether depression and NO levels will disturb retinal hemodynamics is not clear.

Purpose: Associations between the retinal vascular, diastolic ocular perfusion pressure (DOPP) as measure of hyperperfusion, NO metabolites (NOx) and depression symptoms were assessed.

Methods: Chronic VD risk markers [depression symptoms (Patient Health Questionnaire/PHQ-9 >10) and 24h pulse pressure] were determined in a bi-ethnic cohort (n=313; 48±6±9 years; 53.9±0.6 men). At 3 year follow-up, retinal vessel calibre and retinopathy signs were quantified from digital images. Salivary

...
NOx was obtained pre- and post-flicker light-induced provocation (FLIP). DOPP was defined as diastolic blood pressure minus intracocular pressure.

**Results:** Chronic NO deficiency was evident in Blacks opposed to acute risk in Whites (P<0.05). At follow-up, retinopathy (Blacks 60.4%;Whites 39.6%), lower pre-FLIP (μM) and higher post-FLIP NOx (changes from baseline, %), arteriolar narrowing and wider retinal macular volume were evident in Blacks compared to Whites independent of confounders. A wider venular calibre, an index of stroke risk, was associated with chronic depression symptoms [cut point 248 MU: Area under the curve 0.61 (95% CI: 0.51, 0.72); 71% sensitivity; 55% specificity] as well as with hypertension especially in the general population.

**Conclusions:** Chronic depression symptoms may alter NO regulation and facilitate NO-mediated vasorelaxation presumably impeded perfusion, retinal hemodynamics and -remodelling; potentiating stroke risk in Blacks.

**Acknowledgement/Funding:** National Research Foundation, Medical Research Council-, ROCHE Diagnostics-, North-West University-, North-West Department of Education, South Africa,

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**P3406 | BESDIE**

**Observational cohort study on changes in peripheral and central blood pressures**

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**Background:** Standard measurements of brachial blood pressure are the pow-erful markers of cardiovascular morbidity and mortality. Although recent studies suggest that central blood pressure is more closely associated with cardiovas-cular outcomes, their changes in clinical practice is hampered by a limited data of central blood pressure. Their baseline brachial blood pressure was 122.3±14.7/75.0±9.6 mmHg (Systolic/Diastolic) and central blood pressure was 113.0±19.1 mmHg. In this 4-subset analysis of the Japanese population, we assessed the impact of disease length on long term changes in central blood pressure (from 111.5±18.5 to 115.5±18.6 mmHg; p<0.001; yearly change 0.1±3.3 mmHg) were greater than those in central systolic blood pressure (from 122.3±14.2 to 120.8±13.8 mmHg; p=0.3; yearly change 0.1±3.1 mmHg). Interestingly, both central and brachial systolic blood pressure did not change throughout the follow-up period in participants with antihypertensive medication.

**Conclusions:** Central blood pressure more progressively increases with age than brachial blood pressure. Observation of brachial, but not central, blood pressure may overlook a concealed increase of cardiovascular risk. Appropriate antihypertensive medications seem to prevent an increase in both central and brachial blood pressure.

**IMPACT OF STENT DESIGN ON POST PCI OUTCOMES**

**P3406 | BESDIE**

Eight-year clinical outcome of sirolimus-eluting stent implantation for small vessel disease

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**Background:** Late adverse events such as very late stent thrombosis (ST) or late target lesion revascularization (TLR) after sirolimus-eluting stent (SES) implantation remain an important concern. However, there is little data on very long-term outcomes of SES implantation for small vessel disease (SVD).

**Purpose:** We sought to assess the very long-term outcomes of SES implantation for small and large vessel disease.

**Methods:** A total of 985 consecutive patients with 1307 lesions undergoing percutaneous coronary intervention treated only with SES implantation were retro-spectively analyzed. According to the presence of SVD (patients receiving only 2.5-mm stents), we divided the patients into the 2 groups: SES group (n=415 pa-tients with 612 lesions) and non-SVD group (n=570 patients with 695 lesions). The primary endpoint was the cumulative 8-year incidence of major adverse car-diac events (MACE), defined as cardiac death, myocardial infarction (MI), TLR and ST.

**Results:** Cumulative 8-year incidence of MACE was not significant difference between the SVD and non-SVD groups (46.0% vs. 46.1%, P=0.61). No significant differences in the cumulative incidence of cardiac death, MI, TLR and ST in both groups were found (6.6% vs. 7.0%, P=0.7; 5.0% vs. 5.0%, P=0.81; 31.0% vs. 32.9%, P=0.45; 2.3% vs. 2.2%, P=0.98). Hemodialysis (HR 2.68, 95% CI: 1.92–3.75, P<0.01) and vessel disease (HR 1.29, 95% CI: 1.05–1.58, P=0.01) were independent predictors of MACE.

**Figure. Kaplan-Meier curves for 8-year incidence of MACE**

**Conclusions:** Very long-term outcomes of SES implantation for SVD are compara-ble to those for non-SVD lesions.

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**P3407 | BESDIE**

**Paclitaxel- versus zotarolimus-eluting stents in diffuse coronary artery disease; 3-year clinical outcomes**

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**Purpose:** We assessed the impact of disease length on long term clinical outcome following successful PCI with paclitaxel-eluting stents (PES) and zotarolimus eluting stents (ZES).

**Methods:** A total of 656 consecutive patients (pts) underwent PCI who have dif-fuse coronary artery disease were divided into two groups. (PES group = 351, ZES group = 305). Long-term clinical outcome was defined as target lesion longer than 30 mm. Individual and composite clinical outcomes were compared between the two groups up to 3 years.

**Results:** The baseline clinical characteristics were similar between the two groups except previous PCI and cerebrovascular accident (CVA) was more fre-quent in the PES group. In-hospital and procedural complications were similar between the two groups except dissection (23.6% vs. 10.5%, P<0.001). During 3-year clinical follow-up, the PES group showed higher incidence of target lesion.
revascularization (TLR), target vessel revascularization (TVR) and major adverse cardiac event (MACE) than ZES group (table). Following adjustment for baseline confounders, the PES group was still associated with higher incidence of TLR (HR 3.50, 95% CI 1.91 to 6.44; p = 0.001), TVR (HR 3.04, 95% CI 1.74 to 5.30; p < 0.001) and MACE (HR 2.37, 95% CI 1.57 to 3.49; p < 0.005) compared with the ZES group.

Conclusion: For pts with diffuse long coronary artery lesion, ZES rather than PES was associated with improved event-free survival including MACE during 3-year clinical follow-up period.

P3408 | BEDSIDE
Effect of diameter of drug-eluting stents versus bare-metal stents on late outcomes: a propensity score-matched analysis

Introduction: Drug eluting stents (DES) have been shown to reduce major adverse cardiovascular events (MACE) after percutaneous coronary intervention (PCI), as compared with bare-metal stents (BMS). However, the benefits of the use of DES remains uncertain for large diameter stents.

Purpose: We therefore aimed to compare outcomes of DES and BMS for small and large diameter stents separately.

Methods: We evaluated 12785 consecutive patients who underwent PCI from April 2004 to August 2014. Median follow up was 6.4 years. Propensity score matching analysis was used to identify 3119 pairs of patients with at least one small diameter stent (<3.5 mm), and 517 pairs of patients with large diameter stents only (≥3.5 mm). Performance of DES versus BMS was compared separately in each group. Outcomes included all cause death, MI, target vessel revascularization and coronary artery bypass grafting.

Results: Mean age in the large and small stent diameter groups was 68±12 and 69±12 years respectively (p = 0.001) and female gender was 18% and 25% respectively (p = 0.001). Acute cases (i.e. MI or ACS) comprised 63% and 60% (p = 0.016) and STEMI cases 9% and 6.6% (p = 0.001) of large and small diameter stents respectively. After performance of propensity score matching, the placement of a large diameter stent BMS was associated with higher death rate (HR 1.49; 95% CI: 1.28–1.74; p < 0.0001), higher rate of re-MI or death (HR 1.49; 95% CI: 1.3–1.71; p = 0.0001) and higher rate of PCI or CABG (HR 1.5; 95% CI: 1.5 1.28–1.75; p < 0.0001) as compared with DES in small stents. However, there was no significant difference in outcomes between BMS and DES in larger stents.

Figure 1 - Kaplan meier curves for outcomes in respect to stent type and diameter

Figure 1

Conclusions: In the current propensity score matched registry based study, long term outcomes were better with DES as compared to BMS when small stents were used but not when only large diameter stents were used.

P3409 | BEDSIDE
Long-term clinical outcomes of complete versus partial stent fracture after second-generation drug-eluting stent implantation
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Objectives: There were several reports about stent fracture (SF) after first-generation drug-eluting stents (DES) implantation. Though it is still noted in the newer generation DESs, we do not know the long-term clinical significance.

Methods: A total of 1444 lesions of 1040 patients treated with second-generation DES from March 2010 to March 2013 were analyzed retrospectively. Complete fracture (CF) was defined as no visible strut on intra-vascular ultrasound (IVUS), optical coherence tomography (OCT), or plain fluoroscopy and partial fracture (PF) was defined as at least one visible strut on IVUS or OCT in stent segments at 12-month follow-up coronary angiography. All implanted stents were second-generation DESs of which materials were cobalt-chromium, platinum-chromium, and stainless steel. We assessed the cumulative incidence of target lesion failure which included cardiac death, target vessel myocardial infarction (MI), and clinically driven target lesion revascularization (TLR) within 36 months after the index procedure.

Results: At 12-month angiographic follow-up, SF was identified in 60 of 1444 lesions (4.2%). Of 60 lesions of SF, there were complete fractures in 11 lesions (12%) and partial fractures in 49 lesions (82%). At 36 months, the cumulative incidence of TLF was significantly higher in CF group than in PF group (72.7% vs. 6.1%, p = 0.001). However, there was no difference in TLF between PF group and non-stent fracture (NSF) group (6.1% vs. 5.1%). The cumulative incidence of cardiac death was similar between the CF, PF, and NSF group (0.6% vs. 2.6% vs. 0.8%, p = 0.489), however, the cumulative incidence of target vessel MI (0.1% vs. 4.1% vs. 0.4%, p = 0.001) and TLF (63.6% vs. 4.1% vs. 4.3%, p < 0.001) were significantly higher in CF group than in PF and NSF group. The Cumulative incidence of in-stent restenosis was much higher in CF group than in PF and NSF group (81.8% vs. 14.3% vs. 4.4%, p < 0.001). Lesions with overlapping stent more than 3.5 mm (odds ratio [OR]: 16.48, 95% confidence intervals [CI]: 1.62 to 168.00; p = 0.018) or hinge motion (OR: 16.59, 95% CI: 1.28 to 218.34; p = 0.033), and patients with diabetes mellitus (OR: 11.93, 95% CI: 1.22 to 116.42; p = 0.033) or current smokers (OR: 23.36, 95% CI: 2.70 to 220.86; p < 0.005) were independently associated with complete stent fracture.

Conclusions: Complete stent fracture after second-generation DES was highly associated with long-term target lesion failure. Partial stent fracture seems to be comparable to non-stent fracture even in long-term clinical follow-up.

P3410 | BEDSIDE
Long-term clinical impact of stent fracture on second generation drug-eluting stent in comparison with first generation drug-eluting stent

Background: How stent fracture (SF) can affect the clinical outcomes of lesions after the treatment with second generation drug-eluting stent (G2-DES) in the long-term remains unknown.

Purpose: To assess the long-term clinical impact of SF on G2-DES (Xience everolimus, Promus element everolimus, and Nobori biolimus-eluting stents) in comparison with first generation drug-eluting stent (G1-DES, Cypher sirolimus-eluting stent).

Methods: The study sample consisted of 12404 lesions treated with DES (6114 with G2-DES and 6290 with G1-DES) between 2003 and 2013 at a single centre. SF was angiographically defined as the separation of stent segments or struts. The assessment of long-term clinical outcomes was done with the Kaplan-Meier method and log-rank test. Target lesion revascularisation (TLR) was defined as angiographically or clinically driven TLR. Stent thrombosis (ST) was defined according to the Academic Research Consortium definitions.

Results: SF of G2-DES occurred in 2.3% (142/6114 lesions) and that of G1-DES in 4.9% (311/6290 lesions) (p < 0.001). The median follow-up durations of the G2-DES and G1-DES groups were 3.7 and 6.3 years (the first and third quartiles, 3.2 and 4.7, 5.5 and 7.0 years). The 4-year cumulative rate of TLR was not sig-
Minimal lumen diameter (MLD) assessed by Quantitative coronary angiography (QCA) in all (30) patients increased from 0.93±0.35 at baseline to 2.85±0.38 mm post-procedure and the percentage of diameter stenosis was reduced from 68.8±12.6 to 41.2±7.8%. IVUS showed MLD increasing from 0,90±0,38 mm at baseline to 2,6±0,4 mm post-apposition (ISA) in 1 case treated with non-compliant balloon post-dilation. OCT of Medicine and Health Sciences, Campobasso, Italy;6 Ospedale G. Grassi, Bologna, Italy;7 Cattedra A. Cardarelli, Department of Cardiology, Cardarelli, Italy;8 Ospedale F. Vianello, Department of Cardiology, Catania, Italy;9 Campus Bio-Medico University of Rome, Department of Cardiology, Rome, Italy;10 University of Molfese, Department of Medicine and Health Sciences, Campobasso, Italy;6 Ospedale G. Grassi, Department of Cardiology, Ostia, Rome, Italy

Introduction: Biodegradable scaffolds (BRS) represent a great innovation in the field of percutaneous coronary interventions (PCI). These devices provide a temporary vascular support, together with anti-proliferative drug release, before complete disappearance in about 1–2 years. However some technical issues have emerged, mainly related to “structural” weaknesses of the first models, such as too fast resorption resulting in poor vascular support, acute narrowing (recoil) of the scaffold because of insufficient radial stress, strut fracture due to a rapid or excessive dilation over the nominal diameter. These issues have led to the development of new BRS with improved features. The DESolve scaffold may be considered as the “second generation” biodegradable scaffold, due to innovative features such as bioreorption profile, self-correction to nominal diameter and fracture resistance.

Purpose: To describe the performance of a second-generation BRS in various clinical settings.

Methods: From January to December 2015, we performed PCI with DESolve in 30 patients with mean age 51.8±8 years. In 20 patients (66.7% of cases) PCI was performed due to an Acute Coronary Syndrome and in 7 (23.3%) during Primary PCI for ST-elevation myocardial infarction. The scaffold positioning required intravascular ultrasound (IVUS) in 13 procedures (43.3%), Optical coherence tomography (OCT) in 15 procedures (50%) and fractional flow reserve (FFR) was performed to assess functional severity of borderline lesions in 5 cases (16.7%). The measures of implanted scaffolds ranged from 2.5 mm to 3.5 mm of diameter.

Results: Minimal lumen diameter (MLD) assessed by Quantitative coronary angiography (QCA) in all (30) patients increased from 0.93±0.35 at baseline to 2.85±0.38 mm post-procedure and the percentage of diameter stenosis was reduced from 68.8±12.6 to 41.2±7.8%. IVUS showed MLD increasing from 0.90±0.38 mm at baseline to 2.6±0.4 mm post-procedure, whereas MLD raised from 2.34±0.65 mm to 5.2±1.6 mm and ISA in 3 cases of which 2 achieved by self-correction properties of this device and 1 treated with non-compliant balloon post-dilation. No fractured struts were highlighted at OCT. In all STEMI cases (7/7) final TIMI flow 3 was achieved.

Conclusion: PCI with implantation of last generation BRS proved a good post-procedural result in a small group of patients from a single center. Our experience with DESolve scaffolds showed absence of the most common technical problems related to BRS implantation, such as acute recoil or stent struts fracture, confirming some innovative features of this device, consisting mainly in self-correction properties and struts fracture resistance.
Conclusions: There is a beneficial impact of coronary revascularization on long-term survival in patients with an ischemic DSE. Coronary revascularization was associated with a favorable outcome both in patients with limited ischemia and in those with substantial ischemia.

P3414 | BEDSIDE
Review of cardiology guidelines recommendations on revascularization: considerations for clinical practice
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Background: Current guidelines (ACC and ESC) on revascularization recommend selection of CABG over PCI for patients with complex and multi vessel disease. The rankings include Class I/Level A, B or Appropriate for CABG and Class IIa, III/Level B or Uncertain for PCI, respectively. None of the definitions for classes or levels include the “strength” of the evidence. Yet, the rankings are being applied in clinical practice as if the evidence is both accurate and certain. This paper examines the evidence cited by the guidelines with a critical eye to provide clinicians with a clearer picture about appropriate strategies for revascularization.

Methods: The authors conducted a literature review and critical appraisal of each study cited as evidence in support of the guideline rankings. A thorough critical appraisal was conducted by both authors to determine each study’s strengths and weaknesses. Each critical appraisal included a re-calculation of per-protocol and intention-to-treat analyses by the statistician. The results are presented in terms of study limitations effecting evidence rankings and explained in terms of clinical practice implications.

Results: The 5-Year SYNTAX Trial findings were significantly different after the intention-to-treat analysis and the accounting of all patients. Reported MAACE (11.3%) of patients lost to follow up are included in the intention-to-treat analysis, and 16% of the variation for in-hospital mortality (ICC) was attributable to between-hospital differences. Models were adjusted for patient case mix (including demographics and co-morbidities), clinical factors (including the seniority of primary operator and drug treatment before and during PCI), and year of PCI.

Conclusions: Differences in hospital services accounted for 16% of variation for in-hospital mortality after primary PCI for STEMI. Ancillary results for treatment groups are presented in detail in the trials. The SYNTAX Trial and the FREEDOM Trial fail to provide precise and reproducible findings in terms of comparing CABG and PCI for revascularization of patients with multi vessel disease. Yet, the guidelines depend heavily on these two trials for their rankings. There is no clear benefit gained by CABG over PCI from these studies when results are either imprecise or irreproducible. The use of bioabsorbable everolimus-eluting scaffolds (BVS) in myocardial infarction (MI) is limited and its efficacy is unknown. We evaluated the use and results of the Absorb in the STEMI in a tertiary hospital.

Material and methods: Two cohorts of consecutive patients with STEMI were prospectively analyzed. The cohort A of 128 patients with BVS selected between 2012 and 2015 and cohort B of 150 patients treated with everolimus-eluting metallic stents (DES) selected between 2009 and 2012.

Results: Patients of group A vs group B were significantly less diabetics (20% vs 34%), younger (58 vs 53 years) and less multivessel (13% vs 33%). Number of devices released was smaller (1.1 vs 1.3) the length stent was shorter (21 vs 27mm) and predilatation was more common (68% vs 48%) in the cohort A. Procedural success (98 vs 99%), myocardial death at 30 days (1.6% vs 1.4%) and rate of early thrombosis (1.6% vs 0.7%) were similar in both groups. We performed a meta-analysis of the cohort A of 489 days in the BVS group and of 1159 days in the DES group. Kaplan-Meier curves showed a similar survival time free of CV death (Logrank 0.99). However, in the Group A we evidenced a higher rate of TLR (Logrank 0.04) and a tendency for major event composite CV death, definitive device thrombosis and TLR (log rank 0.09).

Conclusion: The use of BVS in the context of STEMI was feasible. Comparing with patients previously treated with DES, patients who underwent an implant of BVS were more selected. During follow-up composite end-point was similar, however we underline a higher TLR in patients with BVS.

P3416 | BEDSIDE
Between-hospital variation in mortality after percutaneous coronary intervention (PCI) for ST-elevation myocardial infarction in England

Background and introduction: Primary percutaneous coronary intervention (PCI) for ST-elevation myocardial infarction (STEMI) is the gold standard of treatment. However, the extent of between-hospital variation in outcomes after PCI remains unclear.

Purpose: To determine between-hospital variation for in-hospital, 30-day, 90-day and 1-year mortality after percutaneous coronary intervention for ST-elevation myocardial infarction in England.

Methods: Data was obtained from the National Institute for Cardiovascular Outcomes Research registry of all PCI in England between 2007–2013. We included all patients for whom 1-year mortality data were available and who had undergone PCI for STEMI without primary thrombolysis; this equated to 85% of all PCI for STEMI in England. We built hierarchical multivariable logistic regression models from which we generated the intra-class correlation coefficient (ICC) to explore the proportion of variation attributable to between-hospital differences. Models were adjusted for patient case mix (including demographics and co-morbidities), clinical factors (including the seniority of primary operator and drug treatment before and during PCI), and year of PCI.

Results: 101,811 patients were analysed. The median (IQR) age of patients was 64 (54–74) and 74% of patients were male. 40% of patients were current smokers, 27% former smokers and 33% had never smoked. Adjusting for patient case mix, median (IQR) in-hospital mortality was 5.1% (4.5–5.8%), rising to 6.6% (5.8–7.3%) at 30 days, 7.8% (6.9–8.5%) at 90 days, and 10.4% (9.3–13.7%) 1 year after PCI. 16% of the variation for in-hospital mortality (ICC) was attributable to differences between individual hospitals after adjusting for patient case mix, clinical factors and year of PCI, reducing to 7% at 30-days, 6% at 90-days and 4% at 1 year after PCI.

Conclusions: Differences in hospital services account for 16% of variation for in-hospital mortality after primary PCI for STEMI. Ancillary results for treatment groups are presented in detail in the trials. The SYNTAX Trial and the FREEDOM Trial fail to provide precise and reproducible findings in terms of comparing CABG and PCI for revascularization of patients with multi vessel disease. Yet, the guidelines depend heavily on these two trials for their rankings. There is no clear benefit gained by CABG over PCI from these studies when results are either imprecise or irreproducible. The use of bioabsorbable everolimus-eluting scaffolds (BVS) in myocardial infarction (MI) is limited and its efficacy is unknown. We evaluated the use and results of the Absorb in the STEMI in a tertiary hospital.

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Results: Patients of group A vs group B were significantly less diabetics (20% vs 34%), younger (58 vs 53 years) and less multivessel (13% vs 33%). Number of devices released was smaller (1.1 vs 1.3) the length stent was shorter (21 vs 27mm) and predilatation was more common (68% vs 48%) in the cohort A. Procedural success (98 vs 99%), myocardial death at 30 days (1.6% vs 1.4%) and rate of early thrombosis (1.6% vs 0.7%) were similar in both groups. We performed a meta-analysis of the cohort A of 489 days in the BVS group and of 1159 days in the DES group. Kaplan-Meier curves showed a similar survival time free of CV death (Logrank 0.99). However, in the Group A we evidenced a higher rate of TLR (Logrank 0.04) and a tendency for major event composite CV death, definitive device thrombosis and TLR (log rank 0.09).

Conclusion: The use of BVS in the context of STEMI was feasible. Comparing with patients previously treated with DES, patients who underwent an implant of BVS were more selected. During follow-up composite end-point was similar, however we underline a higher TLR in patients with BVS.

P3417 | BEDSIDE
Clinical outcome of percutaneous coronary intervention (PCI) in elderly and very elderly patients: 1-year results from a tertiary-centre experience
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Background: Elderly patients represent a rapidly growing cohort for PCI and the results from the Elderly patients experience both in patients with limited ischemia and in those with substantial ischemia.

Objective: To investigate clinical outcome of percutaneous coronary intervention (PCI) in elderly (>75 years old) patients.

Material and methods: 670 unrestricted consecutive >75 years old patients, who underwent elective or urgent PCI, were enrolled in this single-centre observational study between January 2012 and July 2015: 588 patients (88%) were classified as “Elderly” (>75 and ≤85 years old) and 82 (12%) were classified as “Very Elderly” (>85 years old). The primary endpoint of the study was the incidence of net adverse clinical events (NACE), composite of overall death, nonfatal major adverse cardiac events and stroke or major adverse cardiovascular death (MACE). The secondary endpoints were major adverse cardiovascular events (MACE), Bleeding Academic Research Consortium (BARC) type 1, 2, 3, 5 bleeding, at 1-year. Secondary end point was the incidence of each components of primary end point at 1-year.
Impact of stent design on post PCI outcomes

P3418 | BEDSIDE

Twelve versus 30 month dual antiplatelet therapy after percutaneous coronary intervention using national health insurance review & assessment (HIRA) database

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Background: Current PCI (Percutaneous Coronary Intervention) guideline recommends that clopidogrel, at a dose of 75 mg daily, should be given for at least 12 months after implantation of stents if patients are not at high risk for bleeding. However, the optimal duration of dual antiplatelet therapy (DAPT) and the risk–benefit ratio for long-term dual antiplatelet therapy remains unclear. The aim of this study was to evaluate the effect of DAPT on cancer occurrence and death rate using Korean National Health Insurance Review & Assessment (HIRA) database.

Methods: From 2009 to 2013, 240,254 PCI patients were included from HIRA database. We divided patients who had prior PCI, cancer diagnosis detected one year after PCI and irregular doses or interrupted medication history tracked by insurance data records as well as drug store selling records. Finally 26,666 patients, who included, had who DAPT for a year and continued medication of total 30 month’s duration, either DAPT or aspirin. Detection of new cancer occurrence were searched by The International Statistical Classification of Diseases and Related Health Problems, ICD-10 code.

Results: A total of 26,666 patients were enrolled at HIRA data base: DAPT (n=14,510) and aspirin alone (n=12,156). Two groups were well balanced with regards to most baseline characteristics. The mean age was 66 vs 65 yrs, percentage of male, 67.8% vs 68.2%, hypertension 60.7% vs 55.9%, dyslipidemia 37.2 vs 34.0%, and diabetes 29.7 vs 25.0% (DAPT vs aspirin only group each). The total rate and new cancer occurrence rate during the follow up were shown in Table 1.

Table 1. Death and Cancer Rate by Group

<table>
<thead>
<tr>
<th>Group</th>
<th>12-month Cancer</th>
<th>30-month Cancer</th>
<th>Group</th>
<th>12-month Cancer</th>
<th>30-month Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAPT</td>
<td>163 (1.1%)</td>
<td>936 (6.5%)</td>
<td>Group 2</td>
<td>12-month Cancer</td>
<td>30-month Cancer</td>
</tr>
<tr>
<td></td>
<td>93 (0.8%)</td>
<td>727 (6.0%)</td>
<td></td>
<td>256 (1.0%)</td>
<td>1663 (6.2%)</td>
</tr>
</tbody>
</table>

Conclusion: The use of DAPT longer than 12 months have tended to have slightly higher death rate and new cancer incidence rate than aspirin alone group. Detailed information will be presented.

Acknowledgement/Funding: The Ministry of Health & Welfare (No. HI14C1731) and National Research Foundation of Korea (NRF) (No. 2015R1D1A1A09057025)

P3419 | BENCH

Percutaneous coronary intervention in ninety-year-old patients

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Background: Elderly people represent a significant part of the Brazilian population and the population >90 years has tripled in the past three decades. This retrospective study was aimed at analyzing the results of percutaneous coronary intervention in ninety-year-old patients.

Methods: Overall, 31 ninety-year-old patients (G1) undergoing percutaneous coronary treatment from January 1995 to January 2009 were retrospectively evaluated. These patients were compared to 6,222 patients <80 years of age (G2), treated within the same period. Clinical, angiographic and procedure characteristics were assessed as well as early and late major adverse cardiovascular events (MACE) (death, stroke, myocardial infarction, recurrent ischemia).

Results: Ninety-year-old patients had a greater prevalence of diabetes, unstable angina, chronic comorbidities, three vessel coronary disease and left ventricular ejection fraction <50%. Procedure success was different between both groups (87% vs. 95.1%, P=0.049), as well as the incidence of in-hospital death (6.4% vs. 0.3%; P=0.022) and acute myocardial infarction (6.4% vs. 3.6%; P=0.035). In the late follow-up, there were significant differences in survival free from MACE (68% vs. 91%; P=0.001). Left ventricular ejection fraction <50% (RR 1.08, IC 0.99–1.08; P=0.022), <2 vessel disease (RR 1.82, IC 1.04–3.19; P=0.011), left main coronary artery lesion (RR 2.98, IC 0.97–9.17; P=0.001), presence of unstable angina (RR 2.48, IC 0.97–19; P=0.0013) and diabetes (RR 2.35, IC 1.21–4.55; P=0.0015) were MACE predicting variables.

Conclusion: Ninety-year-old patients had a higher incidence of cardiovascular events than younger patients. However, when the technique is feasible and patients have good clinical condition, percutaneous coronary intervention may be effectively used with an acceptable

P3420 | BEDSIDE

Incidence and clinical impact of longitudinal stent deformation after the promus element platinum chromium-everolimus eluting stent implantation

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Background: The PROMUS Element platinum-chromium everolimus-eluting stent (PiCr-EES) has a novel metal and stent design intended to improve deliverability, conformability, and radial strength, whereas such features might have the trade-off of reducing longitudinal stent strength, which would account for the occurrence of longitudinal stent deformation (LSD) as reported previously. However, the incidence and clinical impact of LSD after PiCr-EES implantation in clinical practice have not been fully evaluated.

Methods: A total of 804 patients with 1051 lesions undergoing PiCr-EES implantation between March 2012 and August 2013 were analyzed. LSD was defined as the distortion or shortening and elongation of a stent in the longitudinal axis following successful stent deployment. We assessed the incidence of longitudinal stent deformation and cumulative incidence of major adverse cardiac events (MACE), defined as a composite of cardiac death, non-fatal myocardial infarction, definite stent thrombosis, and clinically driven target lesion revascularization within 2-year.

Results: Of 804 patients with 1051 lesions, we performed an intravascular ultrasound (IVUS) and post-dilatation in 787 patients (97.9%) with 1031 lesions (98.1%) and in 407 patients (50.6%) with 512 lesions (48.7%). In the LSD group, IVUS and post-dilatation were performed in all patients. LSD was observed in 17 patients (2.1%) with 17 lesions (1.6%). The mechanism of LSD was due to the following reasons: compression by post-dilatation balloons (n=2, 11.8%), entrapped IVUS (n=12, 70.6%) and pull back jailed guide wire (n=3, 17.6%). At 2-year, the cumulative incidence of MACE, cardiac death, myocardial infarction, stent thrombosis and clinically driven target lesion revascularization were not significantly different between the LSD and non-LSD groups (6.3% vs. 6.4%, p=0.84; 0.6% vs. 0.9%, p=0.76; 0% vs. 0.6%, p=0.77; 6.3% vs. 5.8%, p=0.77, respectively).

Conclusions: LSD after PiCr-EES implantation occurs in 1.6% of lesions. However, LSD is not associated with MACE within 2-year.

P3421 | BEDSIDE

One-year clinical and angiographic outcomes of everolimus-eluting stent in the very small coronary artery; results of Xience PRIME SV PMS

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Background: Percutaneous coronary intervention (PCI) for small vessels has been one of the worst subsets of lesions in terms of restenosis and target lesion revascularization. Reports with sufficient number of patients and angiographic follow-up data have never been published with regard to the very small vessel (<2.25 mm) so far.

Purpose: Xience Prime (XP) is a second generation Cobalt-chromium everolimus-eluting stent CoCr-EES) with a small size variation of 2.25 mm in diameter. This post marketing study (PMS) Japan is a prospective registry designed to evaluate the safety and efficacy of XP stents for very small vessel in routine clinical practice at 30 centers representative of the clinical environment nationwide.

Methods: Consecutive 312 patients who underwent PCI using at least one 2.25-mm XP with 326 lesions were enrolled and followed up to 1 year. Seven patients were excluded because of lost to follow-up or patients’ refusal. Follow-up angiograms at 8months were assessed by qualitatively and quantitatively in 226
patients with 239 lesions using QCA system (QAngio ver. 7, MEDIS) in the independent corelab.

Results: Seventy-five percent of patients were male, and mean age was 70. Coronary risk factors were 17% of smoking, 85% of hypertension, 71% of dyslipidemia, 54% of diabetes, and 4.5% received hemodialysis. PCI was performed for ACS in 25% of the cases. De novo lesion was 93%. Lesion was located in RCA 22%, LAD 34%, LCx 37%, LM 0.3%, HL 6%, and SVG 0.3%. Complex lesion morphologies assessed by the corelab were as follows: ACC/AHA type B2 42.5%, type C 36.3%, bifurcation 34.7%, ostial 12.2%, moderate/severe calcification 21.6%, GFOC 2.2%.

Mean reference diameter was 2.06 mm and lesion length was 16.9 mm. 83.4% of the lesions were treated with exclusively 2.25-mm XP. DAPT was maintained in 79.7% of the patients up to 1 year. Definite stent thrombosis occurred in 2 patients (0.6%; early 0.3% and late 0.3%). Death, cardiac death, MI, TLR, ischemia-driven TLR rates at 1 year were 1.9%, 0.6%, 4.5%, 2.2%, respectively. Major bleeding complication occurred in 2 patients (1 gastric bleeding and 1 cerebral bleeding). Mean late loss in-stent was 0.23mm and that in-segment was 0.09mm. Binary restenosis rates were 5.4% in-stent and 10.0% in-segment.

Conclusion: Clinical and angiographic outcomes of PCI for very small vessel using XP in the real world setting appears to be similar to those of core size XP.

Acknowledgement/Funding: Abbott Vascular Japan

P3422 | BEDSIDE
One year clinical outcomes after platinum chromium everolimus-eluting stent implantation in patients with bifurcation lesions: sub-analysis from specialist registry

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Background: The clinical outcomes after the deployment of a platinum chromium everolimus-eluting stent (PtCr-EES) to bifurcation lesions have not been fully established.

Purpose: The aim of this study was to evaluate the one year clinical outcomes following PtCr-EES in patients with bifurcation lesions.

Methods: From the prospective multi-center study of SPECIALIST (Study examining the Promus Element everolimus-eluting stent in multi-center Coronary Intervention of complex Arterial Lesion Subsets) registry to assess one year clinical outcomes following PtCr-EES implantation for 996 complex coronary artery diseases in 838 patients, 252 bifurcation lesions were selected for this sub-analysis.

One year clinical outcomes of PtCr-EES were compared with the data from SINGLE KISS (A randomized comparison of sirolimus- [SES] versus paclitaxel-eluting stent [PES] for treatment of bifurcation lesions) trial.

Results: Results are shown in the table.

One year clinical results

<table>
<thead>
<tr>
<th>PtCr-EES group</th>
<th>PES group</th>
<th>p value vs. PtCr-EES group</th>
<th>p value vs. SES group</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of lesions</td>
<td>252</td>
<td>398</td>
<td></td>
</tr>
<tr>
<td>MACE</td>
<td>118 (75%)</td>
<td>320 (80%)</td>
<td>0.12</td>
</tr>
<tr>
<td>Death</td>
<td>100 (40%)</td>
<td>144 (73%)</td>
<td>0.15</td>
</tr>
<tr>
<td>DM</td>
<td>126 (50%)</td>
<td>225 (57%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Stenting for side branch</td>
<td>16 (6.3%)</td>
<td>61 (15%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Final kissing inflation</td>
<td>96 (38%)</td>
<td>398 (100%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MACCE, n (%)</td>
<td>17 (6.7%)</td>
<td>41 (10.5%)</td>
<td>0.16</td>
</tr>
<tr>
<td>Cardiac death, n (%)</td>
<td>2 (0.8%)</td>
<td>3 (0.8%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Myocardial infarction, n (%)</td>
<td>3 (1.2%)</td>
<td>3 (0.8%)</td>
<td>0.09</td>
</tr>
<tr>
<td>Stent thrombosis, n (%)</td>
<td>0 (0%)</td>
<td>0.99</td>
<td>0.33</td>
</tr>
<tr>
<td>TLR, n (%)</td>
<td>8 (3.2%)</td>
<td>15 (3.8%)</td>
<td>0.12</td>
</tr>
<tr>
<td>TVR, n (%)</td>
<td>14 (5.5%)</td>
<td>30 (7.6%)</td>
<td>0.42</td>
</tr>
</tbody>
</table>

Conclusion: In spite of higher rate of double stent strategy and lower rate of final kissing inflation, PtCr-EES demonstrated comparable clinical outcomes to those of SES and PES.

P3423 | BEDSIDE
Direct comparison of biodegradable biolimus-eluting stent versus durable everolimus eluting stent: an updated meta-analysis

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Background: Previous network meta analysis used mixed comparison to evaluate the relative benefit of biodegradable biolimus eluting stent (DES) versus durable everolimus-eluting stent (EES). However, there was no meta-analysis with direct comparison of DES versus EES and EES. Additionally, several new studies about this topic were reported.

Data sources and study selection: We selected 7 studies (4 randomized controlled trials and 3 propensity-matched studies) by electronic search. Data sources in- cluded MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials, and article reference lists.

Data extraction and synthesis: Dichotomous outcome data were analyzed using Manteel-Henzel (MH) risk ratio and its 95% CI with random-effects models. We evaluated the difference between the estimates of the subgroups according to type of study.

Primary and secondary outcomes: Primary end points were major adverse cardio-vascular events (MACES) and secondary end points were probable and definite stent thrombosis, CV death and target lesion revascularization (TLR).

Results: There was no significant difference in MACES between DES and EES (Total RR: 1.077, 95% CI: 0.916–1.266) and the estimates were not different according to type of study (propensity-matched study (PSM); RR 1.041, 95% CI: 0.703–1.541, randomized-controlled trial (RCT); RR 1.084, 95% CI: 0.906–1.296). Heterogeneity between two types of study p for Q=0.853).

The rate of definite and probable stent thrombosis were similar between DES and EES (Total RR: 0.894, 95% CI: 0.505–1.585 (PSM RR: 0.953, 95% CI: 0.323–2.815) (RCT RR: 0.873, 95% CI: 0.445–1.712). The rate of cardiac death or TLR were not significantly different between two types of stents. There was no significant heterogeneity.

Conclusion: The clinical benefit of DES was similar to that of EES.
0.10±0.06 mm² vs. 0.15±0.07 mm² vs. 0.19±0.06 mm², p<0.004). While BP-SES demonstrated a significantly greater number of target lesion than DP-EES in TEM (p<0.05), there were no significant differences between BP-SES and BP-EES. At 10 days, area of fibrin deposition was significantly greater in DP-EES compared with the others (BP-SES vs. BP-EES vs. DP-EES, 0.13±0.04 mm² vs. 0.14±0.06 mm², p<0.007). Similar to the results at 7 days, BP-SES demonstrated a significantly greater number of target lesion than DP-EES in TEM (p<0.05). There were no significant differences in various parameters including inflammatory reaction and neointimal formation among the groups at 7 and 10 days.

Conclusions: The current study demonstrated abluminal biodegradable polymer-coated SES showing the least fibrin deposition and greatest endothelial cell recovery, suggesting that BP-SES have a great potential to prevent early stent thrombosis.

MECHANISMS OF RESTENOSIS – ITS PREDICTORS AND TREATMENT

P3426 | BEDSIDE
Predicting repeat revascularization after percutaneous coronary intervention: target lesion versus nontarget lesion revascularization

Background: Drug-eluting stent (DES) has reduced repeat revascularization, especially target lesion revascularization (TLR). However, there were limited data regarding nontarget lesion revascularization (NTLR) after DES implantation.

Objectives: The aim of this study was to compare the incidence and predicting factors between TLR and NTLR after percutaneous coronary intervention (PCI) with DES.

Methods: Among a total 3085 patients enrolled in single center PCI registry from 2003 to 2012, 293 patients (9.5%) had a repeat revascularization in 24 months. Baseline clinical characteristics, angiographic and procedural outcomes were compared between TLR (151, 4.9%), NTLR (142, 4.6%) and control (2792, 91.5%) groups respectively. Multivariate logistic regression analysis was performed to predict independent factors associated with TLR and NTLR.

Results: TLR group had higher previous history of coronary artery disease (8.6% (TLR) vs. 4.4% (control), p-value<0.001) and myocardial infarction (MI) for PCI indication (43.7% vs. 34.4%, p-value<0.002). In contrast, NTLR group had a higher body mass index. (25.5±3.0 (NTLR) vs. 24.7±3.2 (control), p=0.048) NTLR as well as TLR mostly occurred from 6 months to 12 months after index PCI. In multivariate logistic regression analysis, obesity (HR=2.68, p<0.001) was only predicting factors for NTLR.

Multivariate analysis for TLR and NTLR

<table>
<thead>
<tr>
<th>Predicting factor</th>
<th>Hazard ratio (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TLR logistic regression</td>
<td>1.48 (1.02–2.15)</td>
<td>0.039</td>
</tr>
<tr>
<td>Indication for PCI: MI</td>
<td>1.10 (1.01–1.22)</td>
<td>0.046</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>1.85 (1.01–2.23) +3.7% (p-value=0.006)</td>
<td></td>
</tr>
<tr>
<td>Smoking history</td>
<td>1.95 (1.26–3.01)</td>
<td>0.003</td>
</tr>
<tr>
<td>Number of treated lesion</td>
<td>0.39 (1.03–3.0)</td>
<td>0.037</td>
</tr>
<tr>
<td>NTLR logistic regression</td>
<td>1.31 (1.03–1.67)</td>
<td>0.037</td>
</tr>
<tr>
<td>Obesity (BMI ≥25)</td>
<td>2.69 (1.74–4.20)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

TLR, target lesion revascularization; MI, myocardial infarction; NTLR, non-target lesion revascularization; BMI, body mass index.

P3427 | BEDSIDE
The impact of postprocedural trimetazidine therapy on bare metal stent restenosis in patients undergoing percutaneous coronary intervention
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Background: Besides patient related factors, percutaneous coronary intervention (PCI)-induced reactions like inflammation, granulation, extracellular matrix remodeling and vascular smooth muscle cell proliferation and migration also result in neointimal hyperplasia and in-stent restenosis (ISR). Trimetazidine (TMZ), as an anti-ischemic agent, has also differential effects on vascular smooth muscle cells and endothelial cells.

Purpose: We aimed to evaluate whether post-PCI use of trimetazidine reduced the incidence of bare metal ISR.

Methods: Clinical and angiographic data of 955 patients with stable or unstable angina pectoris (mean age 60.1±10.2 years, 72.6% men) were retrospectively collected and patients were subdivided into the TMZ treatment group (TG, n=279) and control group (CG, n=276). All the patients underwent bare metal stent (BMS) implantation and a further control coronary angiography owing to stable or unstable angina pectoris. Post-PCI, all patients were treated with updated guideline-based medications. TG included patients in whom TMZ has been administered just after index PCI at the dose of 35mg bid.

Results: The TG had a lower incidence of ISR compared to the CG (9.0% vs 79.3%, p<0.001) (Figure 1). While the rate of male gender, smoking, diabetes mellitus were higher in CG, the rate of hypertension was higher in TG (p=0.048). Clinical presentation with unstable angina pectoris for second coronary angiography was significantly higher in CG compared to TG (42% vs 19.4%, p<0.001). Seven diameters and lengths were similar between groups during index procedure. In multivariate logistic regression analysis, trimetazidine use (OR:0.025, p<0.001), diabetes mellitus, smoking, stent diameter and stent length were found as significant predictors for ISR.

Conclusions: Post-PCI trimetazidine therapy is significantly associated with lower incidence of ISR as BMS implantation during follow-up.

P3428 | BEDSIDE
Comparison of acute and 1 year outcome of percutaneous coronary intervention for chronic total occlusion lesion between in stent occlusion and de novo lesion from the Japanese retrograde summit regist
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Objectives: We sought to examine the differences of acute and 1 year outcomes of percutaneous coronary intervention (PCI) for chronic total occlusion (CTO) of between in stent occlusion lesion (ISCO) compared with de novo lesion.

Background: However the long term performances of coronary stent have been improved, stent occlusion lesion is remaining.

Method: A total of 3,147 eligible subjects who underwent CTO-PCI were enrolled from 56 centers by a retrograde summit using a web registry system. They were divided to two groups as ISO (n=466) and de novo (n=2681) groups. Primary end point was major adverse cardiovascular event; MACCE, consisted with all cause death, stroke, any revascularization and myocardial infarction.

Results: There were no several differences in procedural difficulties (indicated by mean J-CTO score) and initial success rate between ISO and de novo lesion (1.57±1.02 vs. 1.54±1.07; p=0.57 and 90.6% vs. 88.1%; p=0.12). However, fluoroscopic time and usage of contrast media dose were higher in de novo lesion.

Conclusions: Repeat revascularization in 24 months after PCI was performed in approximately 1 out of 10 patients. NTLR as well as TLR occurred similarly from 6 months to 12 months after index PCI. While TLR was associated with MI and complex procedures, NTLR was related with obesity.
group compared with ISO group (69.3±46.0 min vs. 57.4±41.4 min; p = 0.001 and 232.6±106.8 ml vs. 197.2±91.5 ml; p < 0.0001).

In acute phase, there were no significant differences in the incidence of MACCE between ISO and de novo group (0.21% vs. 0.48%; p = 0.41). However, 1 year after procedure, the incidence of MACCE were higher in ISO compared with de novo group (7.10% vs. 3.41%; p = 0.01).

Conclusions: Procedural difficulties and initial success rate and acute outcomes were not different between ISO and de novo lesion. However, the chronic clinical outcomes of ISO were deteriorated compared with de novo lesion.

P3429 | BEDSIDE
Anti-inflammatory treatment with colchicine to reduce in-stent neointima growth in patients with drug eluting stents
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Background: Inflammatory processes have been implicated in the pathophysiology of in-stent neointima development and restenosis. Colchicine is an agent with potent anti-inflammatory action, which has been demonstrated to be safe for long-term use in patients with cardiovascular disease and has shown promise in reducing in-stent restenosis in diabetic patients receiving bare metal stents.

Purpose: The objective of this study was to test whether a 9-month course of colchicine would be associated with less neointima formation.

Methods: In this prospective, open-label study patients undergoing primary percutaneous coronary intervention (PCI) in the setting of an acute myocardial infarction were randomly allocated to a course of colchicine 0.5 mg daily for 9 months in addition to standard treatment or standard treatment. In-stent neointima growth was assessed angiographically, using quantitative coronary angiography software to assess late lumen loss, defined as minimal in-stent diameter at baseline minus minimal in-stent diameter on the follow-up angiography — performed approximately 9 months after the index PCI. All patients received zotarolimus- or everolimus-eluting stents. Serum CTRP 5 levels were assayed in 258 patients with and 262 patients without angiographic ISR at approximately one year after DES-based PCI. Late lumen loss was 0.27 mm (1st-3rd quartile 0.14–0.48) in controls compared with 0.26 mm (1st-3rd quartile 0.04–0.39) in those who took colchicine (p = 0.169).

Discussion: Colchicine treatment does not appear to have a significant effect on in-stent restenosis in drug-eluting stents. Considering previous positive results with bare-metal stents, it is possible that the neointima formation process is already strongly inhibited in drug-eluting stents, so that any additive effect of colchicine, if any, is difficult to observe.

Figure 1.

Conclusions: This meta-analysis showed that DEB and DES are equally effective in treating the DES-ISR in terms of MACE rate and the rates of TLR, ST, MI or CD. All-cause mortality was reduced in patients treated with DEB compared to those treated with DES. These data support the treatment of DES-ISR with DEB in order to avoid the double stent implantation and optimize cost-effectiveness.

P3431 | BEDSIDE
CTRP 5 links vascular smooth muscle cell proliferation and inflammation to in-stent restenosis after coronary drug-eluting stent implantation
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Background: CTRP 5 protein is expressed by many tissues particularly in the stromal vascular cell fraction, circulates abundantly in serum, and inhibits the release of adipokines. We investigated whether serum level of C1q/TNF-related protein (CTRP 5) is associated with in-stent restenosis (ISR) after percutaneous coronary intervention (PCI) with drug-eluting stent (DES) implantation, and assessed the biological effects of CTRP 5 in human aortic smooth muscle cells (hASMCs).

Methods: Serum CTRP 5 levels were assessed in 258 patients with and 262 patients without angiographic ISR at approximately one year after DES-based PCI. Multivariate logistic regression analysis was performed to determine risk factors for ISR. We also stimulated hASMCs with CTRP 5 protein to assess its biological effects regarding migration, growth, and inflammation.

Results: There were a higher percentage of type 2 diabetes, dyslipidemia, cigarette smoking, prior history of myocardial infarction and discontinuation of dual anti-platelet therapy at follow-up, higher HbA1c, total and LDL cholesterol, lower serum creatinine and hs-CRP, but lower HDL cholesterol, GFR and LVEF and lower percentage of statin therapy in patients with ISR than in non-ISR counterparts. No significant difference was found in BMI, incidence of hypertension, and other medical treatments between the two groups. Despite similar degree of coronary stenosis before PCI, site of lesion intervened, and type of DES used, patients with ISR more frequently had complicated coronary lesions (class B2/C, CTO and bifurcation lesions) and multivessel disease, and received smaller or longer stents. Serum CTRP 5 levels were higher in ISR patients than in non-ISR counterparts (0.20±0.08 mg/L vs. 0.15±0.07 mg/L; P < 0.001). After adjustment for potential clinical, biochemical and angiographic characteristics, compared with the lowest tertile (<0.126mg/L) of CTRP 5, patients with the mid (0.126–0.196mg/L) and the highest tertile (>0.197mg/L) of CTRP 5 had a
DEB was an independent predictor of TLF (HR 2.07, 95% CI 1.16–3.71, p=0.014).

**Results:**
A total of 628 patients with 697 ISR lesions were treated using newer generation DES after bare-metal stent or DES ISR. All-cause mortality, all-cause myocardial infarction, or any revascularization (TLF, a composite of clinical, lesion and patient-oriented outcomes) at 9-month and 18-month follow-up were compared between DEB and DES group. About 55.1% of patients were pretreated for bare-metal stent or DES ISR.

**Methods:** Patient-level pooled analysis from nationwide multicentre registries was performed with 628 consecutive patients who underwent ISR treatment using 2nd or 3rd generation DES versus DEB. The rates of stent-tethered (target lesion failure [TLF]) and patient-oriented composite outcomes (POCO, a composite of all-cause mortality, all-cause myocardial infarction, or any revascularization) at 1-year follow-up were compared between DEB and DES group.

**Results:**
A total of 628 patients with 697 ISR lesions were treated using newer generation DES (n=409) or DEB (n=219). About 55.1% of patients were pretreated for bare-metal stent or DES ISR. The study thought to investigate the angiographic outcomes after repeat newer generation durable polymer DES implantation for DES restenosis lesions with or without stent fracture. From April 2007 to January 2015, total 8983 lesions implanted DES during PCI at our hospital. Total 766 lesions, 8.5% had restenosis in follow-up angiogram. Subjects of the study were serial 108 patients 137 lesions those implanted either cobalt- or platinum-chromium everolimus- (P/Cr-EES) or Resolve zotarolimus-eluting (R-ZES) stent for DES restenosis lesions during the TLR procedure. Subject was divided into 2 groups with the incidence of SF in the restenosis lesions, SF group: 25 patients 36 lesions and non-SF group: 89 patients 101 lesions. Eighteen-month cumulative incidence of re-restenosis and re-TLR rate of 2 groups was calculated by Kaplan-Meier method and compared with log-rank test retrospectively. Restenosis and re-restenosis were defined as % diameter stenosis >50% in the follow-up angiograms. The patients were defined complete or partial separation of the stent as assessed by plain fluoroscopy.

**Results:** Baseline characteristics were similar. Cumulative incidence of re-restenosis and re-TLR rate in the SF group vs. non-SF group was 42.9% vs. 21.9% (p=0.010) and 34.4% vs. 19.1% (p=0.040), respectively.

**Conclusion:** After newer generation DES implantation, restenosis lesions with SF had significantly poor angiographic outcomes compared with those without.

**Background:**
Drug-eluting DES (DEB) has emerged as a suitable treatment option for in-stent restenosis (ISR) without implanting additional metal alloy. Although DEB has shown enhanced efficacy compared with simple balloon angioplasty or 1st generation drug-eluting DES (DES), evidences comparing DEB with 2nd or 3rd generation DES has been scarce, especially for patients with high-risk clinical and lesion-related characteristics.

**Purpose:**
We sought to evaluate the comparative clinical efficacy and safety of 2nd or 3rd generation DES versus DEB in unselected real-world population who were treated for bare-metal stent or DES ISR.

**Methods:** Patient-level pooled analysis from nationwide multicentre registries was performed with 628 consecutive patients who underwent ISR treatment using 2nd or 3rd generation DES versus DEB. The rates of stent-tethered (target lesion failure [TLF]) and patient-oriented composite outcomes (POCO, a composite of all-cause mortality, all-cause myocardial infarction, or any revascularization) at 1-year follow-up were compared between DEB and DES group.

**Results:**
A total of 628 patients with 697 ISR lesions were treated using newer generation DES (n=409) or DEB (n=219). About 55.1% of patients were pretreated for bare-metal stent or DES ISR. The study thought to investigate the angiographic outcomes after repeat newer generation durable polymer DES implantation for DES restenosis lesions with or without stent fracture. From April 2007 to January 2015, total 8983 lesions implanted DES during PCI at our hospital. Total 766 lesions, 8.5% had restenosis in follow-up angiogram. Subjects of the study were serial 108 patients 137 lesions those implanted either cobalt- or platinum-chromium everolimus- (P/Cr-EES) or Resolve zotarolimus-eluting (R-ZES) stent for DES restenosis lesions during the TLR procedure. Subject was divided into 2 groups with the incidence of SF in the restenosis lesions, SF group: 25 patients 36 lesions and non-SF group: 89 patients 101 lesions. Eighteen-month cumulative incidence of re-restenosis and re-TLR rate of 2 groups was calculated by Kaplan-Meier method and compared with log-rank test retrospectively. Restenosis and re-restenosis were defined as % diameter stenosis >50% in the follow-up angiograms. The patients were defined complete or partial separation of the stent as assessed by plain fluoroscopy.

**Results:** Baseline characteristics were similar. Cumulative incidence of re-restenosis and re-TLR rate in the SF group vs. non-SF group was 42.9% vs. 21.9% (p=0.010) and 34.4% vs. 19.1% (p=0.040), respectively.

**Conclusion:** After newer generation DES implantation, restenosis lesions with SF had significantly poor angiographic outcomes compared with those without.

**Background:**
Contemporary 2nd or 3rd generation DES provided superior clinical and lesional characteristics.

**Purpose:**
The study sought to evaluate the comparative clinical efficacy and safety of 2nd or 3rd generation DES has been scarce, especially for patients with high-risk clinical and lesional characteristics.

**Methods:**
Patient-level pooled analysis from nationwide multicentre registries was performed with 628 consecutive patients who underwent ISR treatment using 2nd or 3rd generation DES versus DEB. The rates of stent-tethered (target lesion failure [TLF]) and patient-oriented composite outcomes (POCO, a composite of all-cause mortality, all-cause myocardial infarction, or any revascularization) at 1-year follow-up were compared between DEB and DES group.

**Results:**
A total of 628 patients with 697 ISR lesions were treated using newer generation DES (n=409) or DEB (n=219). About 55.1% of patients were pretreated for bare-metal stent or DES ISR. The study thought to investigate the angiographic outcomes after repeat newer generation durable polymer DES implantation for DES restenosis lesions with or without stent fracture. From April 2007 to January 2015, total 8983 lesions implanted DES during PCI at our hospital. Total 766 lesions, 8.5% had restenosis in follow-up angiogram. Subjects of the study were serial 108 patients 137 lesions those implanted either cobalt- or platinum-chromium everolimus- (P/Cr-EES) or Resolve zotarolimus-eluting (R-ZES) stent for DES restenosis lesions during the TLR procedure. Subject was divided into 2 groups with the incidence of SF in the restenosis lesions, SF group: 25 patients 36 lesions and non-SF group: 89 patients 101 lesions. Eighteen-month cumulative incidence of re-restenosis and re-TLR rate of 2 groups was calculated by Kaplan-Meier method and compared with log-rank test retrospectively. Restenosis and re-restenosis were defined as % diameter stenosis >50% in the follow-up angiograms. The patients were defined complete or partial separation of the stent as assessed by plain fluoroscopy.

**Results:** Baseline characteristics were similar. Cumulative incidence of re-restenosis and re-TLR rate in the SF group vs. non-SF group was 42.9% vs. 21.9% (p=0.010) and 34.4% vs. 19.1% (p=0.040), respectively.

**Conclusion:**
After newer generation DES implantation, restenosis lesions with SF had significantly poor angiographic outcomes compared with those without.

**Background:**
The role of circulating progenitor cells in the appearance of neointimal hyperplasia after everolimus stent implantation.

**Purpose:**
This study is aimed to assess whether allelic distribution of polymorphisms within encoding proteins related to inflammation and vascular remodeling in Chilean subjects with coronary in-stent restenosis.

**Introduction:**
Coronary artery angioplasty with stent is a common procedure to restore myocardial blood flow. However, 20–30% of those who receive bare metal stents experience 30% to 10% with 30% of the patients develop drug-eluting restenosis (ISR).

**Purpose:**
To assess whether allelic distribution of polymorphisms within encoding proteins related to inflammation and vascular remodeling in Chilean subjects with coronary in-stent restenosis.
phisms in genes Nitric Oxide Synthase (NOS3), tumour necrosis factor (TNF), angiotensin converting enzyme (ACE) and interleukin 10 (IL10), which are involved in inflammation and/or vascular remodeling process of ISR, differ among patients who develop and those that do not develop ISR.

Methods: 192 patients were included. Patients with stenosis >50% in the angiographic site were defined as cases, and those with <50% as controls. Clinical and demographic variables were registered. Six polymorphisms were genotyped: NOS3: rs2070744, and rs1799983; TNF: rs361525 and rs1799984; IL10: rs3024498 and ACE: (I/D) rs4646994. Genotyping was performed by real-time PCR using allele-specific TaqMan® probes for the first five variants, for the ACE I/D polymorphism genotyping was carried out by the polymerase chain reaction (PCR) and subsequent gel electrophoresis. For statistical analysis a p value of <0.05 was considered significant.

Results: Cases and controls were included. We found no differences regarding male sex (79.3% and 70.5% respectively; p=0.16), age (63.2±10 and 65.5±9.8 respectively; p=0.1), Body Mass Index (28.2 vs 27.8 kg/m² respectively; p=0.24), nor for systolic blood pressure (p=0.38), total cholesterol (p=0.6), LDL-cholesterol (p=0.2), and glycemia (p=0.07). Genotypic distribution and allelic frequencies did not differ significantly between cases and controls except for NOS3 rs1799983 which exhibited a protective association (Table 1).

Conclusion: Among the variants studied only NOS3 rs1799983 showed a protective association with ISR, whereas NOS3 rs2070744 and TNF IL10 and ACE polymorphisms were not associated with ISR risk in this population.

Acknowledgement/Funding: Fondecyt 1141292

P3436 | BEDSIDE
Feasibility of drug-eluting balloon for in-stent restenosis lesion in chronic kidney disease patients: The New-Tokyo Registry

Aims: Chronic kidney disease (CKD) is considered to be one of the independent predictor of clinical outcomes after percutaneous coronary intervention (PCI) using drug-eluting stent. This study aimed to investigate the impact of the CKD to the clinical outcome of drug-eluting balloon (DEB) treating for in-stent restenosis (ISR) lesion.

Methods and results: Between March 2014 and April 2015, 233 consecutive patients who underwent PCI using DEB were included. Patients were divided into 4 groups according to estimated glomerular filtration rate (eGFR) as below: 60≤eGFR<90; 90≤eGFR<60; 60, eGFR≥30 (non-hemodialysis [HD]); 11, and HD patients. Study endpoint was major adverse cardiovascular events composed of target lesion revascularization (TLR), target vessel revascularization, and cardiac death. There were no significant differences of baseline patients and procedural characteristics between each group, except of mean age, and chronic total occlusion lesion. TLR was similarly occurred between each groups, except of eGFR<30 (non HD) groups at 1year. (60;eGFR: 35.7%, 30;eGFR: 39.5%, eGFR<30 (non HD): 0%; and HD: 25.6%) In other clinical outcome, there were no significant differences between each group. The number of pre-deployed stent was significantly related to the occurrence of TLR [HR, 1.34 (95% CI, 1.01–1.77), p=0.003].

Conclusion: There was no difference of clinical outcome after DEB treatment for ISR lesion based on the renal function. DEB is acceptable treatment for patients with CKD.

P3437 | BEDSIDE
Clinical relevant chest pain and 3-year clinical outcome in high-risk patients after percutaneous coronary intervention with novel drug-eluting stents: from the randomized DUTCH PEERS trial
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Background/Introduction: After percutaneous coronary intervention (PCI), certain subgroups of patients are known to have an increased risk of adverse events. Data about angina recurrence and clinical outcome in high-risk patients treated with novel drug-eluting stents (DES) are scarce.

Purpose: To evaluate the medium-term safety and efficacy of newer-generation DES in high-risk patients.

Methods: The 3-year clinical outcome and patient-reported chest pain data were compared in all-comer patients of the randomized DUTCH PEERS trial, who were treated with newer-generation zotarolimus-eluting stents (ZES, Resolute Integrity) or everolimus-eluting stents (EES, Promus Element). Patients were categorized as "high-risk", if they fulfilled one of these criteria: 1) diabetes mellitus (17.9%); 2) previous myocardial infarction (21.9%); 3) previous coronary revascularization (25.8%); 4) chronic renal failure (3.5%); 5) left ventricular ejection fraction < 30 (1.5%); or 6) age >75 years (17.3%). Patient-reported chest pain during mild or moderate physical exertion was considered clinically relevant. The "patient-oriented composite endpoint" (POCE) is a composite of all-cause mortality, any myocardial infarction, or any revascularization.

Results: Of all 1,811 patients who were randomized in the DUTCH PEERS trial, 394 patients (21.8%) were categorized as high-risk. These patients presented more often with stable angina, had more often multi-vessel treatment, and underwent more often treatment in a left main or bypass graft than patients who were not classified as "high-risk". After 3 years, high-risk patients had a significantly higher incidence of DES (20.6% vs. 12.3%; Logrank p=0.001). Of the high-risk patients, 481 (50.2%) were treated with ZES and 476 (49.8%) with EES. The rate of POCE was similar for both patients treated with ZES and EES (20.0% vs. 21.2%; Logrank p=0.63). The rates of “any revascularization” were similar (11.2% vs. 14.2%; Logrank p=0.17), and the definite stent thrombosis rates were low and similar (1.3% vs. 1.3%; Logrank p=1.00). More than 90% of the high-risk patients provided chest pain information: at 1, 2, and 3-year follow-up, 86.6%, 86.0%, and 81.4% of high-risk patients treated with ZES, and 84.8%, 82.0%, and 79.6% of high-risk patients treated with EES were free from clinically relevant chest pain (p=0.44, p=0.78, and p=0.52, respectively).

Conclusion: In high-risk patients, who showed a significantly higher event risk after percutaneous coronary interventions, novel ZES and EES were similarly safe and effective until 3-year follow-up.

Acknowledgement/Funding: The investigator-initiated DUTCH PEERS (TWENTE II) study is equally funded by Boston Scientific and Medtronic.

P3438 | BEDSIDE
Predictors of impaired reperfusion after percutaneous coronary intervention in patients in hospital acute stent thrombosis: retrospective analyses of 5-years data

Background: Acute stent thrombosis (STh) is a rare complication of percutaneous coronary intervention, novel DES and ZES were similarly safe and effective until 3-year follow-up.

Methods: All patients with STh treated with novel DES were included.

Results: Of all 1,811 patients who were randomized in the DUTCH PEERS trial, 394 patients (21.8%) were categorized as high-risk. These patients presented more often with stable angina, had more often multi-vessel treatment, and underwent more often treatment in a left main or bypass graft than patients who were not classified as "high-risk". After 3 years, high-risk patients had a significantly higher incidence of DES (20.6% vs. 12.3%; Logrank p=0.001). Of the high-risk patients, 481 (50.2%) were treated with ZES and 476 (49.8%) with EES. The rate of POCE was similar for both patients treated with ZES and EES (20.0% vs. 21.2%; Logrank p=0.63). The rates of “any revascularization” were similar (11.2% vs. 14.2%; Logrank p=0.17), and the definite stent thrombosis rates were low and similar (1.3% vs. 1.3%; Logrank p=1.00). More than 90% of the high-risk patients provided chest pain information: at 1, 2, and 3-year follow-up, 86.6%, 86.0%, and 81.4% of high-risk patients treated with ZES, and 84.8%, 82.0%, and 79.6% of high-risk patients treated with EES were free from clinically relevant chest pain (p=0.44, p=0.78, and p=0.52, respectively).

Conclusion: In high-risk patients, who showed a significantly higher event risk after percutaneous coronary interventions, novel ZES and EES were similarly safe and effective until 3-year follow-up.

Acknowledgement/Funding: The investigator-initiated DUTCH PEERS (TWENTE II) study is equally funded by Boston Scientific and Medtronic.
neous coronary intervention (PCI) and is associated with high-risk of reperfusion failure.

**Purpose:** The data about the risk factors of reperfusion failure in patients undergoing repeat PCI for treatment of STEMI are lacking.

**Methods:** A total of 6,815 patients underwent PCI with a stent implantation from January 2009 to December 2013 were retrospectively reviewed. Among those cases, patients presented with acute STEMI and underwent a repeat PCI for acute STEMI were identified.

**Results:** A total of 108 patients who underwent repeat PCI for the treatment of in-hospital acute STEMI were retrospectively analyzed. Of these, 21 (25%) patients had thrombolyis in myocardial infarction (TIMI) flow <3 after repeat PCI. The median value of pain-to-balloon time was 40 minutes in the TIMI <3 group. It was 35 minutes in the TIMI=3 group (p < 0.001), and first PCI-to-stent thrombosis time was also longer in the TIMI <3 group (10 hours vs. 2.5 hours, p < 0.001). When patients were evaluated according to the PCI time, the percentage of the patients with TIMI <3 was significantly higher in the night period when compared to the daytime period (46.4% vs. 17.5%, p = 0.002). In the multivariable logistic regression analysis, stent length (OR=1.18, 95% CI 1.08–1.38) and pain to balloon time (OR=1.28, 95% CI 1.06–1.54) were the only independent predictors of failed reperfusion.

**Conclusions:** Baseline stent length and pain-to-balloon time were associated with reperfusion failure in STEMI PCI. Moreover, TIMI flow grade showed a circadian variation.

**P3430 | BEDSIDE**

Incidence and impact of cardiac ischemic events in women undergoing percutaneous coronary intervention with new-generation drug-eluting stents

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**Background:** The timing and prognostic significance of cardiac ischemic events (CIEs) in women treated with new-generation drug-eluting stents (DES) is poorly characterized.

**Objective:** We investigated the incidence and independent impact on mortality of CIEs in women undergoing percutaneous coronary intervention (PCI) with new-generation DES.

**Methods:** We pooled patient-level data from 26 randomized controlled trials of new-generation DES.

**Results:** Between 0 and 1 year were 0.9% (0.7% to 1.1%), 3.9% (3.5% to 4.4%) and 3.8% (3.4% to 4.4%), respectively. Finally, between 1 and 3 year were 0.3% (0.2% to 0.5%), 0.9% (0.6% to 1.3%) and 2.6% (2.1% to 3.2%), respectively. The effect of cumulative CIEs at 3 years on all-cause mortality is illustrated in Figure 1. The effect on mortality of ST trended to increase from the early or late period (adjusted HR: 3.72; 95% CI: 2.60 to 5.33) to the very late period (adjusted HR: 1.93; 95% CI: 0.62 to 0.60); trend p-value < 0.001). The effect of TLR was consistent between the early or late and the very late periods (trend p-value = 0.15).

**Conclusion:** In women treated with new-generation DES, ST was rare but associated with a strong effect on mortality that trended to increase over time. The effect of spontaneous MI decreased over time and TLR had no impact on mortality. Measures to mitigate ongoing stent-related thrombotic risk in women are warranted even with use of new-generation DES.

**P3440 | BEDSIDE**

Clinical outcome and mortality predictors in elderly patients with STEMI undergoing primary PCI: Experience from a high-volume single centre


**Background:** Data on real-world outcomes in elderly patients with STEMI are limited.

**Purpose:** To evaluate the clinical profile, outcome and mortality risk factors of elderly patients undergoing primary PCI (PPCI) for STEMI in our contemporary practice.

**Methods:** We studied all consecutive patients with STEMI undergoing PPCI at our institution between 2006–2014 (N = 2,941). Clinical and procedural data were prospectively collected using a computerized database. We investigated the occurrence of death during follow-up. Cox-regression analysis was employed to determine independent predictors of mortality among the elderly.

**Results:** 670 (22.8%) were aged < 75. Older patients were more likely to be female, had more prevalence of comorbidities (diabetes, renal failure, vascular disease and anaemia) and more high-risk features (higher Killip class, lower TLR, higher degree of obstruction of anterior MI and multivessel disease, longer reperfusion times). After median follow-up of 4.1 years, cumulative incidence of death 26.1% for older patients and 8.5% for younger ones (p < 0.001) (Figure 1). Both 30-day (12.7% vs. 3.9%, p < 0.001) and 1-year mortality rates (18.5% vs. 6.0%, p < 0.001) were higher in the elderly. PPCI success rate was slightly lower in aged patients (92.4% vs. 96.0%, p < 0.001). Elderly patients failed with suboptimal PCI had very high 30-day mortality (43.1% vs. 10.2%, p < 0.001) and 1-year mortality (51.0% vs. 15.8%, p < 0.001) (Figure 1). Among aged patients, age, diabetes, creatinine clearance, anterior MI, Killip class, LVEF, total ischemia time and PCI success were independent predictors of mortality.

**Risk factors of mortality in the elderly**

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per year)</td>
<td>1.079</td>
<td>1.032 to 1.128</td>
<td>0.001</td>
</tr>
<tr>
<td>Gender (male vs. female)</td>
<td>0.665</td>
<td>0.463 to 0.955</td>
<td>0.027</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.543</td>
<td>1.065 to 2.236</td>
<td>0.022</td>
</tr>
<tr>
<td>Creatinine clearance</td>
<td>0.988</td>
<td>0.979 to 0.998</td>
<td>0.016</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>0.981</td>
<td>0.968 to 0.995</td>
<td>0.008</td>
</tr>
<tr>
<td>Anterior MI</td>
<td>1.414</td>
<td>0.960 to 2.033</td>
<td>0.080</td>
</tr>
<tr>
<td>Killip class III (vs class I)</td>
<td>2.553</td>
<td>1.359 to 4.795</td>
<td>0.004</td>
</tr>
<tr>
<td>Killip class IV (vs class I)</td>
<td>5.913</td>
<td>3.650 to 9.580</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Total ischemia time</td>
<td>1.001</td>
<td>1.000 to 1.001</td>
<td>0.054</td>
</tr>
<tr>
<td>Successful primary PCI</td>
<td>0.484</td>
<td>0.268 to 0.876</td>
<td>0.017</td>
</tr>
</tbody>
</table>

**Conclusions:** PPCI in the elderly is challenging because of their worse clinical profile and higher mortality. Successful PPCI appears to be crucial for survival of aged patients with STEMI.

**P3441 | BEDSIDE**

Staged revascularization in patients with STE elevation myocardial infarction and multivessel disease is associated with reduced mortality


**Background:** Many patients with STE-elevation myocardial infarction (STEMI) have coronary multivessel disease (MVD). Best revascularization strategy in these patients is still unclear.

**Purpose:** To evaluate the effect of staged percutaneous coronary intervention (PCI) on mortality and recurrent myocardial infarction (MI).

**Methods:** We prospectively studied consecutive patients with STEMI and MVD treated with primary PCI (pPCI) between 2005 and 2013. The outcome of 300
patients undergoing staged, angiography-guided, completion of revascularization (Staged PCI Group) was compared with that of 1:1 propensity-score-matched patients for whom a staged completion was not planned (No Staged PCI Group). Patients with multivessel treatment at the time of PCI were not included. The primary end-point was all-cause mortality. Secondly we assessed the incidence of recurrent MI. Hazard rates were derived from Cox survival analysis. We also performed sensitivity analyses after excluding patients who died within day 5 from the pPCI and according to the timing of completion (during the index hospitalization vs after discharge).

Results: After a median follow-up of 553 days [25th-75th percentile 337–1074] mortality was 2.0% in the Staged PCI Group and 8.0% in the No Staged PCI Group (HR 0.25; 95% CI 0.10–0.60; p=0.002). Mortality was also reduced in Staged PCI group when considering only patients who survived at day 5 (2.0% vs. 11.0% (HR 0.22; 95% CI 0.09–0.57; p<0.001); and 360 ≤ patients with shorter TIT.

Based on our results, routine manual thrombus aspiration during primary PCI for ST -segment elevation myocardial infarction (STEMI) did not reduce the composite primary endpoint. On the contrary, the primary outcome was more often occurred after manual thrombus aspiration in a population did not reduce the composite primary endpoint. We assessed differences in baseline characteristics and outcomes across TIT categories in 653 patients with STEMI, and determined whether TIT modified the treatment effect of manual thrombus aspiration during primary PCI.

Methods: This is a substudy of the POST randomized trial. Patients were catego-

Background: Two large trials have reported routine manual thrombus aspiration during primary percutaneous coronary intervention (PCI) for ST-segment elevation myocardial infarction (STEMI) did not reduce adverse clinical outcomes. However, there are only limited data on the efficacy of thrombus aspiration according to the total ischemic time (TIT).

Purpose: We assessed differences in baseline characteristics and outcomes across TIT categories in 653 patients with STEMI, and determined whether TIT modified the treatment effect of manual thrombus aspiration during primary PCI.

Methods: This is a retrospective unicentric cohort study of 162 consecutive pa-

Results: TIT in POST trial ranged from 36 to 715min (median 184min, IQR [121–303min]). Baseline characteristics varied considerably by TIT. Patients in longer TIT categories were older, more likely to be female, more likely to have history of chronic kidney disease, and more likely to have longer door to reperfu-

Conclusions: Our analysis strongly suggests that after pPCI in patients with STEMI and MVD a staged completion of revascularization is associated with a better long-term survival. This effect was consistent regardless of timing of the staged PCI, although early procedures decreased the reinfarction rate.

P3444 | BEDSIDE

Impact of manual thrombus aspiration for ST elevation myocardial infarction on in-hospital and long-term stroke rates in a single high-volume centre


Recent randomised trials evaluating the strategy of routine manual thrombectomy compared to PCI alone in patients with ST elevation myocardial infarction (STEMI) reported discordant results regarding the risk of stroke.

Purpose: The purpose of this study was to determine the impact of manual thrombus aspiration on the occurrence of in-hospital and 4 years stroke rates in a real world population.

Methods: We identified 4868 consecutive patients undergoing primary PCI from January 2009 to July 2013, from a prospective electronic registry of a high-volume catheterization laboratory. Manual thrombus aspiration was performed at the operator discretion in 690 pts (%) (Group 1) and 3908 patients underwent PCI alone (Group 2). CHA2DS2VASc score was calculated to determine baseline risk for stroke.

Results: Baseline CHA2DS2VASc score high-risk category (≥ 2) of patients and the incidence of previous stroke were similar in groups 1 and 2 (75.9% vs. 75.9%; p=0.96, and 7.2% vs. 6.5%; p=0.46, respectively), while the rates of previous atrial fibrillation (4.1% vs. 2.2%; p=0.001) and previous CAVG (2.9% vs. 1.8%; p=0.03) were more prevalent in Group 1. Rates of in-hospital stroke (0.7% vs. 0.7%; p=0.09) and at a median follow-up of 48 months (IQR 36–56) were similar between groups 1 and 2 (2.9% vs. 2.5%; p=0.33) (Figure 1). Mortality rates were similar in groups 1 and 2, both, in-hospital (4.6% vs. 4.8%; p=0.87) and at 48 months follow-up (16.6% vs. 17.1%; p=0.49). However, higher overall mortality was observed during follow-up in patients with stroke (31.1% vs. 9.2%; p<0.001).

P3444 | BEDSIDE

Multi-vessel revascularization in ST-segment elevation myocardial infarction: in search for the best timing

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Background: Multivessel disease (MVD) diagnosed at the time of ST-elevation myocardial infarction (STEMI) has been associated with a substantially worse outcome as compared with single-vessel disease, although the optimal management strategy for these patients has not been well established.

Aim: We intend to evaluate clinical outcomes of staged multivessel percutaneous coronary angioplasty (PCI) strategy as compared with acute multivessel PCI and non-culprit vessel-only PCI strategy in STEMI patients with MVD.

Methods: This is a retrospective unincenct cohort study of 162 consecutive pa-

Conclusion: Selective use of manual thrombus aspiration compared to PCI alone in patients with STEMI was not associated with an increased risk for stroke, ne-
ther in-hospital or during long-term follow-up, when performed by experienced operators at a high-volume center.
defined as a composite of death from any cause, recurrent myocardial infarction, unplanned revascularization and admission for heart failure.

Results: Sixty-four percent of patients received culprit vessel-only PCI and 36% underwent complete revascularization (19% of patients were treated with multivessel PCI during index hospitalization and 17% received staged PCI under an external pacemaker). Study groups were not significantly different in demographic data, cardiovascular risk factors, infarct location assessed by electrocardiography or left ventricular ejection fraction assessed by echocardiography.

After a mean follow-up of 14 months (IQR 7–25), patients receiving complete revascularization had a lower incidence of MACE (Hazard Ratio (HR): 0.24; 95% Confidence interval (CI): 0.24–0.95, p=0.035), irrespective of culprit vessel, revascularization had a lower incidence of MACE (Hazard Ratio (HR): 0.48; 95% CI: 0.07–0.76; p=0.016). Kaplan-meier curves for incidence of MACE are represented on Figure 1.

Conclusion: In STEMI patients with MVD who underwent primary PCI, complete revascularization for angiographically significant non-culprit lesions was associated with reduction of MACE and a staged PCI strategy was associated with better results.

P3446 | BENCH

The double guidewire approach for transcoronary pacing in a porcine model

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Background: If transcoronary pacing is used for treatment of unheralded brady-cardias in the setting of percutaneous coronary interventions (PCI), it is usually done unipolar with the guidewire in the coronary artery as the indifferent anode and a cutaneous anodal patch electrode connected to an external pacemaker. In the present study we introduced a new concept – the “double guidewire approach” for transcoronary pacing in a porcine model.

Methods: Transcoronary pacing was applied in 16 adult pigs under general anaesthesia in an animal catheterization laboratory. A special guidewire with electrical insulation by PTFE coating except for the distal part of the guidewire was positioned in the periphery of a coronary artery serving as the cathode. As the indifferent anode, an additional standard floppy tip guidewire was advanced into the proximal part of the same coronary vessel. The efficacy of double guidewire transcoronary pacing was assessed by measurement of threshold and impedance data and the magnitude of the epicardial electrogram. It was compared with unipolar transcoronary pacing using a standard cutaneous patch electrode as indifferent anode located at the dorsal thorax of the animal and with bipolar and unipolar transvenous pacing in the right ventricle (using the same cutaneous patch electrode as for transcoronary pacing).

Results: Transcoronary pacing with the new double guidewire technique as with the standard patch approach was effective in all cases. Pacing thresholds obtained with the double guidewire technique (1.5±0.3 V) were similar to those obtained by standard unipolar transcoronary pacing with a cutaneous patch electrode (1.2±0.7 V) and unipolar transvenous pacing against the same cutaneous patch electrode (1.5±1.0 V). Bipolar transvenous pacing yielded the lowest pacing thresholds at (0.8±0.4 V).

The corresponding pacing impedances were 272±46 Ohm for the double guidewire technique, 349±57 Ohm for unipolar transcoronary pacing technique, 299±76 Ohm for unipolar transcoronary pacing and 434±91 Ohm respectively for bipolar and unipolar transvenous pacing.

Conclusions: Transcoronary pacing in the animal model with the novel “double guidewire approach” is a simple and effective pacing technique with comparable pacing thresholds obtained by standard unipolar transcoronary and transvenous pacing. With the availability of insulated coronary guidewires this technique could replace temporary transvenous pacing in emergency situations during PCI, especially when using the radial access.

Acknowledgement/Funding: This study was supported by a restricted grant from Biotronik Cooperation (Biotronik, Berlin, Germany).

P3447 | BENCH

Impact of potent P2Y12 inhibitor loading on resolution of ST-segment elevation in patients with ST-segment elevation myocardial infarction (STEMI)

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Background: Data of relationship between ST-segment elevation resolution (STR) after primary percutaneous coronary intervention (PCI) and potent P2Y12 receptor antagonist are limited.

Objectives: The aim of this study was to examine effect of potent P2Y12 receptor antagonist (prasugrel or ticagrelor) vs. clopidogrel on STR among patients with ST-segment elevation myocardial infarction (STEMI).

Methods: We evaluated the data of index and 60-minute post-PCI ECG in STEMI patients treated with primary PCI (n=320). They were divided into 2 groups by the degree of STR: (1) complete (>70%); and (2) incomplete (<70%).
Results: Complete STR was observed in 188 patients (58.8%). After potent P2Y12 inhibitor loading, prevalence of complete STR was greater compared with clopidogrel loading (71.6% vs. 51.5%; p < 0.001). Interestingly, there was no difference in the level of platelet reactivity pre-PCI according to presence of complete STR (p = 0.357). In multivariate analysis, potent P2Y12 inhibitor vs. clopidogrel loading was the determinant of complete STR (odds ratio, 2.79; 95% confidence interval, 1.54 to 5.05; p = 0.001). Compared with patients with incomplete STR, subjects with complete STR showed the low levels of BNP, LV EF and LV volume index at 30 days (all p values <0.013) and had the lower risk of adverse cardiovascular events during 1 year (Log rank p = 0.044).

Conclusions: Among STEMI patients, potent P2Y12 inhibitor loading before primary PCI increases the chance of complete STR, which may be related with the better outcomes in LV recovery process and clinical events.

Impact of adjuvant ballooning on target lesion revascularization in patients undergoing percutaneous coronary intervention with drug-eluting stents


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Background: There have been limited data regarding the impact of routine adjuvant ballooning after the stenting on target lesion revascularization (TLR). This study sought to investigate impact of adjuvant ballooning on TLR in patients (pts) undergoing percutaneous coronary intervention (PCI) with drug-eluting stents (DESs) up to 12 months.

Methods: A total 4243 pts undergoing PCI with DESs from Jan 2004 to Dec 2015 were enrolled for the analysis. The definition of angiographic success was less than 30% of residual stenosis with good distal run-off. TLR was defined as any revascularization procedure (either PCI or coronary artery bypass graft) of the target lesion in the presence of angiographic restenosis and ischemia. We investigated whether the adjuvant ballooning (n=2518) can favorably impact on the target lesion in the presence of angiographic restenosis and ischemia. We sought to assess the incidence and predictors of late TLR beyond 5 years after DES implantation with those beyond 5 years.

Results: Cumulative incidence of TLR within the first year was 11.7%. Late TLR continued to occur up to 5 years (3.1%/year; cumulative 5-year incidence, 24.0%). Late TLR also occurred constantly up to 10 years (2.2%/year; cumulative 10-year incidence, 35.0%). Predictors of TLR within 5 years were elderly patients (≥80 years), hemodialysis, multivessel disease, ostial lesion, severe calcification, and stent overlap. Of these, elderly patients (≥80 years) and hemodialysis were also predictors of late TLR beyond 5 years.

Conclusions: Late TLR continued to occur without attenuation and acceleration up to 10 years after SES implantation. Elderly patients (≥80 years) and hemodialysis were predictors of late TLR beyond 5 years, which were common to TLR within the 5 years.

Relative impact of clinical presentation and disease extension on outcomes after revascularization with biologically active stents in coronary bifurcation: insights from the P2BiTO registry

M. Zimmero1, C. Briguiu2, R.J. Gil3, F. Radico1, J.Y. Amat-Santos4, E. Barbato5, (DESs) up to 12 months.

Results: The incidence of TLR was 7.0% (176 of 2518) in the adjuvant ballooning group and 9.5% (162/1707) in the non-adjuvant ballooning group (χ² test, P = 0.003). In multivariate logistic regression adjusted by gender, age, ST-segment myocardial infarction (STEMI) or cardiacogenic shock at admission, the history of cardiovascular events, diabetes, dyslipidemia, cerebrovascular accident, peripheral arterial disease, dialysis, current smoking and alcoholics, congestive heart failure, drugs such as clostazol, beta-blocker, calcium channel blocker, renin-aldosterone system blocker, diuretics, and statin, bifurcated lesion, small vessel lesion, ostial lesion, calcification, dissection after pre-balloon, and diffuse long lesion. The adjuvant ballooning was associated with reduction of the incidence of TLR (OR, 0.671; 95% CI, 0.534–0.844; P = 0.001). Also, predictors for TLR was age, STEMI, dialysis, ostial lesion, calcification, dissection after pre-balloon, and diffuse long lesion of more than 3cm (Figure).

Conclusions: In our study, adjuvant ballooning was useful for lowering TLR following PCI even in the DES era.
by Medina classification, rates of MACE were higher in ACS vs stable patients, regardless of looking whether they had Medina true (6.8% for ACS vs 5.1% for stable, p<0.05) or non-true bifurcations (7.8% for ACS vs 5.1% for stable, p=0.05).

Conclusions: As expected, the rate of MACE was higher in patients suffering from ACS, regardless of bifurcation complexity, as assessed by Medina classification.

**P3451 | BEDSIDE**

**Efficacy and safety of high-dose rosuvastatin loading at emergency room following percutaneous coronary intervention among patients admitted with acute coronary syndrome, a pilot study**


**Background:** High-dose statin loading prior to percutaneous coronary intervention (PCI) has been shown to improve outcomes. No conclusive evidence support a very early loading of high-dose statin (in Emergency Room (ER)) among patients presenting with acute coronary syndrome (ACS). Objective: To study the safety and efficacy of early high-dose rosuvastatin loading followed by high-intensity maintenance therapy as compared to standard practice of prescribing statin, among patients presenting with ACS who were intended to undergo PCI.

**Methods:** This is a prospective, randomised, controlled, open-label pilot study. Subjects with ACS were randomised at ER into rosuvastatin group (40mg rosuvastatin loading in ER within the 2 hours diagnosis followed by maintenance 20mg daily), or control group (no loading of statin in ER, statin were prescribed by Medina angiography +/- PCI. We followed up all subjects up to 6 months. The primary end-points were peak cardiac biomarkers within 48 hours post PCI, major adverse cardiac events (MACE), The secondary end-points were incidence of contrast-induced nephropathy (CIN), LDL level reduction and safety.

**Results:** 70 eligible subjects were randomised into rosuvastatin (n=35) and control (n=35) groups. 22 out of 35 subjects in each group underwent PCI. Patients in rosuvastatin group showed a trend to lower peak in cardiac biomarkers at 48 hours post PCI, a lower rate of MACE and CIN, though not statistically significant (p=0.5). The Rosuvastatin group achieved better reductions in LDL (48.3% vs 37.1%) though not statistically significant. There was improvement in left ventricular ejection fraction in rosuvastatin group (mean 4.03% increase), compared to 37.1% though not statistically significant. There was improvement in left ventricular ejection fraction in rosuvastatin group (mean 4.03% increase), compared to 37.1%) though not statistically significant. There was improvement in left ventricular ejection fraction in rosuvastatin group (mean 4.03% increase), compared to 37.1%) though not statistically significant.

**Conclusions:** As expected, the rate of MACE was higher in women compared with men (22.2% vs 16.7%; p<0.0001). Figure). After adjustment using multivariate analysis, female gender was not an independent predictor of mortality (HR 0.96; 95% CI 0.80–1.16; p=0.689), but remained an independent predictor of in-hospital bleeding (OR 2.42; 95% CI 1.76–3.24; p<0.0001) (Figure). Periprocedural BARC type ≥2 bleeding was associated with increased 4-year mortality (HR 1.77; 95% CI 1.35–2.32; p<0.0001) after primary PCI.

**P3453 | BEDSIDE**

**Octogenarians with atrial fibrillation undergoing percutaneous coronary intervention - the AFCAS registry**

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1 North-Kymi Hospital, Emergency Department, Kouvol, Finland; 2 Kuopio University Hospital and University of Kuopio, Heart Center, Kuopio, Finland; 3 Turku University Hospital and University of Turku, Heart Center, Turku, Finland; 4 Martin Luther University Halle-Wittenberg and Paracelsus-Harz-Clinic Bad Suderode, Medical Faculty, Halle, Germany; 5 Maggiore Hospital, Division of Cardiolog, Laboratory of Interventional Cardiology, Bologna, Italy; 6 Satakunta Central Hospital, Heart Center, Petijärvi, Finland

**Introduction:** Octogenarians with atrial fibrillation (AF) undergoing percutaneous coronary intervention (PCI) are high-risk patients with frequent co-morbidities. Little is known on their management and outcomes in contemporary clinical practice and no definite consensus on antithrombotic therapy (AT) exists.

**Purpose:** We evaluated the effects of advanced age and gender on patient management, medication and clinical outcomes in patients with AF undergoing PCI.

**Methods:** A total of 195 octogenarians (≥80 years) were compared to 730 non-octogenarian patients (<80 years) with AF from the prospective AFCAS Registry. The outcomes of interest were bleeding episodes according to the BARC classification and major cardiac and cerebrovascular adverse events (MACCE).

**Results:** Acute coronary syndrome was a more frequent indication for PCI (69.6% vs 53.7%, p<0.001) in octogenarians, and they stayed at hospital twice as long as younger patients (median 4 vs 2.5 days, p<0.05). There was no significant difference in the use of triple therapy (70.3% vs 74.1%, p=0.28), dual anti-platelet therapy (DAPT) (19.5% vs 16.8%, p<0.04) or duration of clopidogrel treatment between the groups (both median 3±11 months). At 12 months follow-up, the incidence of MACCE and its derivative myocardial infarction were significantly higher in octogenarians (27.7% vs 20.1%, p=0.03 and 9.2% vs 4.9%, p=0.04, 0.0001).

**Abstract P3451 – Table 1. Baseline and follow-up parameters**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Rosuvastatin (n=35)</th>
<th>Stable CAD (n=53)</th>
<th>p</th>
<th>Control group (n=35)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL-cholesterol (mmol/L)</td>
<td>4.01±0.15</td>
<td>3.76±0.84</td>
<td>0.20</td>
<td>2.11±0.98</td>
<td>2.31±0.69</td>
</tr>
<tr>
<td>Reduction in LDL (%)</td>
<td>48.3%</td>
<td>38.6%</td>
<td>0.19</td>
<td>42.4%</td>
<td>11 (31.4%)</td>
</tr>
<tr>
<td>Achieved target LDL-cholesterol ≥1.8, n (%)</td>
<td>14 (40%)</td>
<td>11 (31.4%)</td>
<td>0.45</td>
<td>42.4%</td>
<td>11 (31.4%)</td>
</tr>
<tr>
<td>Left ventricular ejection fraction (EF) (%)</td>
<td>53.7±11.9</td>
<td>56.3±10.34</td>
<td>0.01</td>
<td>43.9±11.8</td>
<td>53.1±9.8</td>
</tr>
<tr>
<td>Change in ejection fraction (EF) (%)</td>
<td>+4.03±7.71</td>
<td>+4.06±8.86</td>
<td>0.00</td>
<td>+4.03±7.7</td>
<td>+4.06±8.86</td>
</tr>
</tbody>
</table>

**Purpose:** This study sought to investigate the influence of gender and bleeding on long-term mortality in unselected STEMI patients admitted for primary PCI.

**Methods:** Data of all consecutive STEMI patients admitted for primary PCI between 8/2009 and 12/2011 in a high volume tertiary centre were analysed. In-hospital bleeding events were assessed using the bleeding academic research consortium (BARC) criteria. The primary end point was total mortality at 4 years. The secondary end point was in-hospital BARC type ≥2 bleeding.

**Results:** Of the 3053 pts with STEMI admitted for primary PCI, 921 (30.2%) were female. Compared with men, women were older, with a higher prevalence of diabetes, hypertension and hypercholesterolemia, and had higher rates of in-hospital bleeding compared with men (10.9% vs 3.7%; p<0.0001). Over 4-year follow-up, mortality was significantly higher in women compared with men (22.2% vs 16.7%; p<0.0001) (Figure). After adjustment using multivariate analysis, female gender was not an independent predictor of mortality (HR 0.96; 95% CI 0.80–1.16, p=0.689), but remained an independent predictor of in-hospital bleeding (OR 2.42; 95% CI 1.76–3.24, p<0.0001) (Figure). Periprocedural BARC type ≥2 bleeding was associated with increased 4-year mortality (HR 1.77; 95% CI 1.35–2.32; p<0.0001) after primary PCI.
Comparative results

<table>
<thead>
<tr>
<th></th>
<th>Age ≥ 80 years</th>
<th>Age &lt; 80 years</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>81 (41.5)</td>
<td>194 (26.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age (mean ± SD)</td>
<td>82±2.6</td>
<td>72±6.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CHADS2-VASc (median ± IQR)</td>
<td>5±3</td>
<td>4±2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Triple therapy</td>
<td>137 (70.3)</td>
<td>541 (74.1)</td>
<td>0.28</td>
</tr>
<tr>
<td>Dapt</td>
<td>38 (19.5)</td>
<td>123 (16.8)</td>
<td>0.40</td>
</tr>
<tr>
<td>MACCE</td>
<td>54 (27.7)</td>
<td>147 (20.1)</td>
<td>0.025</td>
</tr>
<tr>
<td>Mortality</td>
<td>29 (14.9)</td>
<td>74 (10.1)</td>
<td>0.07</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>18 (9.2)</td>
<td>36 (4.9)</td>
<td>0.04</td>
</tr>
<tr>
<td>Stent thrombosis</td>
<td>5 (2.4)</td>
<td>10 (1.4)</td>
<td>0.33</td>
</tr>
<tr>
<td>All TIA/stroke</td>
<td>8 (4.1)</td>
<td>15 (2.1)</td>
<td>0.12</td>
</tr>
<tr>
<td>BARC ≥ 2</td>
<td>24 (12.3)</td>
<td>71 (9.7)</td>
<td>0.29</td>
</tr>
</tbody>
</table>

MACCE = major adverse cardiac and cerebrovascular events; BARC = Bleeding Academic Research Consortium bleeding classification.

Conclusions: The use of AT medication was similar in patients with advanced age compared to younger patients. Nevertheless, thrombotic complications ocurred more frequently in the elderly despite apparently similar bleeding rate. This finding underscores the need for adequate and effective antithrombotic therapy also in frail octogenarians.

P3454 | BEDSIDE
Efficacy of everolimus-eluting stent implantation in patients with small coronary arteries: outcomes of 3-year clinical follow-up
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Background: Our aim was to compare in the 3-year clinical impact between second-generation everolimus-eluting stents (EES) and first-generation sirolimus-eluting stents (SES) in small vessel lesions.

Methods: Forty-four-four patients with small vessel lesions defined as reference diameter <2.5 mm were treated with EES (237 patients, 265 lesions) or SES (207 patients, 220 lesions) and completed 3-year follow-up. We compared the major adverse clinical events (MACE) between the two groups.

Results: EES had no significant impact on the MACE rate compared with SES (4.6% vs. 7.2%, p=0.14). No significant differences were observed in the individual components of cardiac death (1.7% vs. 1.9%, p=0.78), myocardial infarction (1.3% vs. 3.4%, p=0.12), and ischemia-driven target lesion revascularization (2.3% vs. 4.6%, p=0.13) in EES and SES, respectively. Stent thrombosis however, was significantly less in the EES group than in the SES group (0.7% vs. 3.4%, HR: 0.53, 95% CI: 0.38 to 0.88, p<0.05).

Figure Cumulative incidences of definite or probable stent thrombosis for 3 years in sirolimus-eluting stent (SES) and everolimus-eluting stent (EES)

Conclusions: EES implantation did not significantly impact 3-year MACE rates compared to SES implantation in small vessel lesions. A significant reduction in the overall rate of stent thrombosis was observed in recipients of EES. While the SES group showed increasing rates of late and very late thrombosis, the EES group did not. EES offers a safe and effective treatment for small vessel lesions.

P3455 | BEDSIDE
Performance of percutaneous intervention using drug-eluting stents versus bare-metal stents in patients with saphenous vein grafts: systemic review
B. Alshammari. QE II Health Sciences Center, Cardiology, Halifax, Canada

Background: Percutaneous coronary intervention (PCI) in native coronary vessels using drug-eluting stents (DES) compared to bare metal stents (BMS) has been shown to reduce restenosis and major cardiac events in both multicenter randomized trials and large registry studies. In contrast, clinical outcomes of saphenous vein graft (SVG) intervention have been poorly represented in the literature or unclear despite up to 10~15% of PCI procedures being performed as SVG interventions.

Objective: To summarize the current evidence of using DES vs. BMS by comparing the performance and effectiveness of DES vs. BMS in saphenous vein graft intervention in stable and unstable coronary artery disease.

Methods: We performed a computerized literature search of all existing studies comparing BMS versus DES by comparing the performance and effectiveness of DES vs. BMS in saphenous vein grafts. A significant reduction in overall death and non-fatal myocardial infarction, and repeat revascularization. Data from both observational studies and randomized trials were included in this systemic review.

Results: A total of 14 studies met the inclusion criteria including 4 randomized clinical trials (RCTs) (812 patients; DES= 416, BMS= 396) and 10 observational studies (9647 patients; DES= 4985, BMS= 4662). Minimum follow-up was 12 months and overall MACCE rate was 10.4% in DES and 15.7% in BMS (P=0.01), major adverse cardiac events was 22% in DES and 26.8% in BMS (P=0.01), non-fatal MI rate was 7.6% in DES and 8.5% in BMS (P=0.03), and the rate of repeat revascularization was 13.4% in DES and 15.4% in BMS.

Conclusion: In this comprehensive review of all available studies including RCTs and observational studies which compared clinical outcomes of PCI using DES vs. BMS in SVG lesions, use of DES in treating SVG lesions appears safe and effective in lowering all cause mortality, reduction in major adverse cardiac events and reduction in rate of repeat revascularization.
large side branch (SB), while standard treatment is stenting of the main branch (MB), with bailout stenting of SB only in case of a threatened need.

**Purpose:** Define the clinical implication of “bailout” stenting of the SB as compared with the “planned” strategy (either 1- or 2- stent).

**Methods:** We retrospectively collected data from patients having coronary bifurcation lesions treated with biologically active - either drug-eluting or bioabsorbable - coronary stents at 12 European centers; 1-year major adverse cardiovascular events (MACE), as the occurrence of death, myocardial infarction (MI) or stent thrombosis (ST) were evaluated.

**Results:** Among 2,602 patients treated at coronary bifurcations and followed for 18±10 months, bailout stenting of the SB was performed in 82 cases, for dissection (42%), plaque shift (40%), unsatisfactory result (15%) or geographical miss (3%); a “planned” strategy was performed in 2,520 cases, and in-hospital and 1-year outcomes in the similar regardless patients received 1 stent (83%) or 2 stents (7%); results according to treatment strategy are summarized in the table.

**Table 1. Results according to treatment strategy (planned strategy as “standard” vs. bailout branch stenting)**

<table>
<thead>
<tr>
<th></th>
<th>Bailout</th>
<th>Standard</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-hospital</td>
<td>82 (3%)</td>
<td>2520 (97%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Death</td>
<td>2 (2.4%)</td>
<td>23 (0.1%)</td>
<td>0.01</td>
</tr>
<tr>
<td>MI</td>
<td>28 (34%)</td>
<td>145 (5.7%)</td>
<td>0.01</td>
</tr>
<tr>
<td>ST</td>
<td>3 (3.7%)</td>
<td>25 (1.0%)</td>
<td>0.056</td>
</tr>
<tr>
<td>Major bleeding (BARC ≥3)</td>
<td>2 (2.4%)</td>
<td>18 (0.7%)</td>
<td>0.01</td>
</tr>
<tr>
<td>1-year</td>
<td>80 (100%)</td>
<td>2060 (82%)</td>
<td></td>
</tr>
<tr>
<td>MACE</td>
<td>14 (1.7%)</td>
<td>117 (5.9%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Death</td>
<td>6 (7.5%)</td>
<td>76 (3.8%)</td>
<td>NB</td>
</tr>
<tr>
<td>MI</td>
<td>5 (6.2%)</td>
<td>54 (2.7%)</td>
<td>0.01</td>
</tr>
<tr>
<td>ST</td>
<td>5 (6.2%)</td>
<td>26 (1.3%)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

**Conclusions:** In the treatment of coronary bifurcations, bailout stenting is associated with an unacceptable higher risk of both in-hospital and 1-year adverse outcomes. Further insights in the technical aspects and antiplatelet regimes are warranted.

**Acknowledgement/Funding:** ClinicalTrials.gov Identifier: NCT01967615

**P3458 | BEDSIDE**

**Malaposition and strut coverage following implantation of the Resolute Integrity stent in patients with ST elevation myocardial infarction assessed by optical coherence tomography**

M. Hoagad, H.S. Hansen, P. Thayssen, A. Junker, L. Antonsen, L.O. Jensen, Odense University Hospital, Department of Cardiology, Odense, Denmark

**Background:** Primary percutaneous coronary intervention (PCI) in ST elevation myocardial infarction (STEMI) is associated with greater risk of late stent malapposition and stent thrombosis despite improvements following development of second-generation drug-eluting stents (DES).

**Purpose:** The aim of this trial was to assess acute and late stent apposition, and coverage post PCI after 1 year following implantation of the Resolute Integrity DES in a STEMI cohort.

**Methods:** Eighty-seven patients with STEMI admitted for primary PCI were enrolled and examined with optical coherence tomography (OCT) of the stented vessel within 48 hours after primary PCI and after 1 year. Endpoints were OCT assessed malapposition: acute, persistent, resolved, and late acquired malapposition after 1 year, and strut coverage.

**Results:** Complete follow-up data was acquired in 74 patients with OCT. A total of 18,875 struts was analyzed post-PCI and 19,208 struts after 1 year. Complete OCT assessed malapposition was 4.0±2.0% (35.4%) patients. Median number of uncovered struts in patients with acute malapposition was 22.0 stent struts (8.0, 52.0) vs. 6.0 stent struts (0.0, 14.0) in patients without acute malapposition (p<0.004).

**Conclusions:** Although strut coverage was well extended, complete strut coverage after 1 year was seen in less than 1 out of 10 patients. Strut coverage was less in patients with acute malapposition.

**Acknowledgement/Funding:** The Danish heart foundation

**P3459 | BEDSIDE**

**Treatment of complex coronary bifurcation. Long term results of Tryton side branch stent vs minicrushing stenting**

A. Nicolino1, R. Rasso1, S. Moshiri1, A. Rognoni2, L. Olivotti1, A. Lupi2, A. Chisari1, A.S. Bongio2, G.B. Danzi1, Interventional Cardiovascular Unit: Santa Corona General Hospital, Pietra Ligure, Italy; 1Hospital Miglio, Della Carta, Cardiologia, Novara, Italy

**Background:** True coronary bifurcation lesions (CBL), defined as Medina classification 1, 1; 1, 0, 1; or 0, 1, 1; account for approximately 15% of all treated lesions and are associated with a lower procedural and long term success when compared with non-bifurcation lesions. Therefore, several dedicated stenting techniques and devices have been developed to improve clinical outcomes in this setting.

**Purpose:** The aim of this study was to compare the long-term clinical outcomes associated with a stent versus the “minicrushing technique” (MCT) with DES for the treatment of CBL.

**Methods:** We performed a retrospective analysis of patients with a true CBL who underwent PCI in two different centers between January 2008 and December 2012. We compared 30 CBL in 30 Patient treated with the Tryton (TR-group) in the side branch (SB) and DES in 30 main branch (MB) versus 30 CBL in 30 Patient treated with MCT (MCT-group). Patients were matched for age, risk factors and baseline characteristics. The measured end-points were cardiac death, follow-up myocardial infarction (MI), target lesion revascularization (TLR), target-vessel revascularization (TVR), and stent thrombosis (ST). The absolute risk of stent thrombosis after premature cessation of clopidogrel is currently not known. Consequently, it remains unclear when it is safe to discontinue clopidogrel.

**P3460 | BEDSIDE**

**Is it safe to discontinue clopidogrel in the first six months after stenting?**

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**Introduction:** Stent thrombosis (ST) remains a feared complication of percutaneous coronary intervention (PCI) with stent implantation. The incidence ranges from 1.2% to over 2% with a tendency to lower incidence rates in more recent studis. Premature discontinuation of clopidogrel administration is a very important risk factor for stent thrombosis. However, the absolute risk of stent thrombosis after premature cessation of clopidogrel is currently not known. Consequently, it remains unclear when it is safe to discontinue clopidogrel.

**Purpose:** To determine the absolute risk of stent thrombosis in patients with premature clopidogrel cessation in specific time frames (<30, <90 and <180 days) after index-PCI.

**Methods:** The current study is a subanalysis of The Dutch Stent Thrombosis Registry (DSTR), a large-scale, multi-centre study conducted in 3 high-volume centers in the Netherlands. Detailed information was obtained on the use of anti-platelet therapy at the time of ST. The proportion of patients who prematurely discontinued clopidogrel and consequently suffered a ST were compared with the proportion of matched controls (with a fictional ST date) who discontinued clopidogrel. The number of patients in the control group was extrapolated to the total number of patients undergoing a PCI in the study period. Consequently, the proportion of patients suffering ST while not on clopidogrel therapy could be related to all patients not on clopidogrel therapy in this specific time frame.

**Results:** The absolute risk of ST after cessation of clopidogrel therapy was 4.6% (95% CI: 3.9–5.4%) as compared to a rate of 1.7% (95% CI: 1.5–1.9%) in patients who did not discontinue clopidogrel (figure 1). A total of 134 out of 437 (30.7%) of ST-patients discontinued clopidogrel, as compared to 117/886 (13.5%) patients in the matched control group. The absolute risk of ST in patients without clopidogrel was calculated to be as high as 35.4% in the first 90 days after index-PCI declining to 11.7% in the first 180 days.
A novel simple experimental model for low-osmolar contrast-induced acute kidney injury using different definitions based on the levels of serum creatinine and cystatin C

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Aims: We aimed to develop a novel simple experimental model in mice for low-osmolar contrast-induced acute kidney injury (CI-AKI) with different definitions for AKI that would be comparable to CI-AKI in humans.

Methods: Fifty Sprague-Dawley rats were divided into five groups of 10 rats each: (1) sham group (normal saline (NS) + NS); (2) NS plus contrast medium (CM15) (NS with CM15); (3) iopromide (FM) plus NS (FM + NS); (4) FM + CM10; and (5) FM + CM15. After they were acclimatized for 7 days, and 6 h before CM administration, FM (10 mL/kg) was administered to groups 3, 4, and 5. Then, after restricted access to water for 6 h in all the groups, groups 2 and 5 received low-osmolarity CM (LOCM) (iopromide, 15 mL/kg) in the tail vein, and group 4 received LOCM (10 mL/kg) under ether anesthesia. Serum creatinine (SCr) and cystatin C (cys-C) levels were measured and histopathological scores were determined in kidney tissues.

Results: In the FM + CM15 group, SCr concentration was significantly higher after CM exposure than that before in the FM+CM15 group (0.08±0.03 vs. 0.18±0.05 μmol/L, p<0.001). In the other groups, there were minor changes in the SCr levels between the pre- and post- CM or NS exposure. In addition, the cys-C levels were also higher after CM exposure than that before in the FM+CM15 group (0.08±0.03 vs. 0.18±0.05 μmol/L, p<0.001). There were minor changes in the FM + NS group before and after NS administration. Furthermore, only rats in the FM + CM15 group developed CI-AKI based on the definitions for SCR or cys-C. The histopathological scores were significantly higher in the FM + CM15 group than in the FM + NS group.

Conclusions: We developed a simple and reliable animal model for LOCM-induced AKI that is similar to clinical CI-AKI based on different definitions for AKI.

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Three-dimensional echocardiographic assessment of mitral valve anatomical variables before and after minimally invasive MV repair with Neochord system on beating heart

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Recently a number of various minimally invasive MV repair techniques appeared in clinical arena, one of them is implantation of artificial chordae on beating heart with a Neochord DS 1000 device. The procedure is performed with a guidance of live 2D and 3D transesophageal echocardiography (TEE).

Aim of the study was to assess anatomical (3D echocardiographic) MV annulus variables in pre-operative and follow-up (FU) (15±6 months) data in patients with degenerative MR after MV repair with implantation of artificial chordae on beating heart. In addition, to investigate the difference of annular changes between successful (residual mild-moderate MR, ≤2) and not-successful (severe MR, >2+) MV repair groups.

Methods: 24 patients after MV repair for severe degenerative mitral regurgitation with Neochord device were studied: 12 patients with residual MR ≤2 (Group A) and 12 with residual MR >2+ during 15±6 months FU (Group B). The acquired preoperative and FU 3D TEE MV volumetric data were analysed using semiautomated MV modeling software. Annular and valvular parameters were measured at end-systole: annulus diameters (antero-posterior (A-P) and mediolateral (M-L)), MV circularity (MVC) index (reflected as min-to-max diameters ratio), annular height, perimeter, valve area, leaflet length, angles between anterior MV leaflet (AML) posterior MV leaflet (PML) with annulus, left ventricle end diastolic diameter (LVEDD), left atrial (LA) index volume.

Results: Among anatomical variables, a significant reduction in LVEDD and LA index volume was found in group A. Furthermore, significant differences were found in the angle between A2 segment of anterior leaflet and annulus, tenting height, where higher numbers were reported for group B compared to group A.

Conclusions: There is tendency of reverse remodeling in LV and LA during the follow-up period in successful group. 3D TEE identify MV anatomical variables predictive of middle term favorable results, mainly related to annulus and leaflet geometry such as angle between anterior leaflet and annulus, restrictive leaflet pattern.
Increase of hs-cTnT level after PCI

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Objectives: Flow-mediated dilatation (FMD) has emerged as a non-invasive baseline and 24 hours after PCI. PCI related myocardial injury was defined as a decrease of FMD group (n=7) as the brachial artery diameter increased maximally by a greater or equal 6% from baseline, and lower percent FMD group (n=34) by a less 6% from baseline. High sensitive cardiac troponin-T (hs-cTnT) was measured at 0.301±0.011–0.114 μm, p=0.047. PCI related myocardial injury was defined as the brachial artery diameter increased maximally by a greater or equal 6% from baseline, and lower percent FMD group (n=34) by a less 6% from baseline. High sensitive cardiac troponin-T (hs-cTnT) was measured at baseline and 24 hours after PCI. PCI related myocardial injury was defined as an increase of hs-cTnT. The primary endpoint is the incidence of PCI related myocardial injury.

Results: Baseline hs-cTnT was not significantly different between both groups, increase of hs-cTnT was significantly greater in lower percent FMD group compared to normal percent FMD group (0.116 vs 0.049, p=0.026). PCI related myocardial injury was detected more frequently in lower percent FMD group (54.5% vs 14.2%, p=0.037).

Conclusions: Based on currently available data, the presence of spotty calcification does not attenuate the response to the lipid-lowering therapy at midterm OCT findings. Spotty calcification probably is not a crucial risk factor in plaque regression when patients are under optimal therapeutic strategy.

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A novel CACNA1C mutation identified in a patient with atypical Timothy syndrome exerts both loss- and gain-of-function effects on Cav1.2

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Background: Timothy syndrome (TS) is a rare multi-system genetic disorder associated with long QT syndrome (LQTS, type B), congenital heart disease, syndactyly, and autism. Specific CACNA1C mutations, G406R or G402S, are causative of TS. More recently, TS patients with only LQTS phenotype without extra-cardiac features have been reported, in whom other CACNA1C mutations were identified.

Purpose: This study aimed to examine the genetic background of an atypical TS patient without syndactyly and assess its functional effect.

Methods and results: Index patient was a 14-year-old boy with prolonged QT interval (QT = 480ms, QTc = 478ms), dysmorphic facial features (but no syndactyly and autism). He had a cardio-pulmonary arrest during sleep at age 13. Genetic test identified a novel heterozygous CACNA1C mutation, S643F. Whole-cell patch-clamp technique in a heterologous expression system using HEK cells revealed that the S643F-CaV1.2 induced a reduction in peak current density (left panel of Fig.) as well as a marked delay of inactivation with subsequent increased late current (right panel) as seen in classical TS. In addition, a confocal microscope showed that there was no difference between wild type- and S643F-CaV1.2 channels in the intracellular expression pattern. S643 is located at the S4-S5 inner loop of domain II, which is linked to the voltage sensor, S4. Substitution of serine to phenylalanine may hinder the smooth movement of activation gate, thereby altering the inactivation.

Conclusions: A novel CACNA1C-S643F mutation exerted both loss- and gain-of-function effects on CaV1.2, thereby causing QT prolongation and arrhythmogenicity.

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Testing in a consecutive series of young athletes with suspected catecholaminergic polymorphic ventricular tachycardia

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Background: Catecholaminergic polymorphic ventricular tachycardia (CPVT; MIM 619138) is a rare inherited disorder due to mutations in RYR2, CASQ2, CALM1 and TRDN genes. It can be both autosomal dominant (RYR2 and CALM1) or recessive (CASQ2 and TRDN). It is clinically characterised by adrenergically induced polymorphic ventricular tachycardia (VT) in absence of structural heart diseases. Presentation includes syncope or sudden cardiac death (SCD) in young patients. Exercise testing is the gold standard for the clinical diagnosis and genetic testing may unravel additional asymptomatic carriers within the family.

Methods: We present a consecutive series of 25 young athletes (aged less than 18) with clinical suspicion of CPVT after undergoing pre-participation testing for competitive sports. Clinical assessment included: physical examination, surface ECG, echocardiogram and exercise testing (Bruce protocol). After genetic counselling, molecular testing was started by means of Next Generation Sequencing (NGS) on an Ion PGM platform with a targeted-resequencing panel of 148 cardiac genes.

Results and conclusion: After testing, we found 8 (32%) mutation-carriers of the RYR2 gene, 4 (16%) mutations-carriers of the CASQ2 gene and 2 (8%) mutation-carriers of the CALM1 gene. Cascade testing revealed additionally RYR2 (n=13), CASQ2 (n=7) and CALM1 (n=3) mutations carriers with (47%) and without (53%) clinical signs. The study proved that proper clinical for sport activity in the young athletes who have CPVT.
athletes is of utmost importance in identifying potentially individuals at risk of life-threatening arrhythmias. However psychosocial evaluations must included in order to overcome the life-style modifications subsequent to the genetic testing for the probands and their relatives.

Acknowledgement/Funding: RF2010 “Hypertrophic cardiomyopathy: new insights from deep sequencing and psychosocial evaluation”; Epidemiologia e Genetica della morte improvvisa

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The burden of complex arrhythmic genotypes in a consecutive series of Sardinian population of patients with primary arrhythmic disorders

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Brugada syndrome (BrS), Long QT syndrome (LQTS), Short QT syndrome (SQTS) and catecholaminergic polymorphic ventricular tachycardia (CPVT), are primary inherited cardiac arrhythmic disorders that can lead to sudden death. Prevalence might change according to the ethnicity and affecting mainly male patients in their third to fourth decade of life. They are inherited as autosomal dominant traits; but recent studies identified complex thought rare genotypes. We aimed to investigate the prevalence of mutations in the disease-genes underlying such inherited disorders in 400 patients of Sardinian ancestry. We analysed -by means of NGS - 148 arrhythmogenic genes in a consecutive series of 400 Sardinian patients enrolled at the San Francisco Hospital form years 2014 to 2015. In addition, to identify genes significantly enriched in the Sardinian series, we performed a mutation burden test by using as control dataset of continental Italians. We confirmed the genetic heterogeneity of the BrS, LQTS and CPVT but in addition we identified: a) a burden of complex genotypes (compound/double heterozygous and triple mutation carriers) with a higher prevalence in Sardinians compared with continental Indians (7.8% vs 3.2%) and b) new potential CPVT/LQTS candidates (such as CACNA1B, CASQ2) thus confirming the idea of a possible genetic overlap between the different disorders. As expected, the use of NGS in the Sardinian population to assess the contribution of genetics to such malignant cardiac traits, can further elucidate causal mechanisms and in addition these results identify a burden of complex genotypes that, in panels derived from more cosmopolitan populations, are missing

Acknowledgement/Funding: Fondazione Fioresta Longo; RF2010 “Cardiomiopatia (ipertrofica); Epidemiologia e Genetica della Morte Improvvisa in Sardegna

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Discrepancy of QTc duration and LQTS risk score for the diagnosis of type 3 LQTS


Clinical and ECG diagnosis criteria have been poorly described in type 3 Long QT Syndrome (LQT3). Patients and methods: Patients from our 2 reference centers with a pathogenic mutation in SCN5A for LQT3 were included. Pre-treatment paper ECGs were scanned and measurements were performed on-screen. Three consecutive RR and QT intervals were used to calculate Bazett corrected QTc interval. T-wave morphology was visually classified as normal, type LQT1, 2 or atypical. The LQTS risk score was calculated.

Results: Our LQT3 cohort included 133 patients. Pre-treatment ECG was available in 124 (93.2%). Mean QTcB was 469±9 ms. QTcB was below 480 ms in 59.7% and below 450 ms in 37.1% of patients (Figure). T-wave morphology was considered as normal in 44%, as typical of LQTS type 1, 2, 3 in 3%, 10% and 21% respectively and as abnormal in 26% of patients. Median LQTS risk score was 2.75 (IQR=3). Score was non diagnostic (-3) in 65% of patients. 70 out of 124 LQT3 patients (56.5%) had neither a QTc Bazett >480 ms nor a LQTS risk score >3.

Conclusion: Type 3 LQT3 patients display a large clinical and ECG spectrum. In our LQT3 cohort, half of patients with an unequivocally pathogenic mutation would not have been diagnosed based on QTcB duration or LQTS risk scoring.

P3470 | BEDSIDE
Complex inherited cardiac diseases inheritance in a family harbouring compound SCN5A and MYBPC3 mutations

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Molecular analyses are recommended for diagnosis, management and therapy of inherited cardiac diseases characterized by genetic heterogeneity and a predisposition to Sudden Cardiac Death (SCD). Here we described a unique Italian family with dilated cardiomyopathy (DCM), hypertrophic cardiomyopathy (HCM) and history of SCD. The index patient (II:5) was diagnosed at 38 years with early stage DCM and frequent polymorphic ventricular ectopy (PVC). During follow-up, addition of amiodarone to the standard therapy resulted in a dramatic reduction of PVC numbers with a recovery of the normal left ventricular function. Interestingly during echocardiographic follow-up evaluations, a progressively thickening of the interventricular septal wall was observed, reaching a thickness value of 17 mm at the age 50 years. The family history revealed that his brother died suddenly at 46 years old and a post-mortem DCM diagnosis was made. A clinical evaluation of other family members, revealed subjects affected by obstructive HCM (III:2) and DCM and PCV (III:3 and III:5).

In order to investigate the genetic basis of these complex and peculiar cardiac phenotypes a Next-Generation Sequencing custom-built panel was used for the detection of sequence variants in all affected family members. We identified two distinct gene variants, p.R222Q within the SCN5A gene and p.K754fsX78 in MYBPC3 gene previously described to be associated with DCM and HCM respectively. Patient II: 5 resulted to be carrier of both p.R222Q and p.K754fsX78 variants. His deceased brother (II:2) was also carrier of both SCN5A and MYBPC3 variants as inferred by segregation analysis. Patient III: 2 carried only the MYBPC3 p.K754fsX78 variant while the other two affected individuals (III:3; III:5) carry only the p.R222Q SCN5A mutation.

At the best of our knowledge this is the first report that describes how the cosegregation of two known specific disease-associated mutations in SCN5A and MYBPC3 determines in individuals bearing them a combined phenotype characterized by dilated cardiomyopathy (DCM), hypertrophic cardiomyopathy (HCM) and SCD. Moreover our study is an important example of personalized medicine confirming the previous data that in p.R222Q SCN5A mutation carriers, PVCS and DCM may be substantially rescued using drug that have sodium channel-blocking properties such as amiodarone. These findings emphasize the complex genetic background of inherited cardiomyopathies and highlight the need of a concerted clinical-molecular approach in the era of Next-Generation Sequencing that undoubtedly works as an efficient and cost-effective tool for molecular diagnosis of heterogeneous disorders in clinical practice.

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P3471 | BEDSIDE
Triple mutations in three major genes for long QT syndrome are very rare and cause complicated phenotypes with ventricular arrhythmia
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Background: Long QT syndrome (LQTS) is characterized by QT prolongation in 12-lead ECG and peculiar ventricular tachycardia called as torsade de pointe (TdP). The disease frequency is estimated around 1 per 2000. The main cause of LQTS is mutations in genes encoding cardiac ion channels and more than 60% of patients carried mutations in KCNQ1, KCNH2 and SCN5A. These gene mutations cause LQT1, LQT2 and LQT3. The frequency of compound or double mutations has been reported as 4 to 10%, however, patients with triple mutations have been rarely reported.

Objective: The aim of this study is to search for the frequency of triple mutation carriers in LQTS and clarify the detailed clinical severity of them.

Methods and results: The cohort of this study consisted of 1015 LQTS probands and their family members. We performed genetic screening for genes related with LQTS including KCNQ1, KCNH2, and SCN5A by Sanger methods or targeted resequencing using next generation sequencing. We identified two unrelated probands with three mutations in three genes (0.2%). The first proband was a 9-year-old boy who experienced syncpe while playing, and KCNQ1-R174C, KCNH2-E1039X, and SCN5A-E428K were identified. Another proband was an 11-year-old boy who suffered cardiac arrest while playing ball game. He carried KCNQ1-T587M, KCNH2-R148W, and SCN5A-K1244N. The minor allele frequencies of all mutations were less than 0.001 in ethnic matched healthy controls. We further performed clinical and genetic analysis of family members for three generations in both families (figure). Only probands were the three mutation carriers except for 2 years-old sister. Several members with one or two mutations showed QT prolongation, however, their symptoms were mild or none. These data suggest that the accumulation of the pathogenic mutations caused severe phenotype.

Family trees

Conclusion: Although the frequency of triple mutation carriers was very rare (0.2%), patients who diagnosed with LQTS, screening for three genes and identification of mutations would be indispensable for the clinical treatment and familial analysis.

P3472 | BEDSIDE
Evaluation of the diagnostic process of arrhythmogenic cardiogenetic disease: how to improve the yield?

Background: Over the past years, knowledge on the genetic aetiology of cardiac arrhythmias has increased enormously. A combination of both genetic and cardiac evaluation is important in the diagnostic approach of patients at risk for inherited cardiac arrhythmias (ICA). In order to obtain an acceptable diagnostic yield, a structured protocol for evaluation of patients at risk is needed.

Purpose: The goal of this study is 1) to evaluate the diagnostic process of ICA in various patient groups at risk and 2) to propose a protocol for cardiogenetic evaluation of these patients.

Methods: In this retrospective study we included 625 patients ≥18 years who visited the cardiogenetic outpatient clinic for cardiac arrhythmia evaluation. Patients were categorized by the reason of their visit: an out of hospital cardiac arrest (OHCA, N=69), unexplained ventricular tachycardia (VT, N=62), symptoms suspected for ICA (N=208), patients with familial arrhythmia (N=18), catecholaminergic polymorphic VT (N=8), short QT syndrome (N=1) and sick sinus syndrome (N=1). Twenty patients were diagnosed with a cardiac disease other than the aforementioned arrhythmogenic cardiogenetic diagnoses, mainly including cardiomyopathies. A mutation or unclassified variant without phenotypic manifestations was found in an additional 3% of patients. In OHCA and VT patients, the cause of the arrhythmia remained unknown in 64% and 52%, respectively. The lowest yield was obtained in patients who came for family screening without a known diagnosis in the index patient (16%). Holter recordings were most often abnormal in LQTS patients, showing a prolonged QT interval in 51%. An MRI was abnormal in >75% of patients with possible/borderline define ARVC or other cardiac diagnoses. A mutation or variant of unknown significance was found in 95% of genetically tested patients with LQTS, in contrast to 28% of patients with Brugada syndrome.

Conclusion: After cardiogenetic evaluation of patients at risk for ICA, a cardiac diagnosis other than a mutation or unclassified variant without a phenotype could be established in 35%. Based on the outcomes of evaluation in all patients at risk, a structured protocol was proposed to increase the yield of cardiogenetic evaluation and to avoid unnecessary (non-)invasive diagnostic testing.

P3473 | BEDSIDE
Clinical characteristics and prognosis of patients with non-type 1 Brugada-pattern electrocardiogram and a history of ventricular fibrillation
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Introduction: The clinical characteristics and prognosis of patients with non-type 1 (saddleback type) Brugada-pattern electrocardiogram (BrP-ECG) in the right precordial leads (V1-V3) and a history of ventricular fibrillation (VF) have not been fully investigated.

Methods: We investigated clinical characteristics and prognosis of consecutive 15 patients (12 males, mean age at the first VF: 38±12.1 years) with a history of VF and non-type 1 BrP-ECG, which never changed to type 1 BrP-ECG in the standard or high costal ECG recordings (2nd and 3rd) even after drug test by a sodium channel blocker, and compared them with those of 36 patients with type 1 Brugada syndrome (BrS) and documented VF. Both the standard and high-costal ECGs were recorded at each follow-up visit, and none of the ECGs of patients with non-type 1 BrP-ECG revealed type 1 BrP-ECG.

Results: During a mean follow up of 111±60 months, the recurrence rate of VF was similar between patients with non-type 1 BrP-ECG and BrS (8/15: 53% vs. 17/36: 47%, p=0.77). Analysis of the onset of VF showed a high incidence of nocturnal VF episodes (non-type 1: 73%, BrS: 53%) and VF with sudden onset pattern (non-type 1: 67%, BrS: 88%) with relatively long-coupled premature ventricular contractions similar to those of BrS (non-type 1: 388±50.6 ms, BrS: 382±59.8 ms). Among 15 patients with non-type 1 BrP-ECG and VF episodes, 13 (87%) showed interolateral early repolarization (ER) at baseline, and all patients with VF recurrence had interolateral ER.

Conclusion: Patients with non-type 1 BrP-ECG, which never changed to type 1 ECG, and a history of VF showed similar clinical characteristics and prognosis to those of type 1 BrS patients. Interolateral ER was identified in most patients with non-type 1 BrP-ECG and VF.

P3474 | BEDSIDE
Prognostic significance of dysrhythmias in patients with familiar amyloid polyneuropathy
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Background: Rhythm disturbances and conduct deficts are common consequences of cardiac amyloid infiltration in familial amyloid polyneuropathy (FAP) V30M-TTR. The occurrence of dysrhythmias appears to increase with the severity of the disease but its prognostic value is still unknown.

Purpose: To evaluate the occurrence of arrhythmias according to the patient’s age and the duration of symptoms and to analyze its prognostic value.

Methods: Prospective observational study with consecutive patients with FAP V30M-TTR who underwent annual cardiac evaluation including Holter recording.

Results: During a median follow-up of 55 months, 223 patients were evaluated (44±14 years; 54.3% female) and a total of 777 Holter recordings were performed. Among 211 patients, 15 patients (12 males, mean age at the first VF: 38.6±12.1 years) with a history of VF were studied. Analysis of VF showed a high incidence of nocturnal VF episodes (non-type 1: 73%, BrS: 53%) and VF with sudden onset pattern (non-type 1: 67%, BrS: 88%) with relatively long-coupled premature ventricular contractions similar to those of BrS (non-type 1: 388±50.6 ms, BrS: 382±59.8 ms). Among 15 patients with non-type 1 BrP-ECG and VF episodes, 13 (87%) showed interolateral early repolarization (ER) at baseline, and all patients with VF recurrence had interolateral ER.

Conclusion: Patients with non-type 1 BrP-ECG, which never changed to type 1 ECG, and a history of VF showed similar clinical characteristics and prognosis to those of type 1 BrS patients. Interolateral ER was identified in most patients with non-type 1 BrP-ECG and VF.

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Acknowledgement/Funding: This work was supported by Fondazione Roma grant (Italy, prot. 43/Al).
1.255, 95% CI 1.255–3.462, P = 0.001) and the number of premature supraventricular contractions (HR: 1.439, 95% CI 1.168–1.774, P = 0.001).

**Conclusions:** Holter monitoring should be integrated in the periodic evaluation of FAP V30M-TTR patients. The presence of brady or tachyarrhythmias and the number of premature supraventricular contractions are associated with unfavorable prognosis in these patients and should be treated timely.

**P3476 | BEDSIDE**

**Effects of cognitive behavioral therapy in cardiac electrophysiology device recipients**

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**Purpose:** Modern cardiac electrophysiology (CE) improves health-related quality of life (QoL), but up to one-third of CE recipients experience psychological distress after implantation, including anxiety or depression. The purpose of this study was to evaluate the effects of custom-designed cognitive-behavioral therapy (CBT) programme in patients undergoing CE.

**Methods:** Patients qualified for CE device implantation were randomized in order to receive either four weeks of CBT or standard medical care. CBT consisted of four one-hour sessions conducted over 30 (±3) days with a psychologist (practice nurse may also perform the therapy), who had received standardized training. Demographic, clinical and psychological factors were assessed. Beck Depression Inventory (BDI), State-Trait Anxiety Inventory (STAI), Acceptance of Illness Scale (AIS), and EuroQol-5D (EQ-5D) health questionnaires were used twice [at baseline (0), and 6 months after the implantation (6)]. Repeated measures analysis was used to assess the changes in effects of the intervention over time.

**Results:** We studied 128 patients (36.7% women, mean age 64.5±8.9). There were no statistically significant differences in psychological parameters between the groups. The proposed CBT programme and structured CBT meeting sessions was well accepted by the patients, which is confirmed by their high turnout for these meetings. After six months, psychological/QoL indices were significantly improved in CE recipients assigned to CBT, including: Visual Analog Scale (VAS) (80.2±11.8 vs 64.9±14.3 (P = 0.0001)), weaker occurrence of depression symptoms (BDI: 8.4±4.2 vs 11.0±5.2 (P = 0.0003), lower anxiety level (STAI-trait: 31.4±5.9 vs 38.1±19.6 (P = 0.0001) and STAI-state: 32.2±5.5 vs 38.5±8.9 (P = 0.0001)), and better acceptance of illness (AIS: 35.6±4.3 vs 28.7±6.1 (P = 0.0001)). Interestingly, these benefits were accompanied by better exercise tolerance [6-minute walk test: 395±128.2 vs 249±3.106.7 (P = 0.02), which equates 144%±28% vs 129%±18% (P = 0.0001)] as compared to the patients subject to standard care following their electrotherapy.

**Conclusions:** Our study had important clinical implications for nursing and medical management, caring for the group of patients in question. Custom-designed protocol of four cognitive-behavioral therapy sessions significantly improved indices of quality of life, depression, anxiety, and acceptance of illness, as well as exercise tolerance (6MWT) six months after cardiac electrophysiology procedure. CBT seem to be a feasible and valuable addition to CE patient population, as well as, ensured the fulfillment of its expected therapeutic effect, while the short duration of the therapy did not prolong hospitalization itself.

**P3476 | BEDSIDE**

**Amiodarone- associated altered sterol metabolism - A possible link to drug-induced steatohepatitis**

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**Introduction:** Amiodarone, a highly effective antiarrhythmic drug is widely used in suppressing atrial and ventricular tachyarrhythmias. The drug is known to have many adverse effects including hepatotoxicity, of which the pathogenetic mechanism is still evolving. Serum desmosterol level is increased in non-alcoholic steatohepatitis, and this cholesterol precursor is suggested to have a prominent role in the pathogenesis of liver inflammation.

**Purpose:** The present study was conducted to evaluate the effects of long-term amiodarone treatment on serum non-cholesterol sterols. We assessed the hypothesis that serum desmosterol levels are increased during amiodarone treatment.

**Methods:** The study population consisted of 56 patients with myocardial inflammatory disease (MID) (40 women, 16 men, mean age 53±1.5 (SE) years, body mass index (BMI) 25±0.9 kg/m²) and 124 healthy controls with similar age, gender and BMI. MID patients were divided into amiodarone (MID drug, n=20) and no amiodarone (MID control, n=36) treatment groups. Serum lipids were determined with gas-liquid chromatography.

**Results:** Serum total cholesterol and serum triglyceride concentrations were similar between both MID drug and MID control groups (eg, total cholesterol 5.7±0.4 vs 5.6±0.2 (SE) mmol/L, NS), respectively. However, desmosterol level was higher in MID drug compared with MID control group (1088±22 vs 92±10 μmol/mmol of cholesterol, p<0.0001), whereas lathosterol, the other cholesterol precursor, was similar between the two MID groups (84±6 vs 92±5 μmol/mmol of cholesterol, NS). In three patients in MID drug group, desmosterol was analysed before and during amiodarone treatment demonstrating significantly lower levels prior to treatment (81±4 vs 858±18 μmol/mmol of cholesterol, p<0.0001). In MID control group, desmosterol levels did not differ from those in the healthy controls (78±7 μmol/mmol of cholesterol, NS). Plant sterol and cholestanol levels were similar between MID drug and MID control groups. In spite of increased desmosterol level in MID drug serum group, serum alanine aminotransferase values were similar to those of MID control group (30±2 vs 26±3 U/L, p = 0.09).

**Conclusions:** The novel observation in the present study was that amiodarone increased thirteen-fold serum desmosterol level. Desmosterol is known to be toxic at high levels and may thus have a role in hepatotoxicity associated with amiodarone treatment.

**P3477 | BENCH**

**Interactions of digitals and class-III antiarrhythmic drugs: amiodarone versus dronedarone**

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**Background:** A post-hoc analysis of the PALLAS-trial recently suggested possible interactions of dronedarone and digitals glycosides. We recently demonstrated proarrhythmic interactions of this combination in an experimental model. The aim of the present study was to compare the effects dronedarone or amiodarone in combination with digitals glycosides in an experimental whole heart model.

**Methods and results:** 11 female rabbits underwent chronic oral treatment with amiodarone (50mg/kg for 6 weeks). 10 rabbits were treated with dronedarone (50mg/kg/d for 6 weeks). 10 rabbits were used as controls. Hearts were isolated and Langendorff-perfused. Eight endo- and epicardial monophasic action potentials (MAPs) were recorded from the 12-lead ECG during ohmic stimulation. Reproducible action potential duration at 90% of repolarization (APD(90)) was chosen as a positive end point. Out of 20 hearts, 9 hearts were inducible with at least 3 episodes of ventricular tachyarrhythmias. An additional 7 hearts were inducible with at least 3 episodes of ventricular fibrillation. The incidence of tachyarrhythmias was well below 5% in 9 of 10 hearts (7 episodes). The incidence of ventricular fibrillation was 14%. Out of 21 amiodarone-pretreated hearts (21 episodes) and 2 of 11 dronedarone-pretreated hearts (6 episodes) showed VF before ouabain inactivation. Additionally, 2 of 11 amiodarone-pretreated hearts (13 episodes) showed VF.

**Conclusion:** In the present study additional treatment with ouabain resulted in an increased ventricular vulnerability in all study groups. Of note, chronically dronedarone-pretreated hearts were significantly more vulnerable than amiodarone-pretreated hearts. Ouabain led to a reduction of APD(90), ERP, and post-repolarization refractory period (PRR). This effect was more pronounced in dronedarone-pretreated hearts that were inducible as compared with all other groups. These results suggest that combination of amiodarone and digitals glycosides might not be as harmful as combining dronedarone and digitals glycosides.
of follow up between group 1 and group 2 (1 month: 12.2±4.1 vs 5.5±5.1 p < 0.05 and 2 months: 19.8±9.1 vs 10.5±3.8 p < 0.05). When assessing effectiveness of AADs for arrhythmia prevention at 1 month there was significantly less arrhythmia recurrence events (AT/AF) noted in propafenone group compared with sotalol group according to the data from ILR. 9.2±4.9 vs 13.9±6.8 (p = 0.05) as well as there was significant difference in number of hospitalizations 18 vs 13 (p = 0.05) and pharmacologic/electrical cardioversions 42/9 vs 54/6 in propafenone and sotalol groups, respectively. But when comparing data at month 2 and 3 of follow up the difference of the same parameters between the two groups was not significant. There was no difference in number of patients treated with propafenone 23.5% (n=16) and sotalol 26.1% (n=17).

Conclusions: Our study showed significant decrease in the rate of AT recurrences during the first month of "blind" period of PVI of AF in patients treated with propafenone compared with sotalol. Higher long-term follow up may showed decrease number of hospitalizations and cardioversions in the first month, but the treatment didn’t affect the number of repeat PVI procedures.

P3481 | BEDSIDE
Efficacy and safety of quinidine in patients with Brugada syndrome
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Introduction: Pharmacological treatment of arrhythmias in Brugada syndrome (BrS) may be challenging due to contra indicated drugs. Quinidine is a class IA antiarrhythmic drug useful in this disease. The aim was to evaluate the efficacy and safety of quinidine in a large cohort of patients with BrS.

Methods: Of a total of 367 patients with BrS in follow-up (43±14 years; 74% male), 12 patients (3.3%) were treated with quinidine 300mg or hydroquinidine 200mg daily (group 1), and 276 patients (75%) were treated with other drugs according to availability. We analyzed the indications and the long-term outcome of this therapy.

Results: After a follow-up of 85±54 months, 6 patients (50%) underwent quinidine treatment due to paroxysmal atrial fibrillation (AF) and 6 patients (50%) due to ventricular fibrillation (VF). Four patients (33%) underwent AF ablation in which quinidine was started due to AF recurrence. Quinidine was started before AF ablation in 1 patient (17%) and 1 patient (17%) had no AF ablation. Although 4 patients (67%) had AF recurrence after quinidine, inappropriate ICD shocks were reduced. Two patients (33%) had 2 recurrences of VF and 1 patient had 9 more VF episodes with appropriate ICD shocks. There were no major adverse effects to quinidine, only 1 patient presented a mild allergic reaction. Basal characteristics and follow-up outcomes are shown in the table.

Conclusion: Quinidine is a safe adjuvant therapy for recurrent arrhythmias in BrS.

P3480 | BEDSIDE
Comparison of propafenone and sotalol effectiveness in prevention of atrial tachyarrhythmias in early postablation period of atrial fibrillation
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Introduction: Currently pulmonary veins antrum isolation (PVAI) is one of the definitive treatments of paroxysmal atrial fibrillation (AF). However follow up and treatment in post-procedural period that is commonly complicated with early recurrence of atrial tachyarrhythmias (AT) still remains one of the difficult questions with ongoing studies.

Purpose: The study was designed to compare the effectiveness and safety of antiarrhythmic drugs (AAD) class IC propafenone and class III sotalol in early prevention of arrhythmias in post-procedural period of PVI.

Methods: Our randomized study included 133 patients with paroxysmal AF who underwent PVI. Mean age 56.9±8.8 yrs, 54% males. Group 1 (n=68) received Propafenone 250mg twice a day, according to availability. We analyzed the indications and the long-term outcome of this therapy.

Results: The rate of arrhythmia events in post-ablation period was 55.6% (n=74). Predominant arrhythmias were AF with regular rhythm – 55.4% of patients (n=41) and 44.6% (n=33) patients experienced paroxysmal AF. There was a significant difference between the number of recurrent arrhythmias in 1 and 2 months post-ablation period: 140/68 vs 70/30, respectively. There was no significant difference in number of hospitalizations at month 2 and 3 of follow up between group 1 and group 2 (1 month: 12.2±4.1 vs 5.5±5.1 p < 0.05 and 2 months: 19.8±9.1 vs 10.5±3.8 p < 0.05). When assessing effectiveness of AADs for arrhythmia prevention at 1 month there was significantly less arrhythmia recurrence events (AT/AF) noted in propafenone group compared with sotalol group according to the data from ILR. 9.2±4.9 vs 13.9±6.8 (p = 0.05) as well as there was significant difference in number of hospitalizations 18 vs 13 (p = 0.05) and pharmacologic/electrical cardioversions 42/9 vs 54/6 in propafenone and sotalol groups, respectively. But when comparing data at month 2 and 3 of follow up the difference of the same parameters between the two groups was not significant. There was no difference in number of patients treated with propafenone 23.5% (n=16) and sotalol 26.1% (n=17).

Conclusions: Our study showed significant decrease in the rate of AT recurrences during the first month of "blind" period of PVI of AF in patients treated with propafenone compared with sotalol. Higher long-term follow up may showed decrease number of hospitalizations and cardioversions in the first month, but the treatment didn’t affect the number of repeat PVI procedures.

Conclusion: Quinidine is a safe adjuvant therapy for recurrent arrhythmias in BrS.
Patterns of amiodarone use and outcomes in clinical practice for atrial fibrillation: insights from the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT AF)

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Background: Amiodarone is the most effective antiarrhythmic at maintaining sinus rhythm in atrial fibrillation (AF), but it has a high incidence of adverse effects.

Purpose: Define patterns of amiodarone use and outcomes in clinical practice.

Methods: Using the US ORBIT AF registry, we analyzed differences in baseline characteristics of patients on amiodarone at enrollment, prescribed amiodarone in follow-up, or never on amiodarone. Hierarchical logistic regression modeling with site-specific random intercepts was used to compare rates of amiodarone use across the 174 sites. A logistic regression model for propensity to receive amiodarone at baseline created a propensity-matched cohort. Cox proportional hazards modeling, stratified by matched pairs, evaluated the association between amiodarone and outcomes.

Results: Among 9,720 AF patients, 1,481 patients (15%) were on amiodarone at any time during the 3-year follow-up. In comparison with those never on amiodarone, those on amiodarone at baseline or started in follow-up were more likely to be male (63% vs 60% vs 57%, p < 0.001), have coronary artery disease (48% vs 36% vs 35%, p < 0.001), have heart failure (43% vs 37% vs 31%, p < 0.001), and have an implantable cardioverter-defibrillator inhibitor (11% vs 10% vs 4%, p < 0.001). Patients in all 3 cohorts had median CHA2DS2-VASc scores of 4. There was significant variability in the proportion of patients at each site receiving amiodarone (Figure). Mortality, cardiovascular hospitalization rates, and stroke were similar among matched patients on and not on amiodarone at baseline (Table).

Association of amiodarone and outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Amiodarone use:</th>
<th>No amiodarone use:</th>
<th>Adjusted HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>133 (6.3)</td>
<td>140 (6.6)</td>
<td>0.99 (0.76, 1.29)</td>
</tr>
<tr>
<td>Cardiovascular death</td>
<td>52 (2.5)</td>
<td>61 (2.9)</td>
<td>0.87 (0.57, 1.33)</td>
</tr>
<tr>
<td>Sudden cardiac death</td>
<td>14 (0.7)</td>
<td>15 (0.8)</td>
<td>0.92 (0.41, 2.09)</td>
</tr>
<tr>
<td>Non-cardiovascular death</td>
<td>72 (3.4)</td>
<td>67 (3.2)</td>
<td>1.16 (0.79, 1.68)</td>
</tr>
<tr>
<td>First cardiovascular hospitalization</td>
<td>347 (21.3)</td>
<td>344 (20.7)</td>
<td>1.08 (0.91, 1.29)</td>
</tr>
<tr>
<td>Stroke</td>
<td>10 (0.5)</td>
<td>21 (1.0)</td>
<td>0.55 (0.23, 1.29)</td>
</tr>
</tbody>
</table>

Figure 1: Proportion of Patients at a Site Using Amiodarone (%)

Conclusions: Approximately 1 in 6 AF patients was treated with amiodarone over the course of the study with significant site-level variation. In comparison to recent literature, long-term mortality and hospitalization rates were similar for matched AF patients on and not on amiodarone in this observational study.

Acknowledgement/Funding: Janssen Pharmaceuticals

Effect of VK-Il-86 in VF activation frequency and electrical heterogeneity modifications induced by acute local stretch

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Introduction: Myocardial stretch can modify the electrophysiological properties of the heart and produce electrical dysfunctions. These interactions are called “mechanoelectrical feedback”. Across this mechanoelectrical interactions, stretch can be arrhythmogenic, and the store-overload-induced Ca2+ release (SOCIR) seems to be implicated in this deleterious effect. VK-Il-86 (a novel selectiveryanodine receptor type 2 agonist) could modulate these effects.

Purpose: We have investigated the effect of VK-Il-86 on the stretch-induced ventricular fibrillation (VF) modifications in a model of acute ventricular local stretch using isolated rabbit hearts.

Methods: 14 adult male White New Zealand rabbits were used. After euthanasia (thionental, 200 mg/kg) according to European ethics laws and heparrinization, their hearts were removed and placed in a Langendorff perfusion type setup. Pacing electrodes and a recording multielectrode (121 electrodes) were placed on the left ventricle epicardium. VF (with continuous perfusion throughout the whole experiment) was triggered pacing the left ventricle at increasing frequencies. Stretch was produced by an “ad hoc” device introduced from the left atria to the left ventricle. VF recordings were obtained before (basal) and at the third minute in control conditions and under drug infusion (0.1μmol/L and 1μmol/L). VF dominant frequency (DF) and VF spectral correlation (SpC) were measured by spectral techniques. Significance was reached when p < 0.05.

Results: Myocardial stretch significantly increased DF in control conditions (15.3±3.4 vs 17.5±2.7 Hz, p < 0.05) and under 0.1μmol/L VK-Il-86 (13.2±2.4 vs 16.2±4.5 Hz, p < 0.05), but not under 1μmol/L VK-Il-86 concentration (7.2±1.4 vs 7.3±0.6 Hz, ns). The significant stretch-induced decrease in SpC observed in control conditions (24.1±6.7% vs 19.6±4.3%, p < 0.05) was slightly attenuated under 0.1μmol/L VK-Il-86 (34.7±5.6% vs 28.8±4.3%, p < 0.05).

Conclusion: The ryanodine receptor type 2 agonist VK-II-86, abolished the changes in VF activation frequency produced by acute local ventricular stretch at the 1μmol/L concentration. It seems that this drug attenuated the stretch-induced activation heterogeneity at the lowest concentration used.

The mechanism of augmented propafenone effect on SCN5A channel with R1193Q polymorphism

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Introduction: Propafenone is a type IC antiarrhythmic drug which has been used widely for cardioversion of paroxysmal supraventricular tachycardia and recent-onset atrial fibrillation. Class IC Na channel blockers may unmask the hidden Brugada syndrome. SCN5A R1193Q is a common polymorphism in Asian. R1193Q has been reported in patients with long QT syndrome or Brugada syndrome. Previously, we reported a patient harboring R1193Q presented Brugada syndrome type I ECG pattern after treatment with propafenone.

Purpose: To investigate the underlying mechanism of the increased sensitivity to propafenone on SCN5A R1193Q channel.

Methods: Variant was engineered using site-directed mutagenesis and expressed transiently in HEK293 cells. Whole-cell sodium currents were measured using the patch clamp technique.

Results: We characterized the tonic block (TB) and use-dependent block (UBD) by propafenone in WT and R1193Q. As shown in Figure A, there was no remarkable difference in the extent of TB. Conversely, when tested the use-dependent block by a protocol that mimic the clinical condition (depolarizing pulse to -10 mV from a holding potential of -100 mV for 400ms) at a clinically relevant concentration of 2 μmol/L propafenone, R1193Q demonstrated a significantly higher block than WT. At 1 Hz, UBD was 10.8±2.6% and 25.1±3.7% for WT and R1193Q respectively with IC50 2 times lower in R1193Q than in WT (Figure B). At 2 Hz, UBD was 24.8±3.5% and 44.2±5.7% in WT and R1193Q respectively with IC50 2 times lower in R1193Q than in WT (Figure C). Figure D showed that R1193Q recovered more slowly than WT from propafenone block. According to the modulated receptor hypothesis and the microscopic reversibility, sodium channel blockers prefer to binding to the inactivated channel and tightly binding of a drug to the inactivated state must be accompanied by a shift in equilibrium from resting toward inactivated states once channels have bound drug. Therefore we compared the shift of steady-state inactivation (SSI) curves of WT and R1193Q with 2 μmol/L propafenone. As shown in Figure E, V1/2 for WT was shifted by...
Purpose: Amiodarone is the most effective antiarrhythmic agent for the treatment of atrial fibrillation (AF) but its use is limited by side effects related to the cumulative drug exposure. Standard weekly doses of 1400 milligrams (mg) are common in practice. Protocol driven down titration is not commonly employed. We sought to demonstrate the effectiveness and safety of such a strategy for AF management.

Methods: There were 124 (70 males, 54 female) consecutive patients in a single cardiology practice deemed eligible for amiodarone therapy for AF management evaluated. Seventy-two patients (58%) had implanted devices (29 IPG, 24 ICD, 17 cardiac pacemaker) and 52 patients (42%) were on anti-arrhythmic drugs. During down titration, most patients were seen in clinic every 6 to 8 weeks or assessed by remote monitoring if they had implantable devices. Successful control of AF was defined as AF burden ≤1% at last follow-up on implantable device patients or lack of symptoms and normal sinus rhythm on last holter monitor or routine 12 lead electrocardiogram on non-device patients.

Results: Ninety-five (77%) patients (52m, 43F, aged 33–102 years, median 80) were included (85%) with 124 (70 males, 54 female) consecutive patients in a single cardiology practice deemed eligible for amiodarone therapy for AF management evaluated. Seventy-two patients (58%) had implanted devices (29 IPG, 24 ICD, 17 cardiac pacemaker) and 52 patients (42%) were on anti-arrhythmic drugs. Down titration achieved much lower weekly doses than the standard practice and with rare side effects. Sustained effective control was maintained over a long follow-up. Implantable device diagnostics and remote monitoring are helpful in evaluating patients for effective AF control. A large, multi-center, prospective study may be warranted.

P3486 | BEDSIDE
Post resuscitation outcomes of one-month in patients with and without anti-arrhythmic drugs
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Background: Anti-arrhythmic drugs (AAD) are often used for fatal ventricular arrhythmias during cardiac-pulmonary resuscitation (CPR). We previously demonstrated the distinct superiority of nifekalant and amiodarone compared with lidocaine, for the survival admission and 24 hour survival (SOS-KANTO study 2012, JCPV 2015). However, the efficacy of initial AAD administration during CPR in improving long-term prognosis remains unknown. This study retrospectively evaluated the effect of AAD administration during CPR on 1-month prognosis in the SOS-KANTO 2012 study population.

Conclusion: AF can be controlled in most patients using a forced down titration monitoring protocol achieving much lower weekly doses than the standard practice and with rare side effects. Sustained effective control is maintained over a long follow-up. Implantable device diagnostics and remote monitoring are helpful in evaluating patients for effective AF control. A large, multi-center, prospective study may be warranted.

P3487 | BENCH
Genetic variants previously associated with catecholaminergic polymorphic ventricular tachycardia are frequently present in the general population
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Background: Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT) is a highly lethal cardiac arrhythmia disease occurring during exercise or psychological stress. It has an estimated prevalence of 1.000 per million and is associated with variants in genes regulating calcium as the main contributors. This study challenges the pathology of variants previously associated with CPVT.

Purpose: Genetic screening is applied more than ever in identification of patients, and new diagnostic CPVT guidelines have recently recommended genetic screening for variants in CASQ2 and RyR2, and proposes it to be used as diagnostic criteria equal to conventional clinical tests. Individuals can be diagnosed on genetic analyses alone without clinical data, and it has therefore become more important to distinguish truly pathogenic variants from innocent bystanders. This is important in preventing incorrect diagnosis of healthy people.

Methods and results: Identification of potential false-positive pathogenic variants was conducted by searching The Exome Aggregation Consortium (ExAC) database (n=60,706) for variants reported to be associated with CPVT. Four different in silico tools predicted the pathogenicity of CPVT associated variants, and we compared the results between variants found in ExAC and those not found in ExAC. Thirty-eight out of 246 variants previously associated with CPVT were identified in the ExAC database. We predicted the prevalence for 30 of these variants. The allele count was 413 out of 54,415 individuals, corresponding to a CPVT prevalence of 1:132. The in silico predictions showed a reduced probability of disease-causing effect for the variants identified in the exome database. Using a requirement of an agreement among ≥3 of the prediction tools, 82% of those not identified in ExAC were predicted correctly while 34% of the variants identified in ExAC were predicted damaging (P < 0.001).

Conclusions: We have observed an overrepresentation of previously CPVT associated variants in a large exome database, indicating that these variants are not identified in ExAC.

Acknowledgement/Funding: The Research Foundation of the Heart Centre Rigshospitalet, The Danish Heart Foundation, Danish Arrhythmia Research Centre

P3488 | BEDSIDE
Cryptogenic stroke: prevalence and predictors of subclinical atrial tachyarrhythmias detected by prolonged continuous Holter monitoring

Background and aim: Ischemic stroke cause remains underestimated in 30% of cases, leading to a diagnosis of cryptogenic stroke. Subclinical atrial tachyarrhythmias (AT) are a major cause of ischemic stroke and may be often undetected.

Prolonged continuous monitoring devices can significantly increase the rate of diagnosis of AT but their use is limited by increasing costs. The aim is to assess prevalence and predictors of subclinical AT with continuous 7-day ECG Holter monitoring applied in patients with cryptogenic stroke.

Methods: In this prospective, observational study, consecutive patients presenting with cryptogenic stroke were included. Patients without documented episodes of AT at presentation and during in-hospital monitoring received 7-day Holter monitoring. All patients underwent ECG, clinical cardiac consultation, and transesophageal echocardiogram (TEE). The CHA2DS2 VASc Score was calculated for each patient without considering the episode of stroke of the index event. Presence of AT was defined as at least 1 period of >30 seconds’ duration of atrial arrhythmia.

Results: Out of 152 patients presenting with symptoms of stroke or transient ischemic attack, 45 patients (mean age 67±10 yrs, 62% males) were discharged
with a diagnosis of cryptogenic stroke and were enrolled in the study. TTE was performed within 7 days from admission. All patients received 7-day Holter monitoring within 7 days after discharge. The mean CHA2DS2-VASc Score was 3.5±1.2. A history of arterial hypertension was reported in 60% of patients, heart failure in 9%. Subclinical AT detected by continuous 7-day Holter monitoring had occurred in 14 patients (31%). Patients with AT were older (70 vs 66; p=0.05), with a significantly higher rate of hypertension (93% vs 56%; p<0.003), compared with patients without AT. At TTE, patients with AT showed a significantly higher left atrium dilatation (83 vs 59 ml; p=0.002) and a significantly higher left ventricular mass (300 vs 179 gr; p<0.001). The univariate analysis demonstrated that higher left ventricular end diastolic volume, left atrium volume, and left ventricular mass were predictors of AT (p<0.05). The rate of change in recommended therapy of 30% of all patients screened transferred into a number needed to screen of 3. Patients to change 1 secondary prophylactic regimen to oral anticoagulation.

Conclusions: In patients with symptoms of cerebral ischemic events 7-day Holter monitoring allows the detection of silent AT in 1 patient out of 3, leading to a relevant change in therapy in a substantial number of patients. Left ventricular hypertrophy, left ventricular and left atrial dilatations may represent predictors of silent AT.

P3489 | BEDSIDE
The diverse management and prognosis of supraventricular tachycardia in pregnant women: Poor prognosis for pregnant outcome in patient with non-PSVT pattern
J.W. Park, T.H. Kim, J.S. Uhm, H.N. Pak, M.H. Lee, B.Y. Joung. Yonsei University College of Medicine, Division of Cardiology, Seoul, Korea Republic of

Background: Supraventricular tachycardia (SVT) can be seen de novo or exacerbated by pregnancy, and can pose risks for both mother and the fetus. However, the diverse management and fate of SVT in pregnant women were not well known.

Purpose: We aimed to evaluate the fate of SVT in pregnant women in this study.

Methods: In 48 consecutive pregnant women with SVT, enrolled between January 2003 and July 2015, (mean age of 33±4 years, mean gestational age of 24±12.1 weeks), clinical characteristics and pregnant outcome were investigated during follow up period (median 60 days, 2–273 days). The primary endpoint was pregnant outcome which was defined as abortion for therapeutic or spontaneous purpose.

Results: PSVT was the most frequent SVT (n=15, 31.3%) in this study. Non-PSVT were consisted of atrial tachycardia (n=8, 16.7%), atrial flutter (n=3, 6.3%), atrial fibrillation (n=10, 20.8%), and pre-excitation (n=12, 25.1%). SVT was first documented in 25 (52%) patients, and preexisting SVT was aggravated in 5 (10%) patients. SVT was most frequently happened during the 3rd trimester (n=16 of 30, 53%). While 8 out of 33 patients (24%) with non-PSVT had abortion, patients with PSVT had no abortion (p=0.044). Preterm delivery was observed in one case of each group (p=0.532). The Kaplan-Meier curve showed that patients with non-PSVT were associated with higher abortion events rather than those with PSVT (Log Rank, P<0.022).

Conclusions: Pregnant women with non-PSVT are associated with poor pregnant outcomes, compared with those with PSVT. Therefore, pregnant women with non-PSVT should be meticulously managed and treated before pregnancy if possible.

P3490 | BEDSIDE
Clinical characteristics and outcomes among haemodialysis patients with newly diagnosed atrial fibrillation: Insight from the RAKUEN study
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Purpose: Using data from the RAKUEN (Registry of Atrial fibrillation in chronic Kidney disease Under hEmodialysis from Niigata) study, we examined the incidence, clinical characteristics, and outcomes among haemodialysis patients with newly diagnosed AF.

Methods and results: Of 423 patients undergoing maintenance haemodialysis, 341 patients without AF at baseline (age 63±12.7 yrs, male 70%, mean duration of haemodialysis 125±111 mo) were enrolled. During observations lasting a mean of 36 months, AF was found in 46 (13%) patients (Picture). This represents an incidence of 4.0 per 100 patient-years. Newly diagnosed AF was independently related to increased age (odds ratio 1.054, 95% confidence interval 1.024–1.084), longer haemodialysis duration (odds ratio 1.003, 95% confidence interval 1.000–1.006), and larger left atrium diameter (odds ratio 1.130, 95% confidence interval 1.062–4.204). The incidence of all-cause death was significantly higher in the newly diagnosed AF patients than in sinus rhythm (n=295) patients (p<0.002), but the incidences of ischemic stroke/systemic embolism, major bleeding and congestive heart failure were similar in both groups of patients. Cardioembolic stroke was found in 1 (2%) of 4 (9%) ischemic stroke patients with newly diagnosed AF during the study period.

Conclusions: In haemodialysis patients, the incidence of newly diagnosed AF was extremely high, with poor mortality.

P3491 | BEDSIDE
The clinical outcomes in atrial fibrillation patients with vascular disease: the Fushimi AF Registry
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Purpose: The clinical outcomes in atrial fibrillation patients with vascular disease (VD) including coronary artery disease and peripheral artery disease. REACH Registry showed that patients with VD had a higher rate of cardiovascular events than those without VD and that the event rate increased with the number of symptomatic VD. However, clinical outcomes of AF patients with VD are not clear.

Conclusions: We investigated clinical characteristics and outcomes of AF patients with VD.

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. We have enrolled 4,441 patients and one-year follow-up was completed in 3,749 patients from March 2011 to November 2015. Median follow-up period was 1,059 days. We defined VD as coronary artery disease (CAD) and peripheral artery disease (PAD). We investigated clinical characteristics of AF patients with VD and the incidence of death, stroke/systemic embolism (SE) and myocardial infarction (MI).

Results: Of 3,749 patients, 3,107 patients had no VD (no-VD group) and 642 patients had VD at baseline. Among 642 patients with VD, 70 patients had both CAD and PAD (poly-VD group) and 572 patients had either CAD or PAD (single-VD group). The mean age was higher in poly-VD and single-VD groups than no-VD group (72.9% vs. 66.9% vs 20.2%; p<0.01). The rate of prescription of antiplatelet drug was higher in poly-VD group than no-VD group (72.9% vs. 66.9% vs 20.2%; p<0.01). The rate of change in recommended therapy of VD and the incidence of death, stroke/systemic embolism and myocardial infarction increased with the number of symptomatic VD. Thus, CHADS2 score also increased with the number of VD (death: 14.3 vs. 7.9 vs. 5.9 per 100 person-years; log-rank p<0.01, MI: 1.9 vs. 0.4 vs 0.1 per 100 person-years; log-rank p<0.01). The incidence of stroke/SE was higher in single-VD group than the other groups (0.8 vs. 2.2 vs. 1.4 per 100 person-years; log-rank p<0.01). Finally, the incidence of composite of death, stroke/SE and MI increased with the number of VD (16.3 vs. 8.4 vs. 4.9 per 100 person-years; log-rank p<0.01).

Conclusion: AF patients with vascular disease, especially with poly-vascular disease, were at significantly higher risk for cardiovascular events.

Acknowledgement/Funding: Boehringer Ingelheim, Bayer Healthcare, Pfizer, Bristol-Myers Squibb, Astellas Pharma, AstraZeneca, Daiichi-Sankyo, Novartis Pharma, MSD
P3492 | BEDSIDE
Safe automatic 1-lead ECG screening for atrial fibrillation
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Background: Opportunistic screening for atrial fibrillation (AF) using pulse palpation in individuals over 65 years of age has been recommended by the European Society of Cardiology in order to reduce AF associated morbidity. Using intermittent ECG recordings as screening method increases AF detection as the condition commonly is paroxysmal in nature. Systematic AF screening using intermittent ECGs has been shown to be cost-effective. However, intermittent ECG screening generates a vast number of ECGs that can become cumbersome.

Purpose: We aimed to evaluate the performance of an automated AF screening algorithm against manual ECG analysis by specially trained nurses and physicians (gold standard) in 30 second intermittent 1-lead ECG recordings.

Methods: The STROKESTOP study is a systematic screening study for AF using intermittent ECG recordings. All individuals in the study without known AF registered 30 sec ECG recordings in lead I twice daily for a fortnight, and all ECGs were manually interpreted. Of these, 80,149 ECG recordings in 3,209 individuals were analysed using a computerised algorithm.

Results: Of the 80,149 ECGs of 30 sec duration, 69,789 (87.1%) were classified as devoid of abnormal rhythm by the algorithm. The manual interpretation (gold standard) was that all except 31 of these ECGs were normal, making the negative predictive value of the algorithm 99.96%. All participants diagnosed with AF in the study were identified by the algorithm as having abnormal rhythm.

Conclusions: Automatic ECG screening using a computerised algorithm safely identifies normal ECGs and reduces the screening workload by >85%, further enabling screening for AF with intermittent ECG recordings.

P3493 | BEDSIDE
The significance of left atrial symmetry to determine structural remodeling and outcome in advanced atrial fibrillation patients
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Introduction: Atrial structural remodeling in atrial fibrillation (AF) is an important prognostic factor in patients undergoing AF ablation, but is only estimated clinically through assessment of left atrial (LA) enlargement.

Purpose: We hypothesized that asymmetrical enlargement of the left atrium in AF patients characterizes less advanced structural remodeling and may help to predict AF ablation outcome.

Methods: Consecutive patients undergoing thoroscopic surgery for AF ablation were included. Two independent observers traced the LA endocardial borders on non-triggered contrast-enhanced magnetic resonance angiography exams excluding the pulmonary veins and LA appendage. We reconstructed a three-dimensional image of the LA cavity from the LA contours using custom made software and calculated the mean distances of all points to the plane of symmetry proportional to the LA volume as a score for asymmetry (*E-100mm/ml) (figure 1). The mean between the asymmetry measurements of the two observers was used for the statistical analyses of atrial asymmetry (AA).

Results: 71 patients (mean age 60±4 years; 69% male) with paroxysmal (n=34) or persistent (n=37) AF had a mean LA volume index on MRI of 50.1±21.8 ml/mm² and atrial asymmetry (AA) of 4.1±1.20. Inter-observer agreement for AA was reasonable (Pearson R: 0.68 p<0.001; intraclass correlation coefficient: 0.79). Patients with paroxysmal AF displayed significantly more AA compared to persistent AF (4.7±1.2 vs 3.7±1.1, p<0.001) and higher AA was associated with success of AF ablation (OR 1.57, 95% CI 1.02–2.40, p=0.039).

Conclusions: We developed a new reproducible index to predict AF recurrence after AF ablation. AA is associated with less AF progression and a better outcome after a thoroscopic surgery for AF. Potentially, decreased atrial asymmetry reflects the tissue loss of structural stability. High wall tension will make the atrium adopt a more spherical shape. A detailed analysis of structural remodeling at the level of the tissue substrate is therefore mandatory.

P3494 | BEDSIDE
Single centre experience in a large cohort of patients undergoing epicardial ventricular tachycardia (VT) ablation

Purpose: Epicardial ablation (EA) is one option to treat VT. Little is known about acute success rate, limitations and follow up of this procedure.

Methods: From 01/2012 to 02/2018, 721 patients underwent EA for VT. A total of 90 EA out of 510 VT procedures were performed: 75/15 m/f (%66/12) for DCM (n=49), CAD (n=21) and other CM (n=20), all in all 7 patients with previous cardiac surgery. In 8% (n=7, none with previous cardiac surgery) an epi approach was not possible due to extensive adhesions. In 4% (n=4) the approach was the only viable one to the left ventricular epicardium (valve replacement (n=1), failed endovascular access to the left ventricle (n=1), thrombus in the left cardiac cavities (n=2)). One procedure (1.2%) was stopped due to a relevant pericardial effusion after gaining epi access. Twenty two pts (24%) had an epi approach after failed previous endocardial ablation (abl) procedures (5 CAD, 13 DCM, 2 inflammatory, 2 ARVC). The remaining 67 pts (75%) had a combined epi-/endocardial approach as initial procedure. In 60 pts (67%) the clinical VT was inducible prior to ablation. Complete acute abl success, defined as non inducibility of any VT was achieved in 55 (92%) of these patients: In 13 pts (24%) due to endocardial abl, in 23 cases (42%) due to EA, and in 19 pts (34%) due to a combination of both abl strategies. Five pts (8%) remained inducible for the clinical tachycardia. In the remaining 29 pts (33%) a substrate modification including abatement of all late potentials in low-voltage areas was pursued but induction of VT was not possible or not performed. Reason for failed complete epi abolishment of all late potential were the proximity of abl to a coronary vessel in 7 (8%) and pulmonary nerve in 2 (2%) pts. Five (6%) minor complications and one (1.1%) major complication (RV perforation) occurred. The median follow up period for 67 pts was 12 (IQR 6, 23) months. 5 pts (7%, 2 CAD, 3 DCM) died due to an arrhythmogenic event, the median survival for DCM was 38 months and for CAD 30 months (log rank 0.4). During follow-up 51 pts (76%, 11 CAD, 30 DCM, 7 inflammatory, 3 ARVC) were free of any arrhythmia. Eleven pts (17%, 3 CAD, 5 DCM, 1 inflammatory, 2 ARVC) suffered of recurrent VT with documented ICD shock or ATR therapy.

Conclusion: Epicardial ablation can be done with a low complication rate including patients after previous cardiac surgery. The limitation for an epi access is mainly given by pericardial adhesions. In our collective the target for successful epi abl was on the endocardium despite an EA approach in 14%. In medium term follow up a combined epi-/endocardial approach for DCM is beneficial.

VENTRICULAR ARRHYTHMIA, ICD AND REMOTE MONITORING

P3495 | BENCH
Optogenetic termination of ventricular tachyarrhythmias in fibrotic myocardial cultures
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Background: Ventricular tachyarrhythmias (VT) are still a large cause of morbidity and mortality. Current investigative and therapeutic approaches are based on pharmacological, rather unspecific (drugs), traumatizing (electroshocks) or irreversible (ablotion). Optogenetics, instead, is a novel biological approach for reversible modulation of electrical function with unmatched spatiotemporal precision using light-gated ion channels. Recent studies have shown that optogenetic engineer- ing of cardiac tissue indeed allows optical pacing and light-induced arrhythmia termination. However, the effects of optogenetic control of cardiac electrical func- tion in pathological conditions, like fibrosis, have not been explored.

Purpose: To optogenetically modulate fibrotic myocardial cultures, by forced expres- sion of light-gated depolarizing ion channels, and study the effects of illumination (i.e. activation of these ion channels) on activation and tachyarrhythmias in these cultures.
Methods: Ventricular cardiomyocytes (vCMCs) and myofibroblasts (vMFbs) from 2-day-old Wistar rats were mixed 3:1 to create confluent fibrotic monolayers and cultured under multi-electrode arrays (MEA). Next, these, but also non-fibrotic control monolayers were transduced with lentiviral vectors encoding red-activatable channelrhodopsin (ReaChR), a light-gated depolarizing ion channel. Tachyarrhythmias were induced by optical burst-pacing, after which the cultures were subjected to programmed global LED illumination. Photocurrents of ReaChR-transduced vCMCs were characterized by whole-cell patch clamp.

Results: Although exposure to 10 ms orange (595 nm) light pulses evoked ac- xial potentials in both control and fibrotic ReaChR-expressing monolayers, the latter group needed a higher light intensity. Sustained monomorphic tachyarrhyth- mias were successfully induced by regional optical burst pacing in all cultures (cycle length 277±70 and 210±38 ms for fibrotic (n=3) and control (n=8) cultures, respectively). Furthermore, light pulses (50 ms) resulted in acute termination of the tachyarrhythmias in 100% of the ReaChR-transduced vCMCs monolayers, both for fibrotic and control cultures. However, illumination threshold (i.e. strength of illumination) for tachyarrhythmias termination was significantly higher in fibrotic monolayers when compared to controls (0.74±0.04 vs. 0.22±0.08 mW/mm², re- spectively, p<0.001). An inward current was recorded upon orange light exposure of single ReaChR-transduced vCMCs, whose strength was determined by level of illumination.

Conclusion: This is the first study to demonstrate successful termination of tachyarrhythmias in fibrotic myocardial cultures through optogenetics. The presence of myofibroblasts in the myocar- dials cultures significantly increased the illumination threshold for monolayer activation and tachyarrhythmia termination, which may have important implications for future translational studies.

Acknowledgement/Funding: Netherlands Organisation for Scientific Research (NWO, Vidi grant 91714336 to D.A.P.)

P3496 | BENCH Safe electrophysiologic profile of the potential novel antiarrhythmic drug antazoline

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Background: We recently demonstrated an antiarrhythmic effect of the antihis- taminic agent antazoline in an experimental model of atrial fibrillation. This drug has been effectively employed to suppress atrial fibrillation in a few small clinical studies. The aim of the present study was to assess potential effects of antazoline on ventricular repolarization.

Methods and results: In 10 isolated rabbit hearts, antazoline (10μM, 20μM and 30μM) was infused after obtaining baseline data. Eight endo- and epicar- dinal monophasic action potentials and a simultaneously recorded 12-lead ECG showed a significant QT prolongation after application of antazoline as compared with baseline (10μM: +20ms, p<0.05; 20μM: +28ms, p<0.05) and temporal dispersion of repolarization remained stable despite the described prolonga- tion of myocardial repolarization. Furthermore, antazoline extremely augmented ventricular effective refractory period (ERP), 10μM: +30ms, 20μM: +52ms, 30μM: +78ms, p<0.05) accompa- nied by an increase of action potential duration (APD90). Spatial and tempo- ral dispersion of repolarization remained stable despite the described prolonga- tion of myocardial repolarization. In addition, antazoline significantly increased the incidence of ventricular arrhythmias in 20% of the hearts, caused ventricular fibrillation in 10% of the hearts and did not significantly affect the incidence of atrial arrhythmias.

Conclusion: Antazoline may be a potential novel antiarrhythmic drug with a safe electrophysiological profile.

P3497 | BENCH Median nerve stimulation reduces ventricular arrhythmias induced by dorsomedial hypothalamic stimulation

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Background: This study tested the hypothesis that median nerve stimulation (MNS) prevents ventricular arrhythmias (VAs) induced by dorsomedial hypotha- lamus stimulation (DMHS) and investigated the electrophysiological mechanisms underlying the anti-arrhythmic effects of MNS by recording left stellate ganglion activity (LSGA).

Methods: Eighteen rabbits were anesthetized, the median nerve was anchored by stimulating electrodes and a bipolar electrode was implanted into the LSG to record nerve activity. The DMH was stimulated to induce arrhythmia. All animals underwent 6 repetitions of DMHS (30sec). The eighteen rabbits were divided into the following three groups: a control group, which underwent only DMHS (n=6); an MNS group, which underwent MNS during both the third and fourth DMHS repetitions (n=6); and an LSGA-recording group, for which LSGA was recorded at baseline, immediately following DMHS and again immediately following MNS and DMHS (n=6).

Results: Repeated DMHS induced multiple VAs, in the rabbits. Compared with the DMHS-only group, the concurrent administration of MNS during DMHS signifi- cantly reduced the incidence of VAs (7±3 and 9±2 beats for the third and fourth DMHS+MNS repetitions vs. 29±8 and 27±9 beats for the first two DMHS repeti- tions, p<0.05). The total duration of the abnormal discharges of the LSG (ADLSG) following MNS and DMHS was significantly reduced compared with that of the DMHS-only group (40±18 sec vs. 14±6 sec, p<0.05).

Conclusion: MNS reduced DMHS-induced VAs by suppressing the ADLSG.

Acknowledgement/Funding: Peking Union Medical College Innovation Fund (10023-1002-1008 to Shuang Zhao)

P3498 | BEDSIDE Ultra-high density mapping with multielectrode catheter vs conventional point by point mapping for ventricular tachycardia substrate ablation

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Introduction: Ventricular tachycardia (VT) substrate ablation is based on detailed electroanatomical maps (EAM).

Purpose: It is unknown whether high-density multielectrode mapping (MEM) is superior to conventional point-by-point mapping (PPM) in VT substrate ablation procedures.

Methods: This is a pilot randomized controlled study (NCT02083016). Twenty consecutive ischaemic patients (95% male, 67.6±10.5 years) undergoing VT sub- strate ablation were randomized to group A (n=10: substrate mapping firstly per- formed by PPM (Navistar) and secondly by MEM (PentaRay), ablation guided by PPM) vs group B (n=10: substrate mapping firstly performed by MEM and secondly by PPM, ablation guided by MEM). Ablation was performed accord- ing to scar-dechanneling technique. Late-potential (LP) pairs were defined as a Navistar-LP and a PentaRay-LP located within a 3D-distance ≤3mm. Data ob- tained from EAM, procedure time, radiofrequency time and VT inducibility after ablation were compared between groups.

Results: Larger bipol ar scar areas were obtained with MEM (55.7±31.7 vs. 50.5±26.6 cm², p<0.017). Substrate mapping time was similar with MEM (19.7±7.9 minutes) and PPM (25.9±12 minutes); p=0.222. No differences were observed in the number of LP identified within the scar by MEM vs PPM (72.7±50.5 mins).
Conclusions: In a multi-centre registry catheter ablation was correlated with significantly lower rate of mortality.

Acknowledgement/Funding: Grant initiated by Polish Society of Cardiology

P3500 | BEDSIDE

Correlation between ventricular arrhythmias and cardiac innervation: clinical impact on ablation procedure

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Aims: We aimed to assess the relationships between regional myocardial perfusion and sympathetic innervation at myocardial scintigraphy, and intra-cavitary electrophysiological parameters in patients with ventricular arrhythmias submitted to invasive electrophysiological study and ablation of the arrhythmic substrate.

Methods and results: Sixteen consecutive subjects referred to our institution for a pre-surgical invasive study underwent scintigraphic mapping (EAM) followed by trans-catheter ablations of ventricular arrhythmias were enrolled. Before the ablation procedure all patients underwent a combined evaluation of regional myocardial perfusion and sympathetic innervation by means of tomographic 99mTc-tetrofosmin and 123I-metaiodobenzylguanidine cadmium-zinc-telluride (CZT) scintigraphies, respectively. Off-line spatial co-registration of CZT perfusion and innervation data with the three-dimensional EAM reconstruction was performed in every patient.

CZT revealed the presence of myocardial scar in 55 (20%) segments. Of the viable segments, 63% exhibited a reduced myocardial perfusion and 62% anxiety at EAM. The potential impact of LVADS on the substrate and characteristics of ventricular tachycardia


Introduction: Ventricular arrhythmias (VA) due to heart failure related mechanism, whereas those related to a pre-existing substrate may remain. We aimed to evaluate the incidence, type of VA and response to ICD therapy in patients operated for destination therapy.

Methods: Consecutive patients receiving continuous flow LVAD (HeartWare) as destination therapy with prior ICD implantation who were discharged alive after surgery were enrolled between 2010 and 2015. All VA episodes occurring 12 months before and after LVAD implantation were reviewed for CL and response to ATP or shocks. VA occurring during LVAD implantation were excluded.

Results: A total of 26 patients (60±10 yrs, 69% male, 9 NICM, LVEF 24±7%, 123I-metaiodobenzylguanidine cadmium-zinc-telluride (CZT) scintigraphies, respectively. Off-line spatial co-registration of CZT perfusion and innervation data with the three-dimensional EAM reconstruction was performed in every patient.
P3502 | BEDSIDE
Prediction of post myocardial infarction ventricular tachycardia

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Introduction: The use of implantable cardioverter-defibrillators (ICD) in post myocardial infarction (MI) and low left ventricular ejection fraction (LVEF) is recommended to prevent cardiac sudden death. However, most of patients never receive ICD therapy and ventricular tachycardia (VT) may occur in patients with subnormal LVEF. Our current risk stratification based on LVEF seems inadequate. We studied whether the characteristics of MI scar, assessed by cardiac magnetic resonance imaging with late gadolinium enhancement (LGE-CMR), could predict the onset of VT in post MI.

Methods: Bi-centric retrospective study.

1. Center 1: Group 1 included 74 patients with a remote MI (>6 months) and a primary prevention indication for ICD implantation and was used to define the best criterion to predict the onset of VT.
   - Group 2 (54 patients, LVEF <40%) and 3 (15 patients, LVEF >40%), included patients hospitalized for VT (secondary prevention indication) and were used to test a criterion determined on group 1.
   - Center 2: Group 4 included 45 patients similar to group 1 and was used to re-test the criterion defined on group 1. Analysis of LGE-CMR was made by center 1 blinded for the follow-up realized by center 2.

Analysis: We performed a LGE-CMR study before implantation to assess scar morphology (surface and extent from endocardial to transmural and epicardial, intramural scar). Post treatment allowed the assessment of total surface of each subtype of scar but also surface of specific separated areas (ie intra and epicardial scar at the infarct border).

Results: In group 1: VT occurred in 23 patients (31%) (follow-up: 54±29 months).
   - There were no differences between patients with VT and without VT for demographic data, LVEF and MI surface. In VT patients, LGE-CMR showed greater total infarct myocardium scar (ISS) (6.2±4.1 vs. 2.7±2.8 cm²; p<0.001) and greater contiguous area of 1+epicardial scar (I+EpiSS), looking like a barrier at infarct borders (4.7±3.6 vs. 2.4±2.9 cm²; p<0.001). ISS and I+EpiSS were associated with the occurrence of VT (respectively: HR 1.20/cm², CI 1.09-1.31 and HR 1.18/cm², CI 1.06-1.31; both p<0.05). ISS >1.6 cm² (Se=80%, Sp=52%, NPV=100%) and I+EpiSS >1 cm² (Se=100%, Sp=52.9%, NPV=100%) were the best predictors of VT.
   - In patients of group 2 and 3 had ISS >1.6 cm² and I+EpiSS >1 cm².
   - In group 4, 22% of patients experienced VT (follow-up: 45±18 months). All VT patients had ISS >1.6 cm² (p<0.0001) and greater contiguous area of 1+epicardial scar/1+epiSS, looking like a barrier at infarct borders (5.7±3.6 vs. 2.4±2.9 cm²; p<0.001) and greater contiguous area of 1+epicardial scar (I+EpiSS), looking like a barrier at infarct borders (4.7±3.6 vs. 2.4±2.9 cm²; p<0.001). ISS and I+EpiSS were associated with the occurrence of VT (respectively: HR 1.20/cm², CI 1.09-1.31 and HR 1.18/cm², CI 1.06-1.31; both p<0.05). ISS >1.6 cm² (Se=80%, Sp=52%, NPV=100%) and I+EpiSS >1 cm² (Se=100%, Sp=52.9%, NPV=100%) were the best predictors of VT.

Conclusion: A critical total surface of IS and a contiguous surface of I+EpiSS, at an infarct border, are key factors for the onset of VT regardless of LVEF and could be area of slow/block of conduction.

P3503 | BEDSIDE
Chronic total occlusion in an infarct related artery: a new predictor of ventricular arrhythmias in patients with implantable cardioverter-defibrillators

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Background: Recent evidences suggest a pro-arrhythmic effect of a coronary chronic total occlusion (CTO), especially when associated with a myocardial infarction in their territory (IRA-CTO, i.e. Infarct Related Artery-CTO).

Purpose: To evaluate the impact of an IRA-CTO on the occurrence of ventricular arrhythmias (VA) in a broad population of ICD patients, both in primary and secondary prevention.

Methods: Observational study that included all consecutive patients that suffered from ischemic cardiomyopathy, had an ICD implanted for primary or secondary prevention at our center and had a coronary angiography before ICD implantation. Patients were followed with regular visits and ICD interrogations. Fast ventricular tachycardia (VT) was defined as a VT with a cycle length of less than 300ms.

Results: 243 patients were included in the study. 110 (45%) had a primary prevention indication. In 116 (48%) had an IRA-CTO. Patients with a secondary prevention indication had significantly higher prevalence of IRA-CTO (89% vs 31%, p<0.001). During a median follow up of 39 months (IQR 17–68), 119 patients (49%) experienced at least one episode of VT correctly treated by the ICD. IRA-CTO was associated with significantly higher rates of any VA (67% vs 32%, p<0.001), fast VT/VF (41% vs 16%, p<0.001) and appropriate ICD discharges (49% vs 20%, p<0.001). At multivariate Cox regression, after adjusting also for the indication for ICD implant, IRA-CTO resulted to be the strongest independent predictor of VT (HR 2.62, 95% CI 1.73–3.96, p<0.001) and fast VT/VF (HR 2.82, 95% CI 1.59–5.03, p<0.001). IRA-CTO was not a predictor of total mortality (HR 1.5, 95% CI 0.91–2.7, p=0.11).

Conclusions: In ischemic patients implanted with an ICD, a coronary chronic total occlusion associated with a previous infarction in its territory (IRA-CTO) is a frequent finding and is significantly more common among patients with a secondary prevention indication. IRA-CTO is an independent predictor of any VA and fast VT/VF and identifies a subgroup of patients with a very high incidence of arrhythmia events at follow up.

P3504 | BEDSIDE
The economic impact of longevity of implantable cardioverter-defibrillator for cardiac resynchronization therapy from a healthcare service perspective


Introduction: Patients receiving implantable cardioverter-defibrillator for cardiac resynchronization therapy (CRT-D) are likely to undergo one or more device replacements after the first implantation, mainly for battery depletion. The economic impact of longevity and device replacement from a healthcare service perspective in a real-world cohort of patients.

Methods: We analyzed data on 1,400 patients implanted with a CRT-D between January 2008 and March 2010 in 10 Italian centers, and followed-up until 2014. Probabilities of replacement for battery depletion, stratified by device generation and manufacturer, were calculated up to 6 years. Public tariffs from diagnosis-related groups were used. All costs are expressed in Euro (€) and refer to the fiscal year 2015.

Results: A total of 1,792 implantation/replacement procedures were performed during the observation period. The generators were from 3 manufacturers: Medtronic (973, 54%), Boston Scientific (667, 37%), and St Jude Medical (152, 8%). The Italian healthcare system spent €34 million for CRT-D therapy in the participating hospitals over the observation period. The initial implant cost was €30,679, the probability of replacement at 6 years was 83% and 68% for earlier- and recent-generation devices (released before and after 2007), respectively. Over 6 years, the cost for replacement per patient decreased by 30%, from €9,092 for earlier-generation to €6,953 for recent-generation devices, with a decrease of 6% in the overall cost of therapy. Among recent-generation CRT-Ds, the probability of replacement from different manufacturers ranged from 12% to 70%. The cost per-patient for replacement over 6 years ranged from €1,258 to €7,214, a difference of 83%. The difference in the overall cost of therapy was €9,092.

Conclusions: This study demonstrated that differences in CRT-D longevity strongly affect the overall cost of therapy and in particular, the cost of therapy decreased with recent-generation devices although significant differences exist among currently available systems.
P3506 | BEDSIDE
The impact of remote monitoring of implanted cardioverter-defibrillator and cardiac resynchronization therapy device patients on healthcare costs in long-term follow-up

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Aims: The population of patients with implanted cardioverter-defibrillators (ICDs) and cardiac resynchronization therapy devices (CRT-Ds) is constantly growing. The use of remote-monitoring (RM) techniques in this group can significantly improve clinical outcomes, but there are limited data about the impact of RM on healthcare costs from a payer’s perspective. The aim of the study was to assess the impact on costs for the healthcare system of RM in patients with ICDs or biventricular-ICDs in a real-world cohort.

Methods: We examined a cohort of 842 patients with ICDs or CRT-Ds. The group was divided into two groups based on RM (or no RM, NRM), matched according to important clinical characteristics. The subjects were followed for a maximum of 3 years after implantation (mean follow-up 2.11±0.83 years). The overall costs for the healthcare provider in the follow-up were defined as the primary endpoint. The secondary endpoint was the use of different types of medical contact: hospitalization and number of in-clinic and general practitioner visits.

Results: In the 3-year follow-up, the reduction in the costs of treatment for National Health Care in the RM group was 33.5% (median value, p<0.001). In patients implanted CRT-Ds, the reduction reached almost 43% (p=0.011) and with ICDs was more than 31 (31.3) % (p=0.007). We observed no significant reduction in the median hospitalization costs in the 3-year follow-up in the RM group (p = NS), despite 25% drop in the mean value. Costs of outpatient visits were lower in the RM group (p=0.013) in the follow-up period, there was no reduction in the number of medical contacts events (p=NS).

Conclusion: Remote monitoring in patients with implanted ICD or CTD-D devices reduces the cost of healthcare.

P3507 | BEDSIDE
Surface electrocardiogram screening for subcutaneous implantable cardioverter-defibrillator: the comparison between Brugada syndrome and non-Brugada syndrome

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Surface electrocardiogram (EKG) screening for subcutaneous implantable cardioverter-defibrillators (S-ICDs) is essential to prevent inappropriate shocks due to T-wave oversensing. It has been reported that in patients with Brugada syndrome (BrS) implanted with an ICD, T-wave oversensing is more frequent than those without BrS.

We assessed the current ICD recipients who are eligible for S-ICD implantation using the surface ECG screening and compared those with and without BrS.

Methods and results: A ECG screening tool was used to determine eligibility for S-ICDs in two different postures (supine and sitting), S-ICD eligibility required at least 1 lead to satisfy the S-ICD screening template in both postures. Patients who needed antiarrhythmic drug therapy were excluded.

Sixty ICD patients were assessed (age 57.0 years, 90% men, body mass index 23±3 kg/m², QRS duration 123±4 ms, QTc interval 437±42, and QRS axis 27±34 degrees). Overall, 9 (15.0%) of patients were considered not suitable for S-ICDs according to the surface ECG screening criteria. There were significantly more unsuitable patients in those with BrS compared to those without (p=0.016; 6/18 [33.3%] in BrS vs. 3/42 [7.1%] in non-BrS). There were no differences in the clinical characteristics and standard ECG measurements between those eligible and ineligible. The S-ICD screening template was satisfied more often by Lead III (primary vector, 77.1%) and Lead II (secondary vector, 68.8%) compared with Lead I (alternate vector, 43.8%).

Conclusion: Among current ICD patients, there was considerably high incidence of patients with BrS unsuitable for S-ICDs after the currently available screening test. There were no predictors associated with ineligibility for S-ICD implantations.

P3508 | BEDSIDE
Gender differences in the outcome of primary preventive implantable defibrillator therapy-data from the EU-CERT ICD study

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Aims:
The population of patients with implanted cardioverter–defibrillators (ICDs) is increasingly growing. Gender differences in the outcome of primary preventive ICD therapy have been consistently underrepresented in all major trials. We therefore analysed the outcome of ICD therapy in women in all 11 countries included in the EU-CERT ICD study.

Methods:
We aimed to identify baseline factors associated with an appropriate ICD therapy within 12 months follow-up. Both LVEF normalization and downgrading to CRT-P were defined as the primary endpoints. The secondary endpoint was the use of different types of medical contact: hospitalization and number of in-clinic and general practitioner visits.

Results:
At the time of replacement, the therapy indication to ICD at the time of first implantation. Overall, clinical indication to ICD did not persist at replacement in 70 (22%) pts. During a median follow up of 365 [25th-75th: 315–415] days, 31 (10%) pts received an appropriate therapy prior to device replacement (OR 3.46, 95% CI 1.44 to 8.28; p=0.005) and low glomerular filtration rate (OR 1.01, 95% CI 1.00 to 1.03; p=0.038) were independent predictors of appropriate ICD therapy within 12 months follow-up. Both LVEF normalization and the persistence of ICD indication were not associated to the occurrence of VTAs after ICD replacement.

Conclusion: Clinical indication to ICD does not persist in approximately 22% of CRTD pts who outlive their first device and about 11% of pts achieved LVEF normalization. Although these pts seem at lower risk and could be considered for downgrading to CRT-P, our post-replacement data showed a non-negligible risk of VTAs within 12 months follow-up.
from a central database. Survival curves and hazard ratios with multivariable correction for baseline parameters and testing for heterogeneity between centers were calculated.

**Results:** During follow-up 885 pts (19%) died. The risk of death for women (n=120) was significantly lower than that for men (n=765; adjusted HR 0.69; 0.43–1.04; p=0.06). Women also received significantly fewer first appropriate ICD shocks than men (60, 7% vs. 48, 14%; 95% CI 0.60–0.93; p=0.02). Women died sooner than men (154, 3% vs. 15, 1%; 95% CI 1.02–1.99; p=0.04).

**Conclusion:** Women have a significantly lower mortality than men, and they receive significantly fewer first appropriate ICD shocks than men. Outcome is affected by gender and the risk of death is lower in women than in men.

**Acknowledgement/Funding:** European Commission within the 7th Framework Programme under Grant Agreement n°602299

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**P3509 | BEDSIDE**

**Ventricular arrhythmia presentation in viral vs. autoimmune myocarditis**

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**Background:** Ventricular arrhythmias (VA) and sudden cardiac death (SCD) represent potential life threatening presentation of myocarditis. However, the relationship between VA and aetiology (viral vs. autoimmune) has never been investigated so far.

**Purpose:** Based on histological data, we aimed to define the relationship between VA and myocarditis according to different aetiology.

**Methods:** We selected 26 patients with a diagnosis of myocarditis by endomyocardial biopsy (EMB). They all presented to ER for palpitation or syncope. All of them had lab exams, echocardiogram, cardiac magnetic resonance (CMR) and coronary angiogram showing normal epicardial arteries. VA at presentation included frequent premature ventricular complexes (PVC >15,000/day), nonsustained and sustained ventricular tachycardia (NSVT, SVT) or fibrillation (VF). Viral or autoimmune myocarditis were diagnosed according to ESC working group consensus paper.

**Results:** Eight patients of 26 (30.7%) had a diagnosis of viral myocarditis (group V) at EMB, while the remaining 18 (69.3%) of autoimmune one (group A). 7/8 group V vs. 6/18 group A patients had acute myocarditis (p=0.03). 9 patients presented with syncope (group V = 4/8, group A = 5/18, p = n.s.) and 13 showed SVT or VF (group V = 5/8, group A = 7/18, p = n.s.). At presentation, VT was polymorphic in 4/6 patients in group V vs. 1/11 in group A (p=0.03). Monomorphic VT was the presenting arrhythmia in the majority of group A patients (10/11). In group V, 2/2 patients with monomorphic VT had parvovirus B19 genome on cardiac tissue. In group A, serum autoantibodies (AHA, AIDA) were found in 12/18 patients: among them, SVT or VF was found in 4/5 patients with predominant AIDA positivity vs. 1/7 patients with AHA prevalence (p=0.07). Left ventricle volumes (EDV and function) (EF) resulted 118±13 mL (V) vs. 135±17 mL (A) and 56±6% (V) vs. 45.5±7% (A) respectively (p=0.02 and p=0.03, respectively). According to EMB, 6/8 group V and 15/18 group A patients had interstitial fibrosis (p = n.s.). Similar results were found at LGE-CMR (6/8 vs. 14/18, p = n.s.), where extension of fibrosis resulted, and 15/18 group A patients had interstitial fibrosis (p = n.s.). Similar results were found in WBC, CRP, troponin T and NT-proBNP levels (all p = n.s.).

**Conclusion:** Significant differences between groups were found in EDV, EF and function vs. 1/7 patients with AHA prevalence (p=0.07). Left ventricle volumes (EDV and function) resulted 118±13 mL (V) vs. 135±17 mL (A) and 56±6% (V) vs. 45.5±7% (A). According to EMB, 6/8 group V and 15/18 group A patients had interstitial fibrosis (p = n.s.). At presentation, VT was polymorphic in 4/6 patients in group V vs. 1/11 in group A (p=0.03). Monomorphic VT was the presenting arrhythmia. Women had significantly lower mortality than men, and they received significantly fewer first appropriate ICD shocks than men. Outcome is affected by gender and the risk of death is lower in women than in men. Research funding has been obtained from the European Commission within the 7th Framework Programme under Grant Agreement n°602299.

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**P3510 | BEDSIDE**

**Effects of cardiac resynchronization therapy in patients with normal or impaired kidney function: a radionuclide study**

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**Background:** The clinical relevance of asymptomatic NSVT detected on pacemaker interrogation.

**Purpose:** To determine whether asymptomatic NSVT detected on PPM interrogation is associated with poorer patient outcome.

**Methods:** As part of an observational prospective, cohort study, 582 patients with long-term PPMs were recruited between January 2008 and December 2012 and followed for a mean (SD) period of 41±1.96 years. Any high ventricular rate episodes detected by the PPMs were reviewed by two independent observers and determined to be ventricular in origin or not. NSVT was defined as ≥3 consecutive ventricular beats at ≥100bpm lasting <30 seconds. The present abstract describes clinical, pacemaker and echocardiographic features associated with the presence of NSVT and a comparison of the outcomes of patients with and without NSVT corrected for important clinical variables. A p value ≤0.05 was considered significant.

**Results:** Of the 582 patients in the cohort, 17 were excluded from the analyses: lost to follow-up (n=7), devices were incapable of providing NSVT information (n=5) and where NSVT information had not been recorded (n=5). The 565 remaining patients had a complete dataset. Those excluded as a group, were not different in terms of age, medication use and important clinical variables. Patients in the final cohort (56.5 ± 57.34 ± 65.20 years, 768±4.4±19.3 years, left ventricular ejection fraction 49.8±11.3%) had their pacemaker for 9.8±5.1 years with mean RV pacemaker for 9.8±5.1 years with mean RV volume of 80±17 mL and mean EF of 54±6% in 22 patients (52%), impaired (48, 41–54 mL/min/1.73 m²) in 20 (48%). At baseline (during spontaneous rhythm), LVEF, intra- and interventricular dyssynchrony were similar between the groups. Immediately after CRT activation, a reduction in interventricular dyssynchrony at rest (from 23, 18–37°, to 18, 8–25°, p=0.05), and a slight improvement in PFR during exercise (p<0.001) occurred only in patients with preserved GFR. Over 3-month follow-up, an improvement in intraventricular dyssynchrony and LVEF was observed at rest and during exercise in both groups, with similar delta values versus spontaneous rhythm at baseline. A decrease in intraventricular dyssynchrony at rest (from 23, 18°–37°, to 18, 8–25°, p=0.05) and a slight improvement in PFR during exercise (p<0.001) occurred only in patients with preserved GFR. Thirteen (59%) patients with preserved GFR and 10 (50%) with impaired GFR were identified as CRT responders (p=0.55).

**Conclusions:** Patients with normal or impaired kidney function and preserved GFR, undergoing CRT, showed an acute decrease in intraventricular dyssynchrony and a mid-term improvement in intraventricular dyssynchrony and diastolic function during exercise, compared with patients with impaired GFR. Kidney function seems to be an additional factor modulating CRT electromechanical effects.

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**P3511 | BEDSIDE**

**The clinical relevance of asymptomatic NSVT detected on pacemaker interrogation**


**Introduction:** Nonsustained ventricular tachycardia (NSVT) is frequently identified in patients with permanent pacemakers (PPMs) during follow up, however its associated features and clinical relevance are unknown.

**Purpose:** To determine whether asymptomatic NSVT detected on PPM interrogation is associated with poorer patient outcome.

**Methods:** Patients with asymptomatic NSVT recorded by permanent pacemakers (PPMs) were reviewed by two independent observers and determined to be ventricular in origin or not. NSVT was defined as ≥3 consecutive ventricular beats at ≥100bpm lasting <30 seconds. The present abstract describes clinical, pacemaker and echocardiographic features associated with the presence of NSVT and a comparison of the outcomes of patients with and without NSVT corrected for important clinical variables. A p value ≤0.05 was considered significant.

**Results:** Of the 582 patients in the cohort, 17 were excluded from the analyses: lost to follow-up (n=7), devices were incapable of providing NSVT information (n=5) and where NSVT information had not been recorded (n=5). The 565 remaining patients had a complete dataset. Those excluded as a group, were not different in terms of age, medication use and important clinical variables. Patients in the final cohort (56.5±57.34±65.20 years, 768±4.4±19.3 years, left ventricular ejection fraction 49.8±11.3%) had their pacemaker for 9.8±5.1 years with mean RV pacing percentage of 72.3%±7.1%. Over the follow-up period, NSVT was noted in
Purpose: To perform a systematic review and meta-analysis of observational studies have suggested a potential role for cardiac magnetic resonance (cMR). Dilated cardiomyopathy (DCM) is far from being optimal. Recently, several reports for sudden death in DCM.

Conclusions: In patients with DCM, the presence of LGE is associated with a significant proportion of patients.

Conclusions: In patients with DCM, the presence of LGE is associated with a significant proportion of patients.

P3512 | BEDSIDE
Association between late gadolinium enhancement at cardiac magnetic resonance and ventricular arrhythmias in patients with non-ischemic dilated cardiomyopathy: a systematic review and metaanalysis
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Background: Risk stratification for sudden death in patients with non-ischemic dilated cardiomyopathy (DCM) is far from being optimal. Recently, several reports have suggested a potential role for cardiac magnetic resonance (cMR).

Purpose: To perform a systematic review and meta-analysis of observational studies that evaluated the association between the presence of late gadolinium enhancement (LGE) at cMR and sudden death or ventricular arrhythmias in patients with DCM.

Methods: A systematic search was performed in PubMed and Ovid using the following keywords: late gadolinium enhancement OR delayed gadolinium enhancement OR magnetic resonance AND cardiomyopathy OR arrhythmias OR ventricular tachycardia OR ventricular fibrillation OR sudden death OR sudden cardiac death. Studies were included in the metaanalysis if they reported the incidence of arrhythmic events in patients with DCM, segmented by the presence or absence of LGE. Sudden cardiac death, resuscitated cardiac arrest, sustained ventricular tachycardia and appropriate ICD therapies were taken into account as arrhythmic events. Specific data were obtained in several cases by asking directly to the corresponding author.

Results: The search allowed the identification of 2660 citations. 28 studies, involving 2787 patients, were finally included in the analysis. These works covered a wide spectrum of DCM patients, from mild to severe left ventricular dysfunction, both with and without implanted ICD. LGE was present in a variable proportion of patients with DCM (21% to 70%). The presence of LGE was associated with an important and statistically significant increase in the occurrence of arrhythmic events (pooled OR 3.9, 95% CI 2.9–5.2, p <0.001). Heterogeneity was not relevant (p=0.40). Egger and Peters tests excluded the presence of publication bias. Meta-regression analysis showed that differences in LVEF across studies did not significantly influence the association between LGE and ventricular arrhythmias or sudden death (p=0.2). The association between LGE and arrhythmic events was still present in all the sub-groups analyzed (mild/moderate vs severe left ventricular dysfunction, primary prevention ICD).

Conclusions: In patients with DCM, the presence of LGE is associated with a relevant and statistically significant increase in the occurrence of ventricular arrhythmias or sudden death. This association is observed across a wide spectrum of DCM patients. LGE could therefore be a useful tool to improve risk stratification for sudden death in DCM.
ventricular unloading, but appropriate ICD shocks still occur in VAD patients. An ICD is associated with improved survival in LVAD-supported HF patients.

P3516 | BEDSIDE
Predictors of in-hospital lethal arrhythmias in acute myocardial infarction: insights from J-MINUET study
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Background: Lethal arrhythmias including ventricular tachycardia and fibrillation (VT/VF) are common complications in acute myocardial infarction (AMI). Predictors of in-hospital VT/VF after AMI are not thoroughly investigated. In this study, we sought to elucidate predictors of in-hospital VT/VF events after AMI in Japan. Lethal ventricular arrhythmias were classified into two groups: QT/RR (J-MINUET), a prospective, multicenter registry conducted in 28 Japanese institutions.

Methods: Of 3,245 patients with AMI in the J-MINUET study, 125 patients had VT/VF episodes (VT/VF group). To adjust for potential confounding and selection bias, a propensity score-matched technique was performed based on age and gender, then identified matched 125 non-VT/VF patients (non-VT/VF group). Patient characteristics, comorbidities, clinical manifestations, and coronary angiographic findings were compared between the 2 groups.

Results: The mean age was 68±13 years. VT/VF group was associated with higher prevalence rate of chronic kidney disease (CKD) (P<0.001), diabetes mellitus (P=0.008), and multi-vascular coronary stenosis (P=0.007). VT/VF group also was associated with higher heart rate (HR) (P<0.001), lower systolic blood pressure (SBP) on admission (P<0.001), shorter time from onset to admission (P<0.001), higher serum potassium (P=0.04), lower high-density lipoprotein cholesterol (HDL-C) (P<0.001), higher maximum creatine kinase (CK) (P<0.001) compared with non-VT/VF group. In a multivariable analysis, HR (Odds ratio (OR), 0.97; 95% confidence interval (CI), 0.958–0.989; P<0.0005), SBP (OR, 1.02; 95% CI, 1.004–1.028; P<0.007), maximum CK (OR, 1.00; 95% CI, 0.9998–0.9999; P=0.0003), and CKD (OR, 3.3; 95% CI, 1.584–7.099; P=0.0015) were identified as independent predictors for VT/VF.

Conclusions: From J-MINUET study, higher HR, lower SBP, broader myocardial damage, and concomitance of CKD were independent predictors of in-hospital VT/VF after AMI.

P3517 | BENCH
Optogenetics to rethink ICD technology
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Introduction: Fatal cardiac arrhythmias are a major medical and social issue in Western countries. Current implantable cardiac defibrillators (ICD) have limited effectiveness and are plagued by frequent malfunctions and complications. Purpose: Here, we set up a new method to map and control the electrical activity of whole isolated mouse hearts and seek new effective interventions for interrupting arrhythmias. We exploit optogenetics aiming to provide novel stimulation patterns that can be translated to the electric strategies used in ICD technology. Methods: We employ a transgenic mouse model expressing Channel Rhodopsin-2 (ChR2) in the heart coupled with voltage optical mapping to monitor and control action potential propagation. The whole heart is loaded with the fluorescent red-shifted voltage sensitive dye (di-4-ANBDQX) and excited in wide-field configuration using a red LED. The wide-field imaging system is implemented with a 473 nm excitation laser for ChR2 activation. Moreover, the system is provided with a random access scanning head, developed using two orthogonally-mounted acousto-optical deflectors (AODs). AODs rapidly scan different sites of the sample, allowing us to design ad hoc ChR2-stimulation schemes. The central portion (100×100 pixel) of a sensor of sCMOS camera operating at frame rate of 2 kHz is used for imaging.

Results: We, first, confirmed that the ChR2 activation represents an effective alternative to the electrical stimulation of the mouse whole heart. Then, we induced arrhythmias by using a hypoxic, no-glucose solution and rapid ventricular pacing. After characterization of the re-entrant circuits by optical mapping, we designed different patterns of ChR2 stimulation aiming at reducing the radiation needed to effectively stop arrhythmias. We found that sinus rhythm is efficiently restored by employing lower-energy ad hoc patterns as compared to whole heart illumination. Conclusion: In this work, we exploited light-induced depolarizations as a work-bench for localized electrical discharges, in order to test novel approaches to interrupt cardiac ventricular arrhythmias. We provide evidences that mechanism-based interventions could reduce ICD electrical entrainment but yet maintaining the same success rate of cardioversion.

Acknowledgement/Funding: (FP7/2007–2013): 2415, 284464; NIH Grant: R01 EB001963; NANOMAX; WFR GR-2011-02350583; GGP13162; Ente Cassa di Risparmio di Firenze; TdRSADE project

P3518 | BEDSIDE
Zero-fluoroscopy approach for catheter ablation of idiopathic ventricular arrhythmias
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Introduction: Although complete elimination of fluorescence (zero-fluoroscopy ap-
SYNCOPE AND DEVICE COMPLICATIONS

P3519 | BEDSIDE
Clinical and electrocardiographical predictors of positive electrophysiological test in patients with syncope and wide QRS


Introduction: Electrophysiological study (EPS) is indicated for evaluation of patients with syncope of unknown origin when arrhythmic mechanism is suspected. Very few data are available about electrocardiographical (ECG) predictors of positive EPS in patients with syncope and wide QRS.

Objective: The purpose of this study is to assess clinical and ECG predictors of a positive EPS in patients with syncope of unknown origin and wide QRS.

Methods: The study included all consecutive patients in the period from 1 January 2011 to 31 December 2015 with wide QRS that underwent EPS for syncope. Syncope was defined as a sudden, unexpected loss of consciousness with or without immediate recovery within 1 minute. The presence of wide QRS (≥120 ms) was defined as the duration of the QRS complex lasting for ≥100 ms after class IC drug challenge, intracardiac block, corrected sinus node recovery time ≥525 ms or tachycardia induction with syncope.

Results: 186 patients were included (66.1% males, age 73.6±12.7, ischemic heart disease 20.8%). Type of bundle branch block were as follow: 38.8% left bundle branch block (LBBB), 38% 57.9% right bundle branch block (RBBB) plus left anterior hemiblock, 16.4% isolated RBBB, 2.7% RBBB plus left posterior hemiblock and 3.4% non specific conduction abnormality. EPS was positive in 33.9% of patients with wide QRS and 30.8% of patients with syncope. The activation of RASS and sympathetic nervous system in patients with vasovagal syncope was measured at (1) and (2). The groups were divided according to presence or absence of vasovagal syncope (2) and 10 minutes after syncope (3). Adrenaline and noradrenalin were measured at (1) and (2). The groups were divided according to presence or absence of vasovagal syncope immediately after syncope (2) and 10 minutes after syncope (3). Adrenaline and noradrenalin were measured at (1) and (2). The groups were divided according to presence or absence of vasovagal syncope.

Conclusions:

(a) The prevalence of wide QRS was higher 33.9% in patients with positive EPS compared to patients with negative EPS 30.8% (P=0.03). Syncope recurrence rate was lower in patients with wide QRS 9.5% compared to patients without wide QRS 30.8% (P=0.002).
(b) The prevalence of wide QRS was higher 33.9% in patients with positive EPS compared to patients with negative EPS 30.8% (P=0.03). Syncope recurrence rate was lower in patients with wide QRS 9.5% compared to patients without wide QRS 30.8% (P=0.002).
(c) The prevalence of wide QRS was higher 33.9% in patients with positive EPS compared to patients with negative EPS 30.8% (P=0.03). Syncope recurrence rate was lower in patients with wide QRS 9.5% compared to patients without wide QRS 30.8% (P=0.002).
(d) The prevalence of wide QRS was higher 33.9% in patients with positive EPS compared to patients with negative EPS 30.8% (P=0.03). Syncope recurrence rate was lower in patients with wide QRS 9.5% compared to patients without wide QRS 30.8% (P=0.002).
(e) The prevalence of wide QRS was higher 33.9% in patients with positive EPS compared to patients with negative EPS 30.8% (P=0.03). Syncope recurrence rate was lower in patients with wide QRS 9.5% compared to patients without wide QRS 30.8% (P=0.002).

P3520 | BEDSIDE
Syncope in patients paced for atrioventricular block

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Aims: Although syncope is the main reason for cardiac pacing in patients affected by atrioventricular block (AVB), very few data are available on the benefit of cardiac pacing in preventing syncopal recurrences.

Methods and results: We retrospectively evaluated 229 consecutive patients who had received a permanent pacemaker from 2009 to 2013 for AVB and syncope (94 patients) or AVB without syncope (135 patients). In patients with AVB and syncope, a third-degree or Mobitz II second-degree AVB had been documented in 73 and was only suspected in another 21, all of whom had bundle branch block. (Table 1). At 5 years, the actuarial syncope recurrence rate was 1% (95% CI, 0–3) in patients with documented AVB plus syncope and 3% (95% CI, 1–5) in those without syncope, whereas it was 14% (95% CI, 0–28) in patients with documented AVB plus syncope (P=0.001). (Fig. 1). All syncope occurred in patients without overt structural heart disease (SHD) (P=0.002 vs. patients with SHD).

Table 1. Patients' characteristics

<table>
<thead>
<tr>
<th>No. of patients</th>
<th>Total population</th>
<th>Syncope and AVB ECG documented</th>
<th>Syncope and AVB not ECG documented</th>
<th>No syncope, AVB</th>
<th>P value (syncope vs. no syncope)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>80±10</td>
<td>80±10</td>
<td>80±10</td>
<td>80±10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1–5</td>
<td>1–5</td>
<td>1–5</td>
<td>1–5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type of AVB</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>persistent</td>
<td>136 (60)</td>
<td>26 (36)</td>
<td>108 (80)</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>intermittent</td>
<td>74 (32)</td>
<td>47 (64)</td>
<td>27 (20)</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>III degree</td>
<td>130 (57)</td>
<td>56 (77)</td>
<td>74 (55)</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>II degree 2</td>
<td>78 (34)</td>
<td>17 (23)</td>
<td>61 (45)</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>Index diagnostic test</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>standard ECG</td>
<td>158 (69)</td>
<td>40 (55)</td>
<td>118 (87)</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>in-hospital telemetry</td>
<td>27 (12)</td>
<td>14 (20)</td>
<td>13 (10)</td>
<td></td>
<td>0.30</td>
</tr>
<tr>
<td>exercise test</td>
<td>8 (3)</td>
<td>4 (5)</td>
<td>4 (3)</td>
<td></td>
<td>0.45</td>
</tr>
<tr>
<td>out-of-hospital monitoring</td>
<td>15 (6)</td>
<td>20 (26)</td>
<td>0 (0)</td>
<td></td>
<td>0.001</td>
</tr>
</tbody>
</table>

Numbers in parentheses are percentages. *Out-of-hospital monitoring includes Holter, external or implantable loop recorders.

Conclusions: Cardiac pacing is highly effective in preventing syncopal recurrences when AVB is documented. Syncope may recur in a non-negligible minority of paced patients when AVB is suspected but not documented and in patients without SHD.

P3521 | BEDSIDE
The role of RASS and sympathetic nervous system in patients with vasovagal syncope

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The renin-angiotensin-aldosterone system (RAAS) and the sympathetic nervous system are important in the maintenance of vertical position. They both are activated with time and the duration of tilt testing may influence the activation. The aim of the study was to assess the activation of RAAS and catecholamines during tilt-induced vasovagal syncope.

The study included all 192 patients (F 140, M 52), aged 49.8±19.3 years, with the vasovagal syncope during diagnostic tilt testing. Plasma renin activity (PRA) and aldosterone were measured in a supine position before test (1), immediately after syncope (2) and 10 minutes after syncope (3). Adrenaline and noradrenaline were measured at (1) and (2). The groups were divided according to the phase of tilt test in which syncope occurred.

Results are shown in the table. There were several differences between the groups listed in the table. The acti-
The most frequent etiology of syncope patients in the outpatient clinic of Mary’s Hospital, Cardiology, Seoul, Korea Republic of three groups. We compared clinical courses and final diagnosis in the patients who visited outpatient clinic. Mean follow up duration was 23.2 months.

Methods: We conducted retrospective, observational study in 269 syncope patients. Measured variables included length of in-patient admission, waiting time. The objective of this study was to evaluate the safety and cost-effectiveness of a novel low-risk syncope assessment unit (SAU) recently introduced at a London Hospital.

Results: Of 262 patients evaluated at the FSDC, 101 patients (mean age 79.7 years, SD 17.7) were diagnosed with syncope. The prevalence of CI was 16.8% using the MMSE, and 60.4% using the MoCA (P=0.000). Only 11.5% of these patients had been diagnosed with CI prior to visiting the FSDC. The MMSE failed to identify 72.1% of patients with CI diagnosed by the MoCA. Mean MMSE and MoCA were 27.5 (SD 2.2) and 23.8 (SD 3.5), respectively. Four subdomains of the MoCA showed markedly lower scores compared with the other subdomains: trail making and cube copy tests, fluency, and delayed recall. There were no significant differences in prevalence of CI or MoCA and MoCA (subdomain) scores compared to FSDC patients with unexplained falls and no syncope.

Conclusion(s): CI was found in 60% of elderly syncope patients, which is more than three times the prevalence reported in the general population aged 75 years or older. Moreover, the MMSE failed as a screening instrument for CI in these patients. These findings suggest that CI may be underdiagnosed in elderly syncope patients. We therefore recommend that screening for cognitive function in older patients with syncope is routinely performed using the MoCA.

P3524 | BEDSIDE

An ambulatory syncope assessment unit is both cost-effective and safe in treating low-risk syncope patients

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Introduction: Up to half of the general population experience syncope in their lifetime. The objective of this study was to evaluate the safety and cost-effectiveness of a novel low-risk syncope assessment unit (SAU) recently introduced at a London Hospital.

Methods: A retrospective analysis of 50 in-patients admitted with syncope was performed. Measured variables included length of in-patient admission, waiting time. The objective of this study was to evaluate the safety and cost-effectiveness of a novel low-risk syncope assessment unit (SAU) recently introduced at a London Hospital.

Results: By initial clinical history, 125 (46.3%) were presumed neurally mediated, 43 (15.9%) were presumed to have other etiology and 101 (37.4%) were uncertain. The number of serious outcome was smallest in the presumed NMS group (2.4%), compared to presumed other etiology group (11.6%) and the uncertain group (4.9%). Hospitalization due to syncope and the syncope recurrence were also less observed in the presumed NMS group compared to the others (1.8% vs. 9.3% vs. 4.9%, respectively, p<0.022) (Table 1). During follow up, the final diagnoses were not changed in all 125 patients of presumed NMS group.

Conclusions: In the syncope patients who are presumed neurally mediated initially, the long term clinical courses are favorable. Also the diagnostic yield of careful history taking is high enough for the diagnosis of NMS.

Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Standard care (n=50)</th>
<th>SAU* (n=50)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (%)</td>
<td>69 (17.7)</td>
<td>63 (17.4)</td>
<td>0.100</td>
</tr>
<tr>
<td>Female (%)</td>
<td>29 (48)</td>
<td>27 (54)</td>
<td>0.870</td>
</tr>
<tr>
<td>Median number of in-patient bed days</td>
<td>4 (4.75)</td>
<td>1 (1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Median number of waiting time days to SAU appointment</td>
<td>2 (3)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Median number of waiting time days to investigation</td>
<td>24-hour holter TTE*</td>
<td>1 (2)</td>
<td>0</td>
</tr>
<tr>
<td>Diagnostic yield of examination (%)</td>
<td>TTE**</td>
<td>2 (1)</td>
<td>0</td>
</tr>
<tr>
<td>Diagnostic yield of investigation (%)</td>
<td>24-hour holter TTE**</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>30-day re-admission with syncope (%)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>–</td>
</tr>
<tr>
<td>90-day mortality (%)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>–</td>
</tr>
<tr>
<td>Diagnosis for syncope on discharge (%)</td>
<td>30 (60)</td>
<td>33 (66)</td>
<td>0.534</td>
</tr>
</tbody>
</table>

Conclusion: In the patients with syncope in the passive phase of tilt test the activation of RAAS is disturbed. The enhanced sympathetic activity in this settings could be responsible for neurocardiogenic reaction induction.

P3522 | BEDSIDE

Cognitive impairment is very common in elderly patients with syncope


Background/Introduction: Syncope is prevalent in older patients. Cognitive disorders may interfere with the diagnostic process of syncope. Although both cardiovascular disease and old age are associated with cognitive impairment (CI), the prevalence of CI in elderly syncope patients is currently unknown. The Mini Mental State Examination (MMSE) may not capture cognitive dysfunction in patients with syncope. The Montreal Cognitive Assessment (MoCA) is developed to identify early amnestic disorders, but also includes executive functions which are particularly important when investigating patients with vascular disorders.

Purpose: To evaluate the cognitive function of elderly syncope patients, using the MMSE in comparison with the MoCA.

Methods: Consecutive patients aged 65 years or older diagnosed with syncope at the multidisciplinary fall and syncope day clinic (FSDC) between November 2011 and the end of May 2014 were included. Main outcome was the prevalence of CI, defined as a composite of death, myocardial infarction, stroke and syncope recurrence. We therefore recommend that screening for cognitive function in older patients with syncope is routinely performed using the MoCA.

P3523 | BEDSIDE

Long term outcome of patients with presumed neurally mediated syncope by initial history taking


Introduction: The most frequent etiology of syncope patients in the outpatient clinic is neurally mediated syncope (NMS). For the diagnosis, initial evaluation with careful history taking is reported to be highly informative. We compared the long term outcome of syncope patients with proper clinical history of neurally mediated syncope to patients who were not certain or presumed other etiology initially.

Methods: We conducted retrospective, observational study in 269 syncope patients who visited outpatient clinic. Mean follow up duration was 23.2 months. Patients were divided into three groups by initial clinical history; presumed neurally mediated, presumed other etiology and uncertain. The serious outcome was defined as a composite of death, myocardial infarction, stroke and syncope resulting in hospitalization. We compared clinical courses and final diagnosis in the three groups.
time to investigation (24-hour holter and transthoracic echocardiogram), 30-day re-admission rate with syncope and 90-day mortality rate. These variables were then assessed prospectively in 50 in-patients referred directly to the SAU. These patients were referred from the ED or from ward at the time of discharge. Accepting referral criteria followed recommendations set out by the European Society of Cardiology (4). SAU took place in the local ambulatory care unit with access to transanatomic echocardiography and continuous ECG monitoring. All 100 patients were low risk as defined by the San-Francisco Syncope Rule (5).

Results: The median length of admission for patients remaining in hospital for as- sessment was 4 days compared to 1 day for those referred to the SAU (p<0.05). There was no significant difference in 30-day readmission rate with syncope or 90-day mortality rate between the two (p<0.05). 93 patients were reviewed in the syncope clinic over the first 6 months (16/6). With an in-patient bed-day cost- ing £110 per day, referral of patients at this rate would save £22492 per month and £269,145 per year.

Conclusions: The introduction of a novel low-risk SAU promotes early discharge from hospital with reduced waiting times for diagnostic investigations and treat- ment. This unit provides a safe and cost-effective patient care

P3525 | BEDSIDE
Hospital admissions for syncope and orthostatic hypotension predict incidence of cardiovascular disease in older middle-aged patients

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Introduction: Middle-aged patients suffering transient loss of consciousness are often referred for cardiac evaluation. However, the most common diagnoses are not car- diac but vasovagal syncope and orthostatic hypotension (OH). The relationship of non-cardiac syncope and OH-related admissions with subsequent cardiovascular (CV) events is an important gap in knowledge.

Purpose: We analyzed the historical hospital admission for syncope or OH with- out concomitant CV disease modifies the risk of subsequent first-ever CV event including coronary disease, stroke, atrial fibrillation, heart failure, and aortic stenosis.

Methods: We analyzed a large population-based prospective cohort of 30,358 individuals (age, 58±8; males, 40%). A total of 524 (1.7%) and 504 (1.7%) partici- pants were hospitalized for syncope or OH, respectively, over a period of 1554 years. During the same period, a first-ever coronary event occurred in 2851, stroke in 2307, new-onset heart failure in 1207, atrial fibrillation in 2824, and aortic stenosis in 489 participants. Clinical determinants of syncope and OH-related hospital admissions were analyzed using a multivariable-adjusted Cox regression model with age and sex as covariates. After exclusion of all cases that were preceded by manifest CV disease, we assessed the predictive value of syncope or OH-related hospital admission in relation to future CV events using multivariable-adjusted Cox regression model and controlling for traditional CV risk factors.

Results: The average time between baseline and first admission for syncope/OH was 7.25 years (age, 69 years). Participants hospitalized for syncope/OH were older, more often male, more frequently treated for diabetes and hypertension and had higher systolic blood pressure (SBP, 147 vs. 140mmHg) compared with the rest of the cohort. Syncope hospitalization was predicted by higher BMI (Haz- ard ratio (HR) 1.06; 95% CI 1.05–1.07), higher SBP (1.08;1.01–1.14), use of diure- urics (1.96;1.50–2.57), and calcium channel-blockers (1.42;1.03–1.97) but not beta-blockers and ACEIs, whereas OH hospitalization was predicted by height (1.01; 1.03;1.01–1.04) and diabetes (1.93;1.33–2.81) but not by antihyper- tension treatment (1.21; 0.98–1.41). History of syncope hospitalization was asso- ciated with higher risk of incident heart failure (2.16;1.52–3.07), atrial fibrillation (1.88;1.50–2.37), and aortic stenosis (2.29;1.36–3.85), while history of OH hospi- talization predicted incident stroke (1.63;1.24–2.14), heart failure (1.53;1.04– 2.25), and atrial fibrillation (1.98;1.58–2.48).

Conclusions: Hospital admissions for syncope and OH in older adults increase with advancing age and are associated with common comorbidities, diabetes and hypertension. Admission for either syncope or OH predicts development of heart failure and atrial fibrillation. Moreover, admission for syncope indicates higher risk of aortic stenosis, whereas admission for OH predicts increased risk of stroke.

P3526 | BEDSIDE
Incidence of pulmonary embolism and upper-extremity deep venous thrombosis in patients submitted to lead extraction and upgrade procedures

C.M.M. Albertini, K.R. Silva, I.C.M. Amaya, G.R.G. Melo, E.S. Crevelari, J.M.M. Leal, M.F. Lima, R.C. Chate, K. Higa, C. Nomura, M. Martinelli Filho, R. Costa, Heart Institute (InCor) – Clinics Hospital of the University of São Paulo Medical School, S. Paulo, Brazil

Introduction: Pulmonary embolism (PE) and upper-extremity deep vein thrombo- sis (UEDVT) are not uncommon after lead replacement or upgrade procedures. Our hypothesis is that the association of these procedures with lead extraction may increase the risk for venous thromboembolism. The purpose of this prospec-
Device complications in patients with ICD and continuous-flow LVAD

Introduction: Continuous-flow left ventricular assist device (CF-LVAD) is a common treatment option for patients with end-stage heart failure. Most of them have an implantable cardioverter defibrillator (ICD) to treat ventricular arrhythmias. Demonstration of survival benefit associated with LVAD implantation is possible, however, device complications and mortality was observed.

Methods: A multicenter analysis (8 institutions) of all ICD recipients implanted with a CF-LVAD between 2008 and 2016 was retrospectively performed. Demographic data of the population and characteristics of ICD and LVAD complications were collected.

Results: One hundred and forty-one patients with CF-LVAD and ICD were enrolled and followed for 610.6±670 days. Among them, 99 (69.5%) had a Heartmate 2, 32 (22.7%) a Heartware, 9 (6.4%) a Jarvik 2000 and 2 (1.4%) a Ventrijet. The mean age was 69±11 years. Survival with or without complication

Conclusion: In this multicenter study, patients with CF-LVAD and ICD have a significant risk of ICD-related complications (17.7%), mainly due to inappropriate shocks. LVAD complications occur more frequently, in more than half of the patients. Occurrences of ICD or LVAD-related complications do not appear to impact patient’s survival.

Acknowledgement/Funding: Federation Française de Cardiologie

Role of the 18F-fluorodeoxyglucose positron emission tomography for diagnosis of cardiac implantable electronic devices infection: initial results of a referral center

Introduction: Cardiac implantable electronic devices (CIED) infections remain a diagnostic challenge, as both the modified Duke Criteria and echocardiography have limitations. Recent studies have demonstrated the value of adding 18F-fluorodeoxyglucose positron emission tomography (18F-FDG-PET/CT) for diagnosing CIED infections. The purpose of this study was to determine whether the addition of 18F-FDG-PET/CT would increase the diagnostic accuracy in patients with suspected CIED infections when other diagnostic findings were inconclusive.

Methods: From July 2012 to July 2015, we enrolled 45 consecutive patients (73.3% male, 62.6±20.0 years) with suspected CIED infection. Patients were submitted to clinical, microbiological and transthoracic echocardiographic (TEE). Cardiac 18F-FDG-PET/CT was performed after low-carbohydrate diet and additional overnight fast. Final diagnosis was defined according to international practice guidelines or modified Duke criteria for endocarditis.

Results: Most patients (77.8%) consisted of pacemaker (PM) recipients. The remaining cases had implantable cardioverter-defibrillator (ICD) or cardiac resynchronization therapy (CRT). Mean time since the initial implantation and the onset of suspected CIED infection was 7.3±7.4 years. Of the included patients, 95.6% presented with bacteremia without inflammatory signs at the generator pocket during the admission. Blood cultures and TEE were positive in 35.6% and 46.6% of the cases, respectively. Final diagnosis was definite endocarditis in 11.2% and lead-related infection in 28.9%. A total of 40% of the patients showed abnormal FDG uptake around the valve or lead. According to the final diagnosis results, the sensitivity, specificity, positive predictive value and negative predictive for diagnosis of CIED infections were 75%, 83%, 75% and 83%, respectively. Overall, PET/CT ruled-out of CIED infections in 51% of the cases, being useful for differential diagnosis identification.

Conclusion: The use of 18F-FDG-PET/CT plays a role in the diagnosis of CIED-related infections by confirming the diagnosis or identifying differential conditions. Our initial results support the addition of this imaging modality in the evaluation of patients with suspected CIED infections.

Predictors of long term complications after transvenous lead-extraction for pacemaker/defibrillator infection: a prospective study

Methods: All patients referred for CIED infection to a high-volume TLE centre between November 2012 to May 2015 were included in this observational prospective study. Data included in the study analysis were: PRE-PROCEDURE: 1) device/leads type; 2) Previous CIED procedures; 3) Previous antibiotic; 4) Clinical characteristics; 5) Transesophageal echocardiography; 6) Laboratory/microbiology tests; 7) 18FDG-PET results.

Procedure: 1) Extraction approaches/tools; 2) TLE duration; 3) TLE complications for Reimplantation procedure; 4) Post-extraction transesophageal echocardiography; POST-PROCEDURE: 1) Leads/generator microbiology; 2) Clinical course; 3) Mid-long-term complications.

Results: 63 patients were included in this analysis, 77% male, aged 68±15 years, 45% with a NYHA class ≥2. Extracted CIED were 59% pacemakers and 41% implantable defibrillators. 76% patients previously underwent a system revision procedure (upgrade, repositioning, hematoma evacuation, pocket plastic surgery). 48% underwent at least a course of antibiotic treatment and/or a local revision procedure as first step: this approach resulted in a mean delay to the extraction procedure of ≥30 days (p=0.02). In the 63 patients were removed 122 leads (53% with active fixation) with a mean implantation time of 75±65 months (range 3–278). Powered sheaths were needed for 54 leads. An alternative extraction approach was required in 4 patients and stenotony in one (to complete lead extraction). 3 of the 63 infections occurred before discharge: 2 pocket hematomas and a death for septic shock (three day after TLE). At a mean follow-up of 18±5 months, 6 death were recorded (1 for myocardial infarction and 5 infection-related) and a patient required a second TLE for infection recurrence. Variables significantly associated with death/infection recurrence at Cox univariate analyses were: procedural serum creatinine >2mg/dl (p=0.011), LVEF <30% (p=0.018) and presence of post-procedural “ghost” at the transesophageal echocardiography (defined as: intracardiac masses observed by echocardiography after device removal in the same site of the extracted lead; p=0.013). At the multivariate analysis only the presence of “ghost” was an independent predictor of death/infection recurrence (p=0.028; HR: 11.85; 95% CI: 4.31–25.48).

Conclusions: Presence of post-extraction “ghosts” represents an important risk factor for long-term outcomes after TLE for CIED infection that should be considered when planning reimplantation strategies.

Venous occlusion and stenosis in CIED carriers: can anticoagulation play protective role? Findings of 1574 TLE procedures

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Conclusion: The use of 18F-FDG-PET/CT plays a role in the diagnosis of CIED-related infections by confirming the diagnosis or identifying differential conditions. Our initial results support the addition of this imaging modality in the evaluation of patients with suspected CIED infections.
present in 60%, of patients, infectious in 40%, 42% of patients had PM DDD system, 13% PM VVI, 21% ICD, 6% CRT-D, 16% other systems. In 15% of patients abandoned leads were found. In 26% of patients had one lead, 55% - two, 15% - three and 4-6 leads in the heart. An average dwell time of all leads was 87.2 mth. The lead entry side was left in 96%, right in 2%. 20 pts had leads both side of the chest.

**Results:** Results are in Table.

<table>
<thead>
<tr>
<th>Location, degree and etiology of lead related venous occlusion</th>
<th>Anticipated procedure</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location of methylprednisolone</td>
<td>Anticipated permanently</td>
<td>Anticipated permanently</td>
</tr>
<tr>
<td>Anterior n=15</td>
<td>n=23</td>
<td>n=12</td>
</tr>
<tr>
<td>Posterior n=22</td>
<td>n=22</td>
<td>n=20</td>
</tr>
<tr>
<td>Anterior side and posterior n=9</td>
<td>n=22</td>
<td>n=20</td>
</tr>
<tr>
<td>Anterior side</td>
<td>n=22</td>
<td>n=20</td>
</tr>
<tr>
<td>Posterior side and anterior n=7</td>
<td>n=22</td>
<td>n=20</td>
</tr>
<tr>
<td>Posterior side</td>
<td>n=22</td>
<td>n=20</td>
</tr>
</tbody>
</table>

**Conclusions:**

1. Lead related venous occlusion is frequently observed phenomenon in CIED carriers (mid-complete occlusion: 67%) and other complications of infection the second CORT implantation is more sophisticated.

**Methods:** Since 2007 to 2015 n=1712 lead extraction in n=537 patients were performed in our center. In n=125 of these patients a CS lead extraction was necessary. In n=62 of these patients a second CORT implantation was performed.

**Results:**

- A total of 2177 patients underwent CIEDs new implantation or replacement were enrolled from April 2011 to December 2015. CIEDs are defined as permanent pacemakers, cardiac resynchronization therapy devices, and implantable cardioverter defibrillators.
- We compared postoperative complications between patients aged ≥80 years and <80 years.
- We defined postoperative complication as hematoma, pocket infection, lead dislodgement, pneumothorax, perforation of cardiac structure, lead fracture and problem with connection screw.

**Results:**

- There were 878 (40.%) patients aged ≥80 years old and no significant difference in postoperative complications between the groups (4.0% vs 4.9%, respectively $P=0.34$).
- Postoperative complications in new implantation or replacement of each device between the two groups did not significantly differ.

**Conclusion:** The CIEDs operation in patients aged ≥80 years could be performed safely without increasing postoperative complication.

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**P3534 | BEDSIDE**

**Transvenous lead extraction in deep analgesia:** A prospective study in 250 consecutive patients

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**Introduction:** Transvenous lead extraction (TLE) is of growing importance. We report our unique experience with TLE in deep analgesia.

**Purpose:** To evaluate the safety and efficacy of TLE performed in deep analgesia.

**Methods:** Patients referred for TLE due to infection or lead malfunction were operated in the cardiac electrophysiology laboratory by an experienced electrophysiologist with cardiothoracic surgery standby available. The intervention was performed in deep analgesia, initiated with intravenous (i.v.) bolus of midazolam, fentanyl and propofol and maintained with continuous iv administration of propofol. Patients were in spontaneous respiration and monitored with invasive blood pressure, oxygen saturation, ECG and arterial blood-gas analysis. A stepwise approach with locking stylies, dilator sheaths and mechanical sheaths using a subclavian, femoral or internal jugular venous access was utilized for TLE. Patient characteristics and procedural data were prospectively collected and analyzed.

**Results:** Extraction of 531 leads (implanted for 83.8±49.7 (12–276) months, 28% ICD leads) in 250 cumulative patients (mean age 65±16 years, 80.4% male) was performed between April 2012 and November 2014. Deep analgesia was initiated with 1.9±0.4 mg midazolam, 0.028±0.008 mg fentanyl and 21.2±10.4 mg propofol and maintained with infusion of 294±92 mg/h propofol. Hemodynamics remained stable in 86% of the patients. 10.8% needed stabilization with cedrine/theodrenaline and 2.8% with continuous infusion of norepinephrine. The operation was finished in spontaneous respiration in 245 patients (98%), 3 (1.2%) needed non-invasive and 2 (0.8%) invasive ventilation during the extraction procedure.

The subclavian venous access was used in 215 (85%), the femoral in 31 (12%) and the internal jugular in 7 patients (3%). We completely removed 510 (96%), partially removed 11 (2.1%), and failed to remove 10 leads (1.9%). Major complications were observed in 7 patients (2.8%), but no procedure related death occurred.

**Conclusion:** TLE in deep analgesia in the EP lab is a safe procedure with a high success rate.

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**P3535 | BEDSIDE**

**Complications of cardiac implantable electrophysiological devices operation in patients 80 or older**

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**Purpose:** We evaluated the safety of CIEDs (cardiac implantable electrophysiological devices) operation in patients aged ≥80 years.

**Methods:** A total of 2177 patients underwent CIEDs new implantation or replacement were enrolled from April 2011 to December 2015. CIEDs are defined as permanent pacemakers, cardiac resynchronization therapy devices, and implantable cardioverter defibrillators.
- We compared postoperative complications between patients aged ≥80 years and <80 years.
- We defined postoperative complication as hematoma, pocket infection, lead dislodgement, pneumothorax, perforation of cardiac structure, lead fracture and problem with connection screw.

**Results:** There were 878 (40.2%) patients aged ≥80 years old and no significant difference in postoperative complications between the groups (4.0% vs 4.9%, respectively $P=0.34$).

**Conclusion:** The CIEDs operation in patients aged ≥80 years could be performed safely without increasing postoperative complication.
P3536 | BEDSIDE
Risk factors of chronically implanted lead extraction. Analysis of 1915 TLE procedures
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Proper evaluation of risk of TLE procedure should have influence on procedure scenario and degree/level of surgical back-up. It was not established which leads an which patients needs especially safe TLE procedure regime.

Objective: The analysis of significance of all (theoretically) possible potential risk factors of major TLE complications.

Methods: Using standard mechanical systems we have extracted ingrown PM/ICD leads from 1915 pts within the last 9 years.

Results: Results are in Table.

Non-significant as risk factors of major TLE complications were: patients age, BM, ejection fraction, NYHA class, LVDD, diabetes, chronic anticoagulation, antiplatelet drugs, CS and CIC lead extraction, utilized approach. Impression: Due to relatively low major complications appearance analysis even 2000 procedures does not permit for proper evaluation significance of number of potential factors.

Conclusions: 1. Female gender, renal failure, long lead dwell time consists known TLE risk factors. 2. RAA, multiple abandoned lead extraction and technical problems appearance during TLE indicates increased risk of procedure. 3. Long lead body dwell time and presence of abandoned lead consist main independent risk factor of major TLE complications.

CELL AND GENE THERAPY

P3537 | BENCH
Prolyl hydroxylase inhibition to enhance SDF-1 and CXCR4 expression for increased CXCR4+ cell homing and myocaridal repair
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Background: Stabilization of the SDF-1/CXCR4 axis facilitates myocardial repair.

Methods: Since DSF-1 upregulation lasts only 3 days after M it limits the targeting of regenerative cells. We aimed to (re)activate the HIF-1α target genes SDF-1 and CXCR4 by inhibition of prolyl hydroxylase to stimulate myocardial repair.

Results: In vitro, DMOG increased predominantly CXCR4+CD11b+ monocyes in the ischemic heart associated with a shift of CD206+DC66 cells in favor of the reparative CD206+ subpopulation. Scarc reduced were serum and myocaridal function was improved.

Conclusions: Our data suggest prolyl hydroxylase inhibition as promising target for HIF-1α mediated SDF-1 activation to increase myocardial repair.

Acknowledgement/Funding: Deutsche Forschungsgemeinschaft (DFG)

P3538 | BENCH
Cardiac regeneration in nonischemic cardiomyopathy
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The massive loss of cardiomyocytes after myocardial injury, e.g. acute myocarditis and acute myocardial infarction, often results in cardiac fibrosis, chamber dilatation and heart failure. Our recent studies confirmed that Nkx-2.5 cardiac progenitor cells contributed directly to postnatal cardiomyogenesis after experimental myocardial infarction. At present, there is no direct evidence that cardiac progenitors participate in cardiomyogenesis in non-ischemic heart failure. We hypothesized that cardiac progenitor cells might mediate cardiac regeneration in non-ischemic heart failure.

To create an animal model of non-ischemic heart failure, we designed a genetic cardiomyocyte-depletion model by interbreeding myosin heavy chain-Mer-Cre-Mer to Rosa26 R26R mice. After animal received low dose tamoxifen i.p. injection, about 30% cardiomyocytes were depleted by Diphtheria toxin fragment A. Tissue analysis confirmed increased cardiomyocyte death and apoptosis and echocardiography demonstrated left ventricular global hypokinesia in the genetic cardiomyocyte-depletion model.

To analyze if cardiac lineage-specific Nkx2.5+ progenitor cells participate in cardiac regeneration in heart failure, we created heart failure by injecting 4-OH tamoxifen to myosin heavy chain-Mer-Cre-Mer Nkx2.5 enhancer-eGFP ROSA26R (cardiomyocyte depletion group) and Nkx2.5 enhancer-eGFP ROSA26R mice (cardiomyocyte non-depletion group). The cell percentage of eGFP+ cells was low (0.015±0.006%) in cardiomyocyte non-depletion group. Also, markedly and significantly in cardiomyocyte depletion group (0.86±0.73%) (p=0.017) in each group.

Our purpose is to document the importance of endogenous cardiac regeneration in heart failure. The discovery of postnatal cardiac progenitors and their contribution to endogenous cardiac regeneration enables the pharmacological targeting of cardiac progenitors and cell therapy for cardiac regeneration.

P3539 | BENCH
The effect of DPP-4 inhibitor on angiogenic regeneration by bone marrow mesenchymal stem cell in hind-limb ischemia ischemia injury model
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Background: Mesenchymal stem cells (MSCs) are known to have a therapeutic potential for severe limb ischemia. However, poor survival of implanted MSCs in the target tissue remains as an important factor that attenuates the angiogenic potential of the cell therapy.

Objectives: We investigated whether sitagliptin, a DPP-4 inhibitor, may enhance the angiogenic efficacy of MSC in a hind limb ischemia murine model by increasing production of SDF-1.

Methods: All male C57BL/6 Mice (n=112) with induced hind limb ischemia were divided into 4 groups: group 1 (n=28) treated with oral saline and local injection of saline, group 2 (n=28) treated with oral sitagliptin (20mg/kg/day) and local injection of saline, group 3 (n=28) treated with oral sitagliptin (20mg/kg/day) and local injection of saline and local injection of MSCs (106 cells/200ul), and group 4 (n=28) treated with oral sitagliptin and local injection of MSCs (106 cells/200ul).

Conclusion: The combined treatment of oral sitagliptin and local injection of MSCs achieved more effective angiogenic response than oral sitagliptin administration or local MSC transplantation alone in a mouse hind limb ischemia model. At 28 days, group 4 with combined therapy of oral sitagliptin and local IMSCs showed the highest blood perfusion ratio (p<0.05 vs. other groups). Histological sections of ischemic tissue showed that capillary density was significantly higher in group 3 and 4 than in group 1 or 2 (p<0.01). Additionally, the mRNA and protein expressions of pro-angiogenic factor (VEGF, CXCR4 and stromal-derived factor [SDF-1]) were higher in group 4 than in the other groups. Also, apoptotic cells assessed by TUNEL were remarkably lower in group 4 than in the other groups. Also, apoptotic cells assessed by TUNEL were remarkably lower in group 4 than in the other groups.

Conclusion: The combination therapy of sitagliptin and local transplantation of MSCs was more effective in enhancing angiogenic responses to ischemia than oral sitagliptin or local transplantation of MSCs alone possibly due to up-regulation of SDF-1.
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Three-dimensional (3D) engineered cardiac tissues (ECTs) are a robust platform technology to investigate cardiovascular (CV) cell function and provide an excellent microenvironment for tissue implantation and cardiac repair. We generated 3D ECTs using cardiomycocytes (CMs), endothelial cells (ECs), and vascular mural cells (MCs) efficiently differentiated from human iPS cells (hiPSCs). We employed 3 different monolayer culture-based differentiation protocols: 1) CM+EC+MC protocol: mes+Dkk1 to induce CMs and MCs; 2) CM+MC protocol: mes+Dkk1 to induce CMs and MCs; and 3) MC protocol: exclusive induction of MCs. We collected the cells on differentiation day 15 and mixed them to generate 3 classes of ECTs composed of different CV cell population patterns: 1) CM+EC; 2) CM+MC, and 3) CM+EC+MC. We seeded the each cell mixture in a collagen/Matrigel mixture to form spontaneously beating ECTs. In vitro force measurement analysis showed that CM+EC+MC ECTs possessed the highest maximum capture rate (4.6±0.6 Hz, P<0.0001) and lowest excitation threshold (1.2±0.3 V/cm, P<0.001). Approximately 75% of active force was maintained at 3.5Hz (210 bpm) pacing in CM+EC+MC, whereas active force in CM+EC or CM+MC at 3.5Hz decreased to approximately 40% of baseline 2Hz-force. We further found that Young’s modulus was higher in ECTs without MCs (CM+MC=CM+EC+MC) compared to those with MCs (CM+EC), indicating that MCs contribute to produce higher tissue stiffness. These results indicate that incorporation of vascular cells augmented tissue maturation and function. We confirmed more preferential alignment of CMs to the ECT long axis in ECTs with MCs. Transmission electron microscopy revealed that incorporation of MCs increased CM sarcomere structure. Incorporation of both ECs and MCs led to vasculature formation within ECTs during 14 days of in vitro culture and activated multiple tissue maturation pathways. These results indicate that incorporation of vascular cells accelerated tissue structural maturation. Next CM+EC+MC ECTs were implanted onto infarcted athymic rat hearts. Echocardiogram revealed a significantly higher cardiac output at 4 weeks after implantation compared to sham-operated rats (137±23 vs 95±23 ml/min, P<0.05). Immunostaining 4 weeks after implantation showed epicardial engraftment of skeletal muscle and mature vasculature. hiPSC-derived ECTs including vascular cells showed novel properties relevant for clinical translation.

Acknowledgement/Funding: This work was supported by a grant from the Kaisar Charities.

P3540 | BENCH

FOXO1A modifies arterial and venous endothelial development from human pluripotent stem cells; they form 3D vascular structures in vitro and quantifiable vascular networks in vivo

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Background and purpose: Endothelial derivatives of human pluripotent stem cells may offer regenerative treatments in ischemic cardiovascular diseases. We aimed to investigate the regulatory role of PI3K/FOXO1A signalling pathway on arterial and venous identity of endothelial subpopulation as well as the fate of generated cells in 3D cultures in vitro and via transplantation into small animals in vivo.

Methods and results: Human embryonic stem cells (hESC) were differentiated either into embryonic body (EB) or monolayer under normoxic and hypoxic conditions. CD31-positive endothelial cells (EC) were sorted by FACS and compared with human induced pluripotent stem cell-derived endothelial cells (hiPSC-EC). Both hESC-EC and hiPSC-EC showed mature endothelial phenotype in vitro, including cobblestone pattern, ac-ADL uptake and tube formation. PI3K/FOXO1A pathway revealed high abundance of angiogenesis-related proteins both in cell lysates and supernatant. Expression of arterial (EphrinB2, Notch1–2) and venous (EphB4) endothelial markers were increased during differentiation, suggesting the presence of mixed endothelial population in culture. Transfection of ECTs with FOXO1A overexpression plasmid encoding CD31-EGFP was carried out by electroporation. Human ECT-EC and hiPSC-EC with high FOXO1A showed downregulated expression of universal (CD31, angiopeptin-2 and -ve-cadherin) as well as arterial and venous markers. Indeed, arterial identity (M1: CD11c+CD206+) or regulatory (M2: CD11c-) polarization, 2) CD45-CD34+ arterial or regulatory macrophages (M1/M2) in SVF was significantly correlated with HOMA-IR, and also negatively correlated with the frequency of LNGFR+MSCs (r=-0.71, p<0.05). The gene expression of stemness markers (Nanog, Oct4/3 and Sox2) and growth factors (VEGF and SDF-1) in ADSCs at passage 2–4 were determined by qPCR. Proliferative capacity of ADSCs was evaluated by colony-forming unit broth (CFU-F) assay. Briefly, ADSCs were plated at low density (20 cells/cm²) and colonies containing more than 50 cells were counted at day 14. All of the properties of MSCs were compared with clinical characteristics at collection of adipose tissue. Results: The frequency of LNGFR+MSCs in ADSCs was greatly increased among study patients, compared with the other markers (median 33.8%[0.3–66.5]). HOMA-IR (calculated by fasting plasma glucose and serum insulin levels), but not the other clinical and laboratory variables, was negatively correlated with the frequency of LNGFR+MSCs (r=–0.60, p<0.05). The ratio of pro-inflammatory to regulatory macrophages (M1/M2) in SVF was significantly correlated with HOMA-IR, and also negatively correlated with the frequency of LNGFR+MSCs (r=–0.71, p<0.05). Gene expressions of stemness markers and growth factors as well as proliferative capacity of cultured cells were positively correlated with the frequency of LNGFR+MSCs in SVF before culture (CFU-F assays; r=–0.67, p<0.05).

Conclusions: These all indicate that the lower yield of LNGFR+MSCs in patients with cardiovascular disease is associated with local adipose tissue inflammation and systemic insulin resistance. This insight might allow prediction of therapeutic efficacy by ADSCs.

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P3543 | BENCH
Adiponectin improves the therapeutic efficacy of mesenchymal stem cells in infarcted myocardium by enhancing their survival through the AMPK pathway
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Background: Poor viability of transplanted mesenchymal stem cells (MSCs) within the ischemic heart has limited their therapeutic potential for cardiac repair. Adiponectin (APN) is an adipocyte-secreted adipokine with pleiotropic actions. It has recently been proposed to participate in tissue regeneration and promote the survival of several types of stem cells. This study investigated whether APN in conjunction with MSCs could improve the stem cell survival and contribute to myocardial repairs after infarction.

Methods: Sprague-Dawley rats were randomized into six groups: Sham operation; AMI control; MSCs; APN + MSCs; APN + MSCs + AMPK inhibitor. MSCs labeled with CM-Di were injected through the jugular vein in 24 hours post AMI. Global APN were injected intraperitoneally (1 g/kg) 20 minutes after AMI. Four weeks after AMI, recruitment and survival of MSCs to the infarcted heart were evaluated. Cardiac function was assessed using echocardiography and left heart catheterization. Apoptosis and fibrosis were measured with TUNEL and Masson’s trichrome staining. AMPK phosphorylation and the expression of Scl-2 and Bax were evaluated by Western blot. Then, MSCs were exposed to hypoxia and serum deprivation (H/SD) conditions to mimic the ischemic environment in vitro. Apoptosis was evaluated with flow cytometry and caspase-3 activity. Downstream molecules were investigated by Western Blotting.

Results: APN enhanced the recruitment and survival of transplanted MSCs in peri-infarct region. This was accompanied by reduced apoptosis and fibrosis. Moreover, MSCs adjuvant with APN improved cardiac performance. The phosphorylation of AMPK was significantly increased in the APN and APN + MSCs group. The protective effects of APN on MSCs survival and cardiac function were partly inhibited by AMPK inhibitor. In vitro, APN decreases the apoptosis of MSCs induced by H/SD, which was partly inhibited by AMPK inhibitor.

Conclusion: APN could improve the survival and therapeutic efficacy of transplanted MSCs through AMPK activation. This study suggests the potential application of APN for stem cell–based heart regeneration.

P3544 | BENCH
Therapeutic effects of adipose-derived mesenchymal stem cells against brain death-induced remote organ damage and post-heart transplant rejection
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Introduction and purpose: We will test the hypothesis that adipose-derived mesenchymal stem cell (ADMSC) alleviated brain death (BD)-induced remote organ damage and reduced the post-heart-transplant (HT) rejection.

Methods and results: Proposed mechanisms underlying the positive therapeutic effects of ADMSC (1.2 x 10^6 intravenous injection 3 h after BD) on reducing BD-induced heart injury and improving successful rate of HT through attenuating the inflammation and immunogenicity. Male Frazier 344 rats (as BD and donor) and Lewis (as recipient) were utilized (n=5 in each group).

Results: (1) ADMSC-treatment reduced rejection rate and improved 5-day post-transplanted LVEF as compared with HT animals without ADMSC treatment (all p<0.001). (2) The circulating levels of Ly6G, IL-6, TNF-α, CD3+, CD8+ & CD3+/CD8+ cells, and protein expressions of TNF-α, NF-κB, IL-6, MIP-1α, MMP-9, caspase-3, PARP, TLR-2/TLR-4 and γ-γH2AX and cellular expressions of F8/80, CD14, CD90+/CRCC1+, CD3+ in kidney, heart and liver were significantly higher than in those of BD-HT with ADMSC treatment (all p<0.0001).

Conclusion: ADMSC therapy against BD-induced remote organ damage and post-HT Rejection.

P3545 | BENCH
Single chamber circulation enhances cell engraftment after intravenous delivery of cardiac progenitor cells in rat models of univentricular heart disease
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Background: We have reported that intracoronary infusion of cardiosphere-derived cells (CDCs) may improve cardiac function in patients with single ventricle physiology. So far, it is reported that intravenous administration of CDCs in bi-ventricular hearts has little effects due to the early loss of transplanted cells captured by the lung. On the other hand, little is known about intravenous administration in single ventricular circulation. CDCs intravenous administration in single ventricular circulation was expected to make more cell engraftment than that in bi-ventricular circulation because the venous blood bypasses the lung and directly flows into the systemic chamber. Moreover, intravenous administration is less invasive method than intracoronary infusion, and recurrent administration is feasible.

Purpose: We sought to investigate whether single ventricular physiology may have the benefits to bypass the lung circulation after intravenous injection of CDCs.

Methods: Single ventricular circulation was created by a novel surgical approach in rats. This complex cardiac surgery was simultaneously performed by generation of atrial septal defect, ventricular septal defect, and right atrial closure above the tricuspid valve. Rat CDCs were labeled with superparamagnetic microspheres (SPMs) and directly injected into jugular vein to verify the cell homing by ex-vivo cardiac MRI and histology. Ten minutes after the administration of 1200/kg CDCs, model heart was removed and T1 emphasized MRI was taken to detect captured by the lung. On the other hand, little is known about intravenous administration in single ventricular circulation. CDCs intravenous administration in single ventricular circulation was expected to make more cell engraftment than that in bi-ventricular circulation because the venous blood bypasses the lung and directly flows into the systemic chamber. Moreover, intravenous administration is less invasive method than intracoronary infusion, and recurrent administration is feasible.

Conclusion: Intravenous injection of CDCs may be useful to directly transplant the cells into the targeted chamber. This lung-bypassed CDC delivery could be applied in patients with single ventricular circulation.

P3546 | BENCH
Donor age impairs the paracrine properties of human mesenchymal stromal cells in a cardiac and renal injury model
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Introduction: It has been demonstrated that adult stem cells repair post-ischemic myocardial and renal damage through paracrine mechanisms. Thus, for translational purposes, it is essential to establish whether donor age influences the paracrine properties of human mesenchymal stromal cells (MSCs).

Purpose: To compare the effects of conditioned medium (CM) derived from fetal MSC (F-CM) with CM derived from the bone marrow (BM) MSC of elderly subjects (≥75 years) in well-established experimental models of acute myocardial infarction (AMI) and renal damage (AKI).

Figure 1

Conclusions: Intravenous injection of CDCs may be useful to directly transplant the cells into the targeted chamber. This lung-bypassed CDC delivery could be applied in patients with single ventricular circulation.
Methods: Human fetal MSC were isolated from amniotic membrane. BM-MSC were isolated from bone aspirate of patients undergoing orthopedic surgery. Three treatment groups were considered: saline, F-CM and o-CM. AMI was induced in rats by temporary ligation of the coronary artery followed by intramyocardial injection of saline or CM. Cardiac function and histological analyses were performed two and three days after surgery. Alternatively, subcutaneous injection of cis-platinum and treatments were administered intravenously. Renal function and histological analyses were performed after 4 days.

Results: A single F-CM administration resulted in improved fractional shortening and ejection fraction at 30 days (both p < 0.05 vs saline; p < 0.001 vs o-CM). Functional data were matched by reduced infarct size (p < 0.01 vs saline and o-CM). Measurement of LV wall thickness demonstrated that administration of F-CM prevented the thinning of the anterior wall compared with both saline and o-CM (both p < 0.001 vs saline). However, the scar area in F-CM-treated hearts was smaller compared with the saline (p < 0.01) and o-CM (p < 0.001) groups, respectively. Furthermore, F-CM seemed to positively modulate cardiac hypertrophy: in hearts injected with F-CM, the myocyte cross-sectional area was significantly reduced compared with saline and o-CM (both p < 0.001). At the contrary, donor age did not affect the pro-angiogenic effect of CM since F-CM and o-CM equally increased the number of vessels at 30 day (p < 0.001 vs saline). F-CM also improved renal function compared both with o-CM (p < 0.05) and with saline (p < 0.001) by limiting tubular injury and cleaved caspase 3 activation (both p < 0.001 vs saline and o-CM). Differently from what observed after AMI, in the AKI model we documented a more robust pro-angiogenic effect of F-CM compared with o-CM (p < 0.001).

Conclusions: Administration of F-CM exerts meaningful cardiac and renal protection. At the contrary, the effect of o-CM was negligible in both models, strongly suggesting that o-CM negatively influences the paracrine properties of MSC. Our results indicate that autologous MSC therapy may not work in elderly patients and that F-MSC represent an ideal alternative source for the development of effective therapies for cardiac and renal injury.

P3548 | BENCH
Comparative study cardiac progenitor cells transplantation into infarcted myocardium by injection of cell suspension or epicardial implantation of cell sheets

Background: Stem cell therapy is emerging as a promising strategy to treat heart failure. Adult heart contains small populations of cardiac progenitor cells (CPCs), which participate in postnatal physiological/pathological cardiac repair and can be isolated and expanded in culture. Several clinical employing direct injections of different types of cells have been already completed. However, low cell survival after injection is a serious obstacle. Therefore, a strategy that limits the benefits of the procedure. Alternative approach is epicardial transplantation of cell sheets, where extracellular matrix and cell-to-cell junction are intact to promote cell survival. The aim of the present study is to compare the efficacy of CPCs transplantation to myocardium by injection of cell suspension or epicardial implantation of cell sheet.

Methods: After ligation-induced myocardial infarction, rats were randomly allo-
cated to receive intramyocardial injections of c-kit+ (CD45+) rat CPC marked with vital fluorescent dye (Cell Tracker CM-DIL) or control medium or infarcted area covered with scaffold-free cardiac progenitor cell sheet (epicardial cell sheet implantation). Morphometry analysis of left ventricular remodelling, quantification of cell engraftment, assessment of CSC survival, apoptosis, differentiation, myo-
cardium fibrosis and angiogenesis were analyzed by immunostaining on day 14 after transplantation.

Results: Quantitative analysis showed that at 2 weeks after transplantation the number of engrafted CPC in injection group was significantly lower compare with cell sheet group. No significant differences in number of cells expressing prolifer-
ation (Ki67) and apoptosis (Casp3) markers have been found. CPC transplanted in cell sheets had more pronounced migration ability compared to injected cells. Histological analysis of myocardium frozen sections revealed that CPC sheets induced better vascularization of underlying myocardium compared to injected cells. Morphometry analysis also showed better cardiac remodeling profile in cell sheet group.

Conclusion: Epicardial transplantation of cell sheets from CPC is associated with better cell survival, graft structural integration and myocardial vascularisation compared to conventional direct intramyocardial delivery of equivalent amount of CPC suspension. This data strongly supports the potential of CPC sheet transplantation for treatment of damaged heart.
Calcific aortic valve disease (CAVD) is the defining feature of aortic stenosis (AS), with accumulating evidence for heterotopic ossification. This study was to determine whether expressions of ossification-related microRNAs are related to osteogenic differentiation of circulating progenitor cells in patients with CAVD. This study included 46 patients with AS and 46 controls. Twenty-nine patients underwent surgical valve replacement (AVR) and 17 underwent transcatheter aortic valve implantation (TAVI). Blood samplings were performed at baseline and 2 and 12 weeks after AVR or TAVI.

The number of circulating progenitor cells (COPCs, CD133+/CD34-/KDR+/osteocalcin+) was higher in AS group than in controls (P<0.01). Levels of miR-30c were higher in AS group than in controls (P<0.01), whereas levels of miR-106a, miR-148a, miR-204, miR-211 miR-31 and miR-424 were lower in the AS group than in the controls (P<0.01). The number of COPCs and levels of osteocalcin protein in COPCs were positively correlated with levels of miR-30a and negatively correlated with levels of miR-106a, miR-148a, miR-204, miR-211, miR-31 and miR-424 (all P<0.05). The degree of aortic valve calcification was weakly positively correlated with number of COPCs and miR30c levels, and negatively correlated with number of COPCs and miR30a levels higher than those after TAVI (all P<0.05). In-vitro study using cultured peripheral blood mononuclear cells transfected with each ossification-related miRNA showed these ossification-related microRNAs controlled levels of osteocalcin.

In conclusion, dysregulation of ossification-related microRNAs may be related to differentiation into COPCs and may play a significant role in the pathogenesis of CAVD.
Background: Remote ischaemic conditioning (RIC) protects against ischaemia-reperfusion injury through cellular protective pathways. However, RIC may also modulate platelet function and fibrinolysis.

Purpose: We investigated whether long-term RIC treatment affects platelet function, platelet turnover, and fibrinolysis in patients with chronic ischaemic heart failure and matched controls without IHD.

Methods: In a prospective, outcome-assessor blinded, paired study, 20 patients with chronic ischaemic heart failure and 21 subjects without IHD matched on age and gender were treated with RIC once daily for 28±4 days. RIC was performed as 4 intermittent cycles of 5 minutes upper arm ischaemia and 5 minutes reperfusion.

Results: Long-term RIC treatment did not affect platelet function or platelet turnover in patients with chronic ischaemic heart failure or matched controls without ischaemic heart disease (IHD).

Conclusions: Long-term RIC treatment did not affect platelet function or turnover in patients with chronic ischaemic heart failure or matched controls without IHD but reduced fibrin clot lysis time in subjects without IHD. The clinical implication of these findings needs to be further investigated but suggest that the effect of RIC may not be restricted to cellular protective pathways.
P3557 | BENCH
Brain-derived neurotrophic factor improves exercise capacity and mitochondrial function in the skeletal muscle in mice with post-infarct heart failure

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Background: Exercise capacity is decreased in patients with heart failure (HF), which is due to skeletal muscle abnormalities. We previously reported that serum brain-derived neurotrophic factor (BDNF) was reduced in HF patients and decreased serum BDNF levels were significantly associated with low peak VO2 and reduced exercise tolerance. BDNF is known to be produced not only in the brain but also in the skeletal muscle in response to exercise. We thus examined the role of BDNF in the regulation of mitochondrial function in the skeletal muscle from mice with HF after myocardial infarction (MI).

Methods and results: MI was created in male C57BL/6j mice by ligating the left coronary artery, and sham operation was also performed. After two weeks after operation, exercise capacity was significantly decreased in MI mice compared to sham mice (n=7 for each group). BDNF protein levels examined by western blot analysis were significantly decreased by 62% in the skeletal muscle from MI compared to sham mice (p<0.05). Mitochondrial complex I and II-linked respiration measured by high-resolution respirometry was significantly decreased by 54% in the permeabilized skeletal muscle fiber from MI (n=6 for each group). Two weeks after surgery, MI mice were randomly divided into two groups and subcutaneously treated with recombinant human (rh) BDNF (5 mg/kg BW/day) or vehicle for two weeks. The administration of rhBDNF did not affect the cardiac function in MI mice. Left ventricular end-diastolic diameter and fractional shortening evaluated by echocardiography were similar between MI+vehicle mice and MI+rhBDNF mice (5.1±0.2 vs. 5.1±0.2 mm, 11±1.3 vs. 9.7±1.0%, n=10 for each group). The work and the run time were significantly improved in MI+rhBDNF mice compared to MI+vehicle mice (10.3±0.8 vs. 17.1±1.0 J, 1255±47 vs. 168±146 sec, p<0.05, n=10 for each group). Mitochondrial complex I and II-linked respiration of electron transport system in the skeletal muscle was significantly improved in MI+rhBDNF mice compared to MI+vehicle mice (433±7 vs. 72±7 pmol O2/sec/mg fiber, p<0.05, n=7 for each group).

Conclusions: The administration of rhBDNF can improve the exercise capacity and mitochondrial function in skeletal muscles from mice with heart failure. BDNF may be a potential therapeutic target against exercise intolerance in patients with heart failure.

P3558 | BENCH
Induction of heart failure by chronic beta-adrenergic stimulation in larvae and adult zebrafish

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Background: Impaired beta-adrenergic signal transduction is a common molecular alteration found in heart failure (HF). Chronic catecholamine release and overstimulation of beta-adrenergic receptors (beta-ARs) in the failing heart results in their desensitization, largely mediated through upregulation of the G-protein coupled receptor kinase 2 (GRK2), and consequently to the progression into HF. Normalization of beta-AR signaling represents a potent and common therapy to treat HF. Other drugs are developed to inhibit key components of the beta-adrenergic signal transduction that interfere with the receptor desensitization is highly desirable. Zebrafish represents an established model to evaluate genetic causes of HF and to screen for novel therapeutic targets. However, the contribution of the beta-adrenergic system in zebrafish models of HF is not known. Hence, this study seeks to systematically characterize development and function of the beta-adrenergic signaling in developing and adult zebrafish both at the molecular and functional level.

Methods and results: Zebrafish larvae hearts first responded at 3 dpf to acute isoproterenol (ISO) stimulation when key components of the beta-adrenergic signaling (i.e. beta-AR and beta-arrestin mRNA) and catecholamine synthesis (i.e. tyrosine hydroxylase mRNA) pathway, respectively, were sufficiently expressed. Chronic beta-AR stimulation for 5 days induced signs of HF accompanied by similar but not identical expression changes as seen in mice and humans. Echocardiography revealed that in adult zebrafish hearts, ISO robustly enhanced cardiac function. However, chronic beta-AR stimulation for 14 days efficiently induced HF symptoms. Consistent with mice and humans, we found reduced expression of beta-ARs and elevated expression of GRK2, BNP and ANP. Additionally, these zebrafish models develop essential characteristics accompanying HF in mice and humans, including increased cell death, elevated inflammation and reduced cardiomyocyte calcium transients.

Conclusion: We show that beta-AR function in zebrafish is comparable to that in mammals. Further, we present the first ISO-induced HF model in adult zebrafish, thereby introducing adult zebrafish as a particularly valuable model to study the pathogenesis of HF and to screen and test for novel therapeutic strategies as a resource efficient alternative to mouse in a preclinical setting to treat HF.

Acknowledgement/Funding: Charité Clinical Scientist Program

P3559 | BENCH
Cytosolic calcium removal in cardiac myocytes during atrial remodeling

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In heart failure atrial remodeling (AR) leads to impaired contractility, relaxation and atrial fibrillation and contributes to negative clinical outcomes. In myocardies, atrial Ca removal after systolic ejection is primarily achieved by SERCA pump and Na/Ca exchange (NCX) activity, allowing atrial relaxation. In atrial myocytes that lack a transverse tubule system, NCX is located exclusively in the cell periphery where it is exposed to high concentrations of Ca during the cardiac cycle.

Previously we found that the relative contribution of NCX to Ca removal increased in AR and was associated with a higher propensity of arrhythmogenic Ca waves, i.e. Ca waves that triggered action potentials (APs). We hypothesize that dys synchrony of Ca removal globally (whole cell) and locally (peripheral sub sarcolemmal (SS) and central (CT) domains) is altered in atrial remodeling, influenced by the special atrial ultrastructure and related to increased arrhythmogenicity. We used confocal line scan imaging and Ca sensitive dyes to investigate Ca removal in remodelled atrial myocytes from a rabbit left ventricular volume-pressure overload systolic heart failure model. In control atrial myocytes Ca removal (assessed by the time constant of decay (TAU) of local SS and CT AP induced Ca transients) is slower in the cell center (CT region) compared to the SS domain (135±11 vs. 187±13 ms, n=33 cells) and this was related to local differences of NCX and mitochondrial activity. In AR myocytes, however, CT TAU was not different from SS TAU (110±10 vs. 104±9 ms, n=13 cells). Moreover, in AR cells local dys synchrony (defined as the standard deviation of TAU divided by mean TAU) in the CT domain was significantly increased compared to control (0.11±0.03 vs. 0.04±0.01, n=10 AR and CTRL cells). However despite the increased dys synchrony, CT Ca removal was 77% and SS Ca removal 59% faster in AR myocytes as compared to control cells. In summary, AR myocytes show accelerated but dys synchronous diastolic Ca removal and altered local NCX and mitochondrial activity which may result in impaired relaxation and increased susceptibility to rhythm disorders.

Acknowledgement/Funding: Charité Clinical Scientist Program

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comeric protein phosphorylation 3 weeks after TAC surgery for cardiac myosinbinding protein C (cMyBP-C), cardiac troponin I (cTnI) and phospholamban (PLN), which was attenuated 6 weeks after TAC. In contrast, Tm phosphorylation increased significantly in hypertrophic hearts and maintained high also in failing hearts. Tm phosphorylation was reversed to basal levels in response to mechanical unloading. Increased Tm phosphorylation during hypertrophic and cardiomyopathic heart failure development was paralleled by enhanced MEF-dependent and ERK-autophosphorylation, suggesting MAPK kinase involvement in this scenario.

**Conclusions:** Tm phosphorylation reflects disease progression in cardiac remodeling and remodeling. Interestingly, Tm phosphorylation pattern during heart failure development is distinct from other known cardiac sarcromeric proteins, which show reduced phosphorylation in hypertrophic and failing hearts. Preliminary results suggest involvement of ROS-mediated MAPK kinase modulation in the development and progression of cardiomyopathic heart failure.

**Purpose:** To determine the biological effects of the novel calcium (Ca²⁺) channel and to investigate the modulating effects of bradycardia on arrhythmogenic mechanisms.

**Methods:** Next generation sequencing was used to screen for variants in J wave syndrome associated genes. The CACNB2b gene was cloned, and the wild-type or variant transfected into human embryonic kidney cells. Whole cell patch clamp experiments were used to characterize its biophysical properties. Rate-dependent changes in the proband's ECGs were compared to data from canine ventricular wedge preparations displaying similar variations in R-R interval to gain insight into the cellular basis of rate-dependent augmentation of J wave amplitude. Action potential (AP) clamp experiments were used to assess the effects of a prominent transient outward current (Ito)-mediated AP notch, as occurs during bradycardia, on calcium channel current (ICa) and the total Ca²⁺ charge during phase 2 of the AP in wild-type and mutant cells.

**Results:** Genetic screening uncovered an S557L variant in CACNB2b, encoding the β-subunit of the cardiac L-type calcium channel. The minor allele frequency (MAF) of this variant was 0 in the NHLBI GO Exome Sequencing Project (ESP) and 0.0014 in the 1000 Genomes Project. Functional expression of the variant revealed a loss of function in Ca²⁺ channels by altering their gating properties. The mutant had a significantly faster decline in channel availability between depolarising voltage steps (<0.001) and a positive shift in the voltage-dependence of activation (<0.05). Data from canine ventricular wedge preparations highlighted the presence of a prominent transient outward current (Ito)-mediated AP notch, developing during periods of bradycardia, in the pathogenesis of phase 2 re-entry. AP clamp experiments showed a larger decrease in ICa and total charge during phase 2 of the AP in mutant cells activated by a notch AP, as occurs during bradycardia, compared to an AP with a minimal notch.

**Conclusion(s):** The presence of a prominent Ito-mediated AP notch during bradycardia accentuates modulation-mediated decrease in ICa. This likely serves to create a positive feedback loop of progressive ICa loss in successive beats, culminating in prominent J waves, phase 2 re-entry and polymorphic ventricular arrhythmias.

**Acknowledgement/Funding:** Many thanks to the Sharpe-Strumia Research Foundation, the WW Smith Foundation and the National Natural Science Foundation of China who supported this study.

**P3563 | BENCH**

**Antirhythmic drugs target atrial TASK-1 K⁺ channels: mode of action and implications for AF therapy**

**Purpose:** This study was designed to systematically elucidate inhibitory effects of clinically established antiarrhythmic drugs on TASK-1 channels compared to an experimental high affinity blocker of TASK-1.

**Methods:** Whole-cell patch clamp and two-electrode voltage clamp electrophysiology was used to study K2P channel pharmacology in Chinese hamster ovary (CHO) cells and Xenopus laevis oocytes. In silico modeling of drug-channel interactions was employed to identify and visualize individual drug docking positions. Effects of TASK-1 inhibition on atrial action potential duration (APD) and conduction were evaluated in human atrial cardiomyocytes.

**Background:** The human TASK-1 channel was systematically tested in Xenopus oocytes for its sensitivity to clinically established AADs (amiodarone, d-cisnerone, ranolazine, ibutilide, dofetilde, ajmaline, mexiletine, propafenone, digoxin, digoxin) and to the specific TASK-1 inhibitor A293. TASK-1 was sensi-
tive to all drugs tested, with the exception of dofetilide and ajmaline. The IC50 levels were determined in Xenopus oocytes and CHO cells, which are commonly used for experimental conditions. However, the IC50 values in these cells do not necessarily correlate with clinical effectiveness. In conclusion, clinically relevant AADs target human atrial TASK-1 and impaired L-type Ca2+ channel inactivation is a promising candidate drug for treating LQT8 resulting from impaired L-type Ca2+ channel inactivation.

### P3564 | BENCH

**I-cis diltiazem rescues impaired calcium channel inactivation in a patient-specific stem cell model of long QT syndrome with a CACNA1C mutation**


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**Background:** Timothy syndrome is a highly malignant inherited arrhythmogenic disorder caused by mutations in the L-type Ca2+ channel gene, CACNA1C, and characterized by a myriad of multisystem abnormalities, including long QT syndrome (LQTS), syndactyly, immune deficiency, and autism. However, we recently reported a new disease entity of LQT8 without extra-cardiac phenotypes.

**Purpose:** The purpose of this study is to establish and analyze human induced pluripotent stem cell (hiPSC)-based model of LQT8 without typical phenotypes of Timothy syndrome that can promote the development of new pharmacotherapies.

**Methods:** We generated hiPSCs from a 48-year-old female carrying a CACNA1C-A582D mutation with familial bradycardia and QT prolongation without extra-cardiac phenotypes. The hiPSCs were differentiated into cardiomyocytes (hiPSC-CMs) using an embryoid body differentiating system and electrophysiological functional assays were performed at day 42–56 of differentiation.

**Results:** Action potential (AP) recordings revealed that AP durations (APDs) were significantly prolonged in LQT8-hiPSC-CMs compared to control (APD90 (ms); LQT8: 1388±83, control: 1045±77 at 0.5Hz pacing; P < 0.05) (Figure A). In L-type Ca2+ current recordings (Figure B), the ratio of current remaining after 300 ms depolarization (r300) of L-type Ca2+ current was significantly larger in LQT8-hiPSC-CMs (0.30±0.02, control: 0.23±0.01 at 0 mV; P < 0.01). These results indicate that this hiPSC-based model of CACNA1C-A582D recapitulated the disease phenotype of delayed repolarization due to impaired L-type Ca2+ channel inactivation and might explain the milder phenotype of the patient than typical Timothy syndrome. Furthermore, we found that L-cis diltiazem, the stereoisomer of clinically used d-cis diltiazem, restored both the prolonged APD and impaired L-type Ca2+ channel inactivation in LQT8-hiPSC-CMs (APD90 (ms); rest: 1388±83, with L-cis: 1171±114 at 0.5Hz pacing; P < 0.01; Figure C; r300; rest: 0.12±0.05, with L-cis: 0.07±0.001 at 0 mV; P < 0.01; Figure D). On the other hand, d-cis diltiazem couldn't rescue the electrophysiological parameters of LQT8-hiPSC-CMs.

**Conclusions:** These results suggest that late INa-mediated focal activities in the ischemic border zone (BZ, Figure, left panel). After ranolazine perfusion, the incidence of BEs was decreased from 22.1±13.1 (per 1.5 s, baseline, n=8) to 7.5±4.1 (ranolazine), and unstable rotors (average number of atrial level, n=3) decreased from 1.5±4.3 (per 1.5 s, baseline, n=8) (P < 0.05, Figure, right panel). In a separate series of experiments, VT was induced by intramuscular injection of acolinine, which enhances the late INa, into the ventricle without coronary ligation. Ranolazine (10 μM) reduced the excitation frequency of atrial-induced spontaneous VT from 4.8±0.4 Hz (baseline, n=3) to 3.6±0.1 Hz (ranolazine) and terminated VT in all 3 hearts tested.

**Ischemic activation mass of Ischemic VT**

**Conclusion:** These results suggest that late INa-mediated focal activities in the ischemic border zone play important roles in VT associated with acute myocardial ischemia.

### P3566 | BENCH

**Influence of Toll-like receptor 4 during sepsis on refractory periods and atrial fibrillation in an in vivo mouse model**


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**Background:** Activation of Toll-like receptor 4 (TLR4) during lippopolysaccharide (LPS)-induced sepsis has been shown to result in alterations of potassium and calcium ion currents in excitable animal models.

**Purpose:** The purpose of this study was to assess the impact of TLR4 activation on myocardial electrophysiological (EP) parameters as predisposing factors for new onset arrhythmias in vivo, during LPS-induced sepsis.

**Methods:** Sepsis was induced in 11 wild type mice (WT-LPS) (background C57BL/6; age 12 weeks) with intraperitoneal (i.p.) administration of LPS (5 mg/kg body weight). A group of TLR4 knockout mice (TLR4–/–) also received LPS i.p. and a group of 17 control mice received saline i.p. Mice were further treated with i.p. fluid resuscitation every 8 hours (35 ml/kg body weight saline + 5% glucose).

**Results:** WT-LPS mice exhibited clinical signs of mild sepsis, including reduced physical activity, reduced food intake and weight loss (19.7±1.1 g vs. 24.1±2.9 g; P < 0.01; Figure A). On the other hand, TLR4–/– mice exhibited a significant reduction of refractory periods only on atrial level (12.5±2.7 ms vs. 40.6±3.1 ms; P < 0.05). Ischemia-induced VT terminated in 6 of 8 hearts in 13.2±7.7 min in average after ranolazine application (vs. in 1 of 6 hearts in controls without ranolazine perfusion, P < 0.01) (Figure, right panel).
as compared to control mice (41.7%). After administration of LPS, TLR4−/− mice did not show clinical signs of sepsis, no prolongation of the QTc interval, and no shortening of the atrial refractory period.

**Conclusion:** LPS-induced sepsis led to an increased inducibility of atrial fibrillation. Furthermore, a shortening of the atrial refractory period was present in these mice, representing a predisposing mechanism for sepsis-induced atrial fibrillation. This pathomechanism was neutralized in TLR4−/− mice, indicating the true TLR4-dependency of this sepsis-induced EP alteration.

**Results:** Compared with I/R group, the infarct size of left ventricle was markedly decreased by a third in I/R+Vimentin group (21.13±17.2% vs. 0.6±0.1%). The cardiomyocyte contraction was decreased in hypoxia condition by 0.5±0.2 μm (p<0.05). However, after cotreatment with vimentin, the contractility was recovered nearly up to control level (1.0±0.9 μm vs. control, p<0.01). Compared with control (1.0±0.0 F/F0), the amplitudes of the Ca²⁺ waves were markedly increased in both I/R group (4.8±1.0 F/F0, p<0.01) and I/R+Vimentin group (4.9±1.1 F/F0, p<0.01). The frequencies of the Ca²⁺ waves were not different among 3 groups (1.0±0.0 Hz in control, 0.9±0.5 Hz in I/R group and 1.1±0.3 Hz in I/R+Vimentin group, p=0.9). While spontaneous ventricular arrhythmias were not observed in control rats, they occurred frequently in I/R group (6 out of 10, 60%) and in I/R+Vimentin group (5 out of 7, 71%). APD was shortened, and the steepness of the CV restitution slope was increased in both I/R and I/R+Vimentin group.

**Conclusions:** The injection of vimentin one hour after I/R injury increased myocardial contractility and Ca²⁺ release. However, vimentin was related with more frequent ventricular arrhythmias after I/R injury. This result suggested that vimentin might be used as a therapeutic tool to increase cardiac contractility. However, arrhythmogenic effect should be further evaluated.

**Acknowledgement/Funding:** Grants from the Young Investigator’s Award funded by the Korean Society of Cardiology.
Background: Risk stratification in patients referred to mitral valve surgery for chronic ischemic mitral regurgitation (CMR) remains unexplored.

Purpose: The aim of our study was to evaluate echocardiographic parameters of left and right ventricular structure/function to define independent predictors of outcome at long-term follow-up.

Methods: One-hundred and thirty-seven (137) patients underwent mitral valve repair and CABG surgery for CMR, of whom 63 received restrictedavitral annuloplasty (RMA) and 74 mitral valve replacement (MVR). Standard 2D and Doppler echocardiography, six-minute walking test (6-MWT) and BNP levels were collected (RMA) and 74 mitral valve replacement (MVR). Standard 2D and Doppler echocardiography, six-minute walking test (6-MWT) and BNP levels were collected (RMA) and 74 mitral valve replacement (MVR). Standard 2D and Doppler echocardiography, six-minute walking test (6-MWT) and BNP levels were collected.

Results: The primary outcome was all-causes mortality only. Patients referred to MVR were older and had higher EF (RMA: 32±8% vs. MVR: 37±6%, p<0.01). Median follow-up was 7 years (range: 3.3–15.4). In the RMA group 42% of patients experienced MR re-currence. Fifty-nine patients developed primary outcome (35 in RMA and 24 in the MVR group, p<0.05). Baseline dyssynchrony indices in HF were increased after operation (27±8% vs. 31±8%, 310±72 vs. 219±78 ml; 230±71 vs. 153±65 ml, respectively; all p<0.05) but deteriorated at early and late follow-up (rho = -0.52, p value = 0.02).

Conclusions: Preoperative LGE extension and distribution and LV and RV mass and wall thickness were added to the previous parameters creating the Integrated CMR score (I-CMRscore).

Results: We studied 19 patients (mean age 65±10 years, 17 males). G-CMRscore did not show any significant statistical correlation with post-operative LV function at follow-up (rho = -0.25, p value = 0.29) while I-CMRscore showed an improved significant statistical correlation with LV ejection fraction (LVEF) (rho = -0.61, p value <0.01) and with right ventricular ejection fraction (RVEF) at 6-month follow-up (rho = -0.52, p value = 0.02).

Conclusions: Preoperative LGE extension and distribution, together with other preoperative anatomical and geometrical CMR variables, predict the effect of SVR on LV and RV function. Moreover, scar tissue analysis adds pivotal information in predicting LV response to SVR and should be included into preoperative evaluation and selection of patients candidate to SVR.
P3573 | BEDSIDE
Does the operative technique play a role on long-term myocardial function in valve-preserving aortic root surgery?

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Background: Ectasia of the aortic root, particularly in patients with Marfan syndrome, is treated by prophylactic aortic surgery to prevent an aortic dissection or rupture. Various surgical techniques have been developed to fully eliminate or stabilize the diseased aortic wall tissue. We hypothesized that surgical techniques preserving some residual aortic root compliance (Windkessel) lead to a sustained reduction of left ventricular afterload resulting in a better diastolic cardiac function and possibly less hypertrophy.

Methods: Of 863 patients seen at the Marfan clinic between 3/2010 and 9/2015, 413 had Marfan syndrome, and 238 had undergone cardiovascular surgery. We excluded patients with aortic dissection or repeat surgery. Looking closer exclusively at the aortic root, 25 had a composite graft replacement, 13 had a valve-sparing procedure as described by Tyrode David, 25 had a wrapping procedure using a Florida sleeve-like prosthesis surrounding the aortic root, and 15 (predominantly non-Marfan patients) had a supra-coronary ascending replacement, with or without aortic valve replacement. Fractional shortening (FS), relative wall thickness (RWT, a normalized posterior wall thickening), NT-proBNP, its logarithm, and early relaxation in tissue Doppler (e') were analyzed.

Results: In patients with wrapping using Florida sleeve as compared to composite graft replacement, we found significantly higher values for e' (p=0.009), and lower values for NT-proBNP (p=0.022) and Ln NT-proBNP (p=0.025), p = 0.089 for RWT. This effect could not be seen after David procedure. A similar trend in supra-coronary replacement did not reach significance.

Conclusion: Surgical technique to root surgery modulates aortic root impedance and thereby might have an impact on myocardial diastolic function and hypertrophy in long-term follow-up.

P3574 | BEDSIDE
The effect of sublingual nitroglycerin on resting and exercise left ventricular filling pressure in patients with heart failure with preserved ejection fraction (invasive hemodynamic study)

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Background: It is well known that nitroglycerin effectively lower left ventricular end diastolic pressure (LVEDP) in patients with heart failure at resting condition. But most patients with heart failure with preserved ejection fraction (HFpEF) have dyspnea only during exertion by exercise induced elevation of LVEDP. Thus study evaluate whether sublingual nitroglycerin could prevent aggravation of LVEDP during exercise in patients with HFpEF.

Method: Among patients with unexplained dyspnea referred for cardiac catheterization, 17 patients diagnosed with HFpEF owing to elevated LVEDP (>15mmHg) was enrolled from October 2015 to January 2016. LVEDP was measured by pigtail catheter and at point after A wave inflection on LV pressure tracing. After measuring resting LVEDP, 0.6mg sublingual nitroglycerin was given and LVEDP was rechecked 5 minutes later and then supine bicycle (Lode instruments) exercise with 20 watt was performed for 3 minutes. At 3 minutes of exercise, LVEDP was measured again and then exercise was terminated.

Results: In 17 HFpEF patients enrolled, mean age was 64±10 years and half (48%) was female. Hypertension was present in 42% of patients and most patients (88%) complained of NYHA class II–III dyspnea. Mean LV ejection fraction was 62±3% and mean NT proBNP was 76±54pg/ml. Resting blood pressure was 143±23/81±13mmHg and heart rate was 79±11BPM. In invasive hemodynamic study, resting LVEDP was 24±5mmHg. Five minutes after giving 0.6mg sublingual nitroglycerin, systolic blood pressure was decreased to 132±14mmHg (p<0.004) and LVEDP was markedly reduced to 17±4mmHg (p<0.001). At supine bicycle exercise was performed. At 3 minutes of 20 watt exercise with effect of nitroglycerin, systolic blood pressure and heart rate were increased to 159±20mmHg and 105±12BPM compared to both resting (p<0.01) and nitroglycerin phase (p<0.01) and there was abrupt elevation of LVEDP to 30±15mmHg compared with both resting (p<0.001) and nitroglycerin phase (p<0.001) (Figure 1).

Conclusion: Although sublingual nitroglycerin effectively decreased resting LVEDP in patients with HFpEF, it failed to suppress aggravation of LVEDP during exercise in HFpEF patients.

P3575 | BEDSIDE
Clinical outcomes at one year follow up in cardiac resynchronization therapy with acute optimization of left ventricular pacing site and multipoint pacing

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Introduction: The clinical response to cardiac resynchronization therapy (CRT) is variable. The optimization of the left ventricle (LV) pacing site increases the number of responder to CRT. The Multipoint (MPP) pacing could further increase hemodynamic response to and clinical outcome of CRT. The purpose of our study was to test the hypothesis that pts optimized at implant and treated with MPP experience superior long-term clinical outcomes than conventional CRT pts.

Methods: 110 HF pts treated for 1 year with either conventional CRT (STD, N=54), CRT with hemodynamic and electrical optimized LV pacing site (OPT, N=36), and with optimized LV pacing site + MPP (OPT-MPP, N=20) were evaluated to determine CRT response relative to baseline. Responders were classified in terms of 1-year reduction in end-systolic volume index<15%, reduction in NYHA class<1, and PACKER score variation (NYHA response with no HF-related hospitalization or death).

Results: In terms of ESV, 55.6% of STD, 72.2% of OPT, and 90.0% of OPT-MPP pts were responders. In terms of NYHA, 66.7% of STD, 77.8% of OPT, and 95.0% of OPT-MPP pts responded, with more MPP pts experiencing a NYHA downgrade of 2 classes or beyond. Likewise, 59.3% of STD, 66.7% of OPT, and 90.0% of OPT-MPP pts exhibited a 1-year PACKER response.

Conclusions: Optimization of LV pacing sites by means of Hemodynamic and electrical delay plus MPP showed an enhanced potential to reverse the progression of HF and improve clinical outcomes, relative to conventional CRT.

P3576 | BEDSIDE
Evaluation of baseline right ventricular function on clinical significance and change of right ventricular function on cardiac resynchronization therapy

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Background: Right ventricular (RV) function can be affected by the left ventricular (LV) function. The present study focused on RV systolic dysfunction which has been associated with a worse clinical outcome in heart failure with reduced ejection fraction. We evaluated the prognostic significance of baseline RV systolic function and their change in patients underwent cardiac resynchronization therapy (CRT).

Methods: We enrolled 330 patients (198 males, mean 65±11 years old) treated with CRT from February 2005 to August 2007, who had good baseline and follow-up echocardiograms. Echocardiographic parameters were analyzed and RV global longitudinal strains (RVLGS) were measured from the apical images.
Results: Baseline LV end-systolic (ESV) and end-diastolic volumes (EDV), and LVEF were 74±32ml/m², 96±37ml/m², and 24±7%, respectively. RVFAC, TAPSE, and RVGLS were 37±15%, 1.5±0.5cm, and -12.6±4%, respectively. One hundred and forty seven patients (49%) showed LV reverse remodeling within 6 months after CRT. Female gender, non-ischemic etiology, higher LVEF, smaller LVESV and LVEDV, and smaller left atrial area were associated with LV reverse remodeling. Also, baseline RV indices were significantly associated with remodeling (RVFAC: HR=1.11, p<0.01, TAPSE: HR=3.32, p<0.01, and RVGLS: 0.77, p<0.01). LV volumes decreased and LVEF improved significantly after CRT. However, RVFAC did not change (37±15 to 36±14%, p=0.11) and TAPSE decreased (1.5±0.5 to 1.4±0.5cm, p=0.02) after CRT. RVGLS improved slightly (-12.6±4 to -14.0±4.8, p<0.01). Change of LVEF significantly correlated with change of RVGLS. However, LVEF change did not correlate with changes of RVFAC and TAPSE (Figure).

Conclusion: Baseline RV systolic indices can be used as predictors of LV remodeling after CRT. While CRT improves RVGLS, it does not influence conventional RV systolic indices such as TAPSE and RVFAC.

P3578 | BEDSIDE
Surprisingly frequent findings of subclinical dysfunctional left ventricle in COPD without pulmonary hypertension
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Background: There is little and contradicting knowledge on how chronic obstructive pulmonary disease (COPD) affect left ventricular (LV) function.

Methods: The present study therefore aimed to elucidate the prevalence of dysfunctional LV in a cohort of stable COPD where left sided heart disease had been thoroughly excluded.

Results: 112 COPD outpatients in GOLD stages I-IV and 34 controls were prospectively recruited. Patients were divided by invasive mean pulmonary artery pressure (mPAP) > or = 25 mmHg in COPD-PH (pulmonary hypertension) and COPD-non-PH, respectively. LV myocardial performance index (LVMI) and longitudinal strain at basal septum and lateral wall by tissue Doppler imaging, as well as 3D dimensional LVEF, were acquired. Descriptive data are given as median (25%, 75%). A composite score value based on combined normalized LVMI (septal + lateral) and strain values (septal-lateral) were calculated. Abnormal values were defined as values below average -2 SD for controls (≤-2.4 % - dysfunctional LV).

Results: Prevalence of subclinical LV dysfunction based on combined score was 2.9%, 94.6%, and 100% in controls, COPD-non-PH and COPD-PH, respectively. LV strain and MI show concordant findings, with the most abnormal values at septal site, with significant difference between COPD-non-PH and PH (p<0.001), however, significantly (p<0.001) reduced at lateral segment also compared to controls (*).

Table 1. LVMI and longitudinal strain by tissue Doppler imaging at LV basal septum and lateral wall in controls, COPD-PH (pulmonary hypertension) and COPD-non PH

<table>
<thead>
<tr>
<th>Variables</th>
<th>Controls (n=34)</th>
<th>COPD-PH (n=74)</th>
<th>COPD-PH (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEF %</td>
<td>61 (57, 64)</td>
<td>57 (54, 60)*</td>
<td>57 (54, 61)</td>
</tr>
<tr>
<td>Septal strain</td>
<td>-21.7 (-23.0, -20.4)</td>
<td>-15.9 (-16.9, -14.2)**</td>
<td>-13.7 (-15.6, -12.5)**</td>
</tr>
<tr>
<td>Lateral strain</td>
<td>-22.3 (-24.0, -20.7)</td>
<td>-15.3 (-16.8, -14.2)**</td>
<td>-14.1 (-16.2, -12.9)*</td>
</tr>
<tr>
<td>Septal LVMI</td>
<td>0.35 (0.29, 0.43)</td>
<td>0.54 (0.46, 0.61)*</td>
<td>0.62 (0.53, 0.70)</td>
</tr>
<tr>
<td>Lateral LVMI</td>
<td>0.36 (0.32, 0.39)</td>
<td>0.53 (0.48, 0.60)*</td>
<td>0.62 (0.53, 0.67)*</td>
</tr>
</tbody>
</table>

Conclusion: Subclinical dysfunction is frequent present in COPD-non PH as in COPD-PH. LVMI was increased and LV strain reduced similarly equally both at the lateral and septal wall. Pressure load from the right side and interventricular interdependency might explain the septal findings; however additional mechanism must be present to explain the dysfunctional lateral wall, in particular in the non-PH group.

P3579 | BEDSIDE
Early predictors of weaning failure from veno-arterial extracorporeal membrane oxygenation in patients with acute myocardial infarction-induced cardiac arrest
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Background: Weaning failure from veno-arterial extracorporeal membrane oxygenation (VA-ECMO) for patients with acute myocardial infarction (MI) with cardiac arrest is increasing. However, early predictors of weaning failure from VA-ECMO, which is crucial for application of ventricular assist device or termination, are little known.

Methods: This study aimed to determine early predictors of weaning failure from VA-ECMO in patients with acute MI-induced cardiac arrest.

Methods: Of 396 patients with acute MI, 28 patients had received primary percutaneous coronary intervention (PCI) and VA-ECMO for refractory cardiac arrest between January 2012 and January 2016. We evaluated baseline characteristics, laboratory findings and echocardiography parameters at index, 24 hours, and 48 hours after initiation of VA-ECMO.

Results: Mean age was 64.0±10.6 years and 24 patients (85.7%) were men. All patients received PCI and 26 (92.9%) were successfully revascularised. Of 28 patients, 14 (50%) were successfully weaned from veno-arterial extracorporeal membrane oxygenation (group S), whereas 14 (50%) failed to wean (group F). 3 were bridged to a ventricular assist device, 10 died for insufficient recovery of cardiac or brain function, and 1 died for intra-cranial haemorrhage. Group S was significantly higher index-CKMB (50.1±81.0 vs. 26±72.5 ng/ml, p=0.024) compared to group S. At 24 hours, group F had significantly lower left ventricular ejection fraction (LVEF) (7.7±3.6 vs. 19.5±13.1%, p=0.009) and higher serum lactate acid (5.7±2.5 vs. 2.9±1.7 mmol/l, p=0.005) compared to group S. In univariate analysis, LVEF <10% at 24 hours (OR; 11.25, 95% CI; 1.647–76.849), and 4 mmol/l at 24 hours (OR; 8.4, 95% CI; 1.274–55.394, p=0.027) were identified as significant predictors of weaning failure from VA-ECMO.

Conclusions: 24-hour LVEF <10% and serum lactate acid ≥4 mmol/l predict weaning failure from VA-ECMO for acute MI-induced cardiac arrest. In those situations, therefore, application of ventricular assist device or early termination should be considered.
Objective: Left ventricular global longitudinal strain (LV GLS) is an important predictor of post-discharge adverse outcomes in patients with myocardial infarction (MI). GLS is more sensitive than LV ejection fraction (LVEF) as a measure of systolic function and may be used to detect reduction in LV function prior to failure in LVEF. Pulse wave velocity (PWV), a marker of arterial stiffness, can predict cardiovascualr events. The aim of the study was to investigate the relations between GLS and carotid-femoral PWV in patients with MI successfully treated with percutaneous coronary intervention (PCI).

Methods: 93 patients with first MI (57 (61.3%) with ST-elevation MI, 70% male, age 61.5±10.1 years (Ms±SD), smokers 25%, arterial hypertension 20%, blood pressure 129±6/82±7 mmHg, LV ejection fraction 47±4±3%) underwent conventional and speckle tracking echocardiography and applanation tonometry at initial presentation and 4 weeks after PCI. GLS was calculated in a 16-segment LV model as the average segmental value on the basis of three apical imaging planes. Mann-Whitney and Spearman tests were considered significant if p<0.05.

Results: Baseline GLS >16% was not detected in any patient. GLPS decreased from 11.5±1.9 to 10.1±2.3 m/s, p<0.01. Mean carotid-femoral PWV decreased from 11.5±1.9 to 10.1±2.3 m/s, p<0.05. Patients without vs with GLS normalization were older (63.2±9.1 vs 56.6±11.4 years, p<0.02), more frequent smokers (83 vs 50%, χ²=7.8; p<0.01), smokers (83 vs 50%, χ²=6.5; p<0.05), STEMlD (60 vs 67%, χ²=4.6; p<0.03), had higher diastolic BP (84±7 vs 80±8 mmHg, p<0.02), baseline PWV (12.9±6.9 vs 9.9±2.1 m/s, p<0.03). A significant correlation was found between changes of GLS and baseline PWV (r=-0.21, p<0.05).

Conclusion: Improvement of systolic function assessed by GLS was revealed in 25% of patients with first MI treated with PCI. Higher baseline PWV was associated with less improvement of GLS. Arterial stiffening may result in a less effective recovery of LV longitudinal function after MI.

P3581 | BEDSIDE

The prognostic implications of echocardiographically estimated elevated systolic pulmonary arterial pressures in a large cohort of patients undergoing cardiac rehabilitation

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Background: Regardless of the underlying etiology, pulmonary hypertension (PH1) is a condition diagnosed via direct measurement of pulmonary arterial pressures (PAP). Since invasive hemodynamic evaluation is not always feasible, echocardiographic measurement of systolic PAP (SPAP) often serves as a surrogate. Whether the prognostic implications of echocardiographically elevated SPAP measurements are as powerful as those of the invasive measurements is a matter of ongoing debate.

Aims: Evaluate the association between echocardiographically estimated SPAP and occurrence of mortality and heart failure (HF) related events at mid-term follow up period.

Methods: Medical records and echocardiographic studies of patients undergoing cardiac rehabilitation for various etiologies at our hospital were screened. Age adjusted rather than empirical cut off values, likely have more accurate prognostic implications.

P3582 | BEDSIDE

Prediction of left ventricular diastolic dysfunction in asymptomatic patients with diabetes mellitus type 2

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Introduction: Diabetes mellitus (DM) type 2 is a common cause of preclinical diastolic dysfunction (DD) of the left ventricle with the tendency of progression into diabetic cardiomyopathy and heart failure.

Objective: Aim of this study is to identify predictors of diastolic dysfunction in asymptomatic diabetic patients that should be treated for the prevention of later heart failure.

Methods: We recruited consecutive asymptomatic adults with previously diagnosed DM type 2 without any signs of ischemic or other heart disorder. All patients received standardized evaluation including interview, laboratory tests and echocardiogram with conventional and tissue Doppler studies. We used univariate and stepwise multivariate logistic regression models to identify risk factors for diastolic dysfunction, with Hosmer-Lemeshow goodness-of-fit statistics for model calibration and receiver operating characteristic (ROC) curve for model discrimination.

Results: Our study enrolled 114 asymptomatic patients, mean age 59.2±8.8 years, 47 males (41%) among them. DD was diagnosed in 65 patients (57%). Univariate logistic regression identified several parameters of statistical significance for prediction of DD including: age (56.3±8.5 yrs without DD vs 61.4±8.7 yrs with DD), diastolic arterial pressure (75.9±3.9 mmHg vs 86.3±2.9 mmHg), duration of diabetes mellitus (8.8±3.2 yrs vs 11.±4.3 yrs), hemoglobin A1C (7,0±2.5% vs. 8.7±2.2%), smoking status (75 vs 50%, χ²=13.5; p<0.001), use of aspirin (67 vs 46%, p<0.03), and left atrium diameter (35±3.1 mm vs. 38±3.8 mm). In the multivariate logistic regression model, which included these variables, the following were significant predictors of DD: duration of diabetes (OR, 1.303 [95% CI 1.083 to 1.567]), hemoglobin A1c (OR, 1.441 [95% CI 1.099 to 1.885]), LDL cholesterol (OR, 0.04 [95% CI 0.006 to 0.274]) and left atrium diameter (OR, 1.198 [95% CI 1.011 to 1.40]). The model discriminated well (p<0.001), with a ROC of 0.92 (95% CI: 0.87 to 0.97).

Conclusion: It appears that clinical, laboratory and basic echocardiographic parameters are sufficient to identify asymptomatic patients with diabetes mellitus type 2, as high risk for left ventricular diastolic dysfunction.

P3583 | BEDSIDE

Association of cardiovascular autonomic neuropathy and left ventricular diastolic function

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Background: The association of cardiovascular autonomic neuropathy (CAN) with heart failure by reduced ejection fraction (HFREF) has been well documented. But the relation between CAN and heart failure with preserved ejection fraction (HFpEF) or diastolic function has not been clearly elucidated. The aim of this study was to evaluate the relationship between CAN and left ventricular (LV) diastolic function in asymptomatic patients.

Methods: 324 patients (F:M=226:98, mean age=57.3±7.9 years old) who had no critical coronary stenosis by coronary angiography from the KoRean wOmen’S chest pain rEgistry (KoROSE) study were enrolled. All patients underwent treadmill exercise test (TET), echocardiography (TTE); LV mass index, LV ejection fraction, left atrial (LA) diameter, trans-mitral early (E) and late velocity (A) were measured by TTE. Mitral annular tissue velocity (e’) were measured by TTE. CAN was defined as corrected QT (QTc) prolongation (>440ms for male, >460ms for female) or less than 48 heart rate recovery (HRR) from peak heart rate in 2 minute post-exer-
cise recovery EKG. Patients with e’ <8 were categorized as patients with diastolic dysfunction (DD).

Results: Hypertension was present in 198 (61.1%) cases and diabetes was present in 38 (11.7%) cases. Patients with DD were 224 (69.2%). The patient who had DD had larger left ventricular mass index (LVMI) and LA size (LVMI: 83.4±15.5 vs 94.8±24.1 g/m², P=0.005, LA: 34.0±3.9 vs 36.7±5.6 mm, P=0.001). HRR of patients with DD was lower than that of patients without DD (54.5±15.0 vs 51.1±14.8 beats, P=0.038). QTc interval of patients with DD was significantly prolonged than that of patients without DD (422.1±41.7 vs 430.1±28.5 msec, P=0.048). The CAN was more frequently present in patients with DD than patients without DD (Impaired HRR: 40.0% vs 25.0%, P=0.001; QTc prolongation: 15.9% vs 2.7%, P=0.003). Exercise capacity measured during TET was lower in patients with DD than that of patients without DD (101.9±11 vs 112.1±2 MEQs, P=0.039). The 223 (68.8%) patients with E’e’<8 showed lower HRR than patients with E’e’≥8 (54.8±14.0 vs 51.0±15.7 beats, P=0.05). Multivariate analysis adjusting age, gender showed that impaired HRR and QTc prolongation were independently related with the presence of DD (HRR: odd ratio 2.099, P=0.041; QTc prolongation: odd ratio 6.902, P=0.012).

Conclusion: In asymptomatic patients, the CAN is frequently associated with LV diastolic dysfunction and accompanied with low exercise capacity. This finding suggests that CAN may be the early sign of HFpEF and could be used as a prognostic parameter for developing overt heart failure.

P3584 | BEDSIDE
Correlation between ST2 levels, Doppler echocardiographic parameters and prognosis in patients with heart failure and preserved ejection fraction
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Background: Although Doppler echocardiography has been used to identify abnormal left ventricular (LV) diastolic filling dynamics, inherent limitations suggest the need for additional measures of diastolic dysfunction. We hypothesized that ST2 levels could predict diastolic abnormalities in patients with heart failure and preserved ejection fraction.

Methods: We studied 52 patients admitted for HF PEF with the following criteria: signs and symptoms of HF, EF >50% and NT-pro BNP >300 pg/mL. Patients had complete evaluation of diastolic function according to the ASE guidelines along with ST2 level quantification. Survival curve is given with ST2 cut-off of 45 IU (logrank=0.06)

Results: There were 26 men: mean age was 72.0±10.0 years. ST2 level average 42.9±17.9 IU. ST2 levels increased with the thickness of the left ventricle (r=0.011) and left atrial enlargement (r=0.033) while transmitral peak early velocity (r=0.24), transmitral E deceleration time (r=0.49), transmitral E/A ratio (r=0.69), and mitral flow to tissue ratio E/e’ (r=0.34) were not correlated to percentage of pts on beta-blocker therapy (12% vs 2%; p<0.01). A ST2 value of ≥45 IU had a sensitivity of 62%, a specificity of 64%. Cumulative survival curve is given with ST2 cut-off of 45 IU (logrank=0.06).

Conclusions: A rapid assay for ST2 can reliably detect LV remodeling but not increase preload in HF-PEF patients. Elevated ST2 levels ≥45 IU tends to reinforce the prognosis of HF-PEF.
pared these echocardiographic parameter before and after 6 months trastuzumab chemotherapy with other echocardiographic parameters. Paired t-tests were used to compare all parameter at 6month with baseline.

Results: There were significant elongation of time in RVEMDi, RVEMDp, LVEMDi, LVEMDp, AEMDi at TDI, and AEMDp at TDI between baseline and after 6 months follow up echocardiographic data (RVEMDi, 90.31±20.11 vs. 97.09±19.34, p value=0.04, RVEMDp, 220.81±35.57 vs. 237.74±34.91, p value<0.001, 84.77±14.83 vs. 95.91±18.31, p value=0.009, LVEMDi, 179.18±25.60 vs. 199.82±25.01, p value=0.004, AEMDi at TDI, 57.88±15.71 vs. 63.50±15.73, p value=0.001, AEMDp at TDI, 54.02±19.84 vs. 119.84±18.94, p=0.001). Particulary, LVEMDi and LVEMDp showed an increase of 10% or more. GLS average was also changed after trastuzumab chemotherapy, but mean difference was very small (GLS average, −16.15±3.69 vs. −15.10±3.64, p value =0.05). LVEMDi and LVEMDp showed a significant increase (r=0.637, p<0.001) and Global LS (-22,33±2,40% vs -22,54±2,24%, P>0,05) results.

Conclusion: AEMDp and VEMDp was a good parameter to early detect of Trastuzumab cardiac toxicity in breast cancer patients before LV systolic dysfunction occurred. Especially, LVEMDi and LVEMDp showed great difference at 6 months follow up after initiation of trastuzumab chemotherapy.

P3585 | BEDSIDE
Acute anthracycline cardiotoxicity: carvedilol and omega-3 effects on cardiac and redox biomarkers
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Background: Acute anthracycline cardiotoxicity increase biomarkers, some of which are correlated with chronic cardiotoxicity. Generation of reactive oxygen may contribute to chronic cardiotoxicity development. We assessed the effect of carvedilol and omega-3 on cardiac dete- rioration and redox changes through the determination of cardiac and redox biomarkers, exploring the strengthening of antioxidant defense system by carvedilol or omega-3 fatty acids (iC3).

Methodology: A placebo-controlled, randomized, double-blind clinical trial was conducted in 120 patients with breast cancer undergoing chemotherapy through the determination of cardiac and redox biomarkers. Blood samples were collected prior to interventions initiation (baseline), 2 days (+2day) and 4 days (+4day) after the first anthracyclines cycle. Cardiac biomarker assessed was NT-ProBNP. Redox status was evaluated by determining the erythrocyte thiol index (GSH/GSSG). Enzymatic antioxidant defense mechanisms of erythrocytes were evaluated through superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GSH-Px) activities. Lipid oxidative damage was evaluated by measuring the F2-isoprostanes. Potential long-term effects of intervention on acute cardiotoxicity were evaluated by ECHO ejection fraction (LVEF) at baseline and at 12 months.

Results: There were no differences in baseline characteristics. Both carvedilol (baseline 47 [19–79] pg/ml vs +2day 246 [54–647] pg/ml) and placebo groups (baseline 44 [29–84] pg/ml vs +2day 112 [54–518] pg/ml) showed a statistically significant difference between baseline and 6 months (p=0.001, 62.55±2.98 vs. 60.16±3.64, p=0.044). LVEF was significant statistical difference between baseline and 6 month follow up echocardiographic data, but both data was in normal value, this results was no clinical significance (62.55±2.98 vs 60.16±3.64, p<0.001).

Conclusion: AEMDp and VEMDp was a good parameter to early detect of Trastuzumab cardiac toxicity in breast cancer patients before LV systolic dysfunction occurred. Especially, LVEMDi and LVEMDp showed great difference at 6 months follow up after initiation of trastuzumab chemotherapy.

P3589 | BEDSIDE
Degree of nocturnal blood pressure in pregnancy might be associated with enlargement of the left atrial volume
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Purpose: Few studies have been accessed the association between diastolic function and left atrial volume (LAV) in pregnancy. The aims of this study access the association between diastolic function and dipping pattern in pregnancy.

Methods: The study was a retrospective analysis of the findings in 125 pregnant patients performed 24hr ambulatory blood pressure monitoring (ABPM) and echocardiography. All pregnant patients were referred for initial evaluation of high BP and dyspnea in late third trimester of pregnancy. We enrolled the pregnant patients with normal ABPM result (mean ABPM <130/80mmHg) between 20 and 34 years. We exclude the pregnant patients with antihypertensive medication or past history of hypertension. Degree of night BP reduction was calculated as (1- (Mean SBP in night/Mean SBP in day time)) × 100

Result: The patients were mean gestational age of 29±3months. Mean ABPM was 123.4±8.4mmHg (mean day ABPM: 126.3±8.4 mmHg, mean night ABPM: 117.5±7.6 mmHg). Mean degree of night BP reduction was 8.8±6.1%. In echocardiography, mean left atrial volume index and Global CS (-25,03±4,39%, P>0.05) were included in the study upon their verbal decleration, and these substances were mostly not encountered in urine when qualitative tests were applied.

Conclusion: The addition of systolic dysfunction with preserved ejection fraction. However, these changes can be detected using 2D-speckle tracking strain imaging method. The limitations of the study are almost all of the patients who admitted to Alcohol and Drug Addiction Center were males, only male patients who used synthetic cannabinoids were included in the study upon their verbal decleration, and these substances were mostly not encountered in urine when qualitative tests were applied.
P3590 | BEDSIDE
Assessment of diastolic function in hypertrophic cardiomyopathy by computed tomography derived analysis of left ventricular filling
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Introduction: Hypertrophic cardiomyopathy (HCM) is characterized by abnormal left ventricular (LV) filling, resulting in diastolic dysfunction. Echocardiography is the clinical standard for assessment of diastolic dysfunction, but only modestly correlates with invasively derived LV filling pressures in this condition. Since retrospective ECG gated cardiac computed tomography angiography (CTA) is ideally suited for accurate measurement of simultaneous LV and left atrial (LA) volume changes, we hypothesized that CTA would be useful in the assessment of diastolic function in HCM.

Purpose: To characterise diastolic function in HCM by analysis of simultaneous LV and LA volume changes.

Methods: We studied 21 patients with HCM, age 57±14 previously diagnosed by echocardiography, and 21 age-matched controls with normal diastolic function by echo, who had undergone CTA to rule out coronary artery disease. Phases were reconstructed every 10% of the cardiac cycle and end-diastole, end-systole and diastasis identified. From these LA and LV volumes, normalized for body surface area were calculated and early and late diastolic volume changes derived.

Results: As expected, HCM patients had significantly larger LV mass (108±28 vs. 57±10 g/m², p<0.0001) and LA volumes (p<0.001). The HCM group had reduced LA total emptying fraction (30±7% vs. 42±6%, p<0.0001) while conduit volume, which represents LV filling directly from the pulmonary veins, independent of LA volume change, was increased (30±7 vs 22±4 ml/m², p<0.001). In fact, conduit volume contributed 60±10% vs. 47±6% (p<0.001) of the total LV diastolic filling, suggesting that passive filling of the LV compensates for LA dysfunction, but at the expense of increased pulmonary filling pressure. In contrast, atrial contractile function did not differ from normal subjects (11±3 vs 6±9 ml/m²) in HCM vs. 11±4±0.6 (ml/m²).

Typical examples of volume curves for a control and HCM patient

Conclusions: This study suggests that accurate simultaneous depiction of CT-derived LV and LA volume changes throughout the cardiac cycle can characterize diastolic dysfunction in HCM.

P3591 | BEDSIDE
CHADS2-VASc score identifies patients with diastolic dysfunction and heart failure with preserved ejection fraction

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Background: Heart failure with preserved ejection fraction (HFpEF) is increasingly common and often associated with systemic co-morbidities such as arterial hypertension and diabetes, advanced age and female gender. As symptoms are unspecific (dyspnea, exercise intolerance), diastolic dysfunction is often associated with systemic co-morbidities such as arterial hypertension and diabetes, advanced age and female gender. As symptoms are unspecific (dyspnea, exercise intolerance), diastolic dysfunction is often not assessed and the diagnosis of HFpEF is delayed. CHADS2-VASc, a simple risk score used in atrial fibrillation, also includes risk factors for HFpEF. We evaluated whether CHADS2-VASc identifies patients at risk for HFpEF.

Methods: We analysed medical history and echocardiographic data of 623 consecutive patients (all comers) transferred for echocardiography to our clinic, 521 with symptoms of heart failure at the time of exam (NYHA ≥2) and 102 without heart failure. Echocardiographic data was available in 266 of symptomatic and 82 of asymptomatic patients. Advanced diastolic dysfunction with increased left ventricular end-diastolic pressure (DD_advanced) was defined as E/E' ≥15 mmHg (oesophageal involvement), representing a preclinical vascular internal organ disease, in about 40% of the patients. The present study is devoted to assess the prevalence of right (RV) or left ventricle (LV) systolic and/or diastolic dysfunction as assessed by tissue Doppler imaging (TDI).

Results: Fifty-three patients with UCTD-risk-SSc (46 female, aged 45±12 years, range 16–67) and 52 age- and sex-matched controls underwent cardiac assessment by standard echocardiography and TDI.

Conclusions: Our study shows that UCTD-risk-SSc patients present a previously unrecognized, mild biventricular systolic and diastolic dysfunction as compared to controls.

Summary and conclusion: In patients with dyspnea, CHADS2-VASc score correlates with diastolic dysfunction and the prevalence of HFpEF. A CHADS2-VASc score ≥4 identifies the majority of patients with HFpEF.

P3592 | BEDSIDE
Systolic and diastolic biventricular function in patients with undifferentiated connective tissue disease at risk for systemic sclerosis
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Objectives: Undifferentiated connective tissue disease at risk for Systemic Sclerosis (UCTD-risk-SSc) is a condition characterized by Raynaud’s phenomenon (RP) and positive autoantibodies without fulfilling classification criteria for the disease. UCTD-risk-SSc patients have been reported to show mitral E/A ratio <1 (heart involvement), increasing lung capacity for CO >80% of the predicted value (lung involvement) and low esophageal sphincter pressure <15 mmHg (oesophageal involvement), representing a preclinical vascular internal organ disease, in about 40% of the patients. The present study is devoted to assess the prevalence of right (RV) or left ventricle (LV) systolic and/or diastolic dysfunction as assessed by tissue Doppler imaging (TDI).

Methods: Fifty-three patients with UCTD-risk-SSc (46 female, aged 45±12 years, range 16–67) and 52 age- and sex-matched controls underwent cardiac assessment by standard echocardiography and TDI.

Results: UCTD-risk-SSc patients and controls did not show any difference at standard echocardiographic evaluation. In particular, an inverted E/A ratio was pointed out in 14/53 patients and 12/52 controls (p<0.01). TDI showed a mild impairment of LV and RV diastolic function (Em 16±5 vs 19±5, p<0.01; E/E' 6±3±3.0 vs 4±8±1.4, p<0.005; E/A 14±3 vs 18±3, p<0.03; E/A(1±1±0.4 vs 1±3±0.4, p<0.001) and systolic function (Sm 11±3 vs 14±2 cm/sec, p<0.001; S1 14±3 vs 16±3 cm/sec, p<0.01) in UCTD-risk-SSc patients in comparison to controls. Estimated pulmonary artery systolic pressure (27±5 vs 25±5, p<0.07) and TAPSE (23±3 vs 23±5, p<0.20) were not significantly different between the 2 groups.

Conclusions: Our study shows that UCTD-risk-SSc patients present a previously unrecognized, mild biventricular systolic and diastolic dysfunction as compared to controls.
**P3593 | BEDSIDE**

Noninvasive assessment of heart failure with preserved ejection fraction: new results in echocardiographic measurement of diastolic stiffness and intraventricular vortex

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**Background:** The prevalence of heart failure with preserved ejection fraction (HFpEF) has increased in the past 2 decades. The pathophysiology is complex and specific diagnostic criteria have evolved over time. Limited data are available of quantification of diastolic function using two-dimensional (2D) real time echocardiography and a simple parameter has not yet been established, as it is the ejection fraction to assess systolic function. We believe that Diastolic wall strain of posterior wall (DWS PW) and Vortex formation time (VFT) may play an important part of an integrated approach to the non-invasive assessment of diastolic function. DWS is a parametr, that reflects resistance to deformation in diastole and thus increased myocardial stiffness. VFT represents the impact of intraventricular flow patterns on filling of the left ventricle during early diastole.

**Methods:** We have outspred our file to total number of 111 subjects with expetional dyspnea having normal left ejection fraction (Group A) and 20 healthy volunteers (Group B). In addition to the standard parameters used in the diagnos- sis of HFpEF, DWS PW and VFT were assessed in all patients. HFpEF has been proved in 38 patients with dyspnea (Group A1). The remaining 73 patients have not met established criteria for positive diagnosis of HFpEF (Group A2).

**Results:** Patients with HFpEF (Group A1) were compared with other sub- jects with dyspnea (Group A2) and significantly different values were found: DWS PW (0.261±0.064 vs 0.329±0.066, p<0.001), e' (7.10±1.47 cm/sec vs. 9.10±1.89 cm/sec, p<0.001), LV mass index (106.70±25.90 g/m² vs. 83.30±17.04 g/m², p<0.001), NT-proBNP (326.60±280.41 pg/ml vs. 119.70±63.82 pg/ml), s' (peak mitral annular systolic ve- locity, 7.40±2.98 cm/sec vs. 8.80±1.49 cm/sec, p<0.001) and VFT (3.00±1.14 vs 4.11±1.50, p<0.001). No difference was observed between the group A2 and the control group B. Multivariate analysis, which includes standard parameters for the diagnosis of HFpEF as well as new parameters, revealed, that NT-proBNP (Odds Ratio 1.136, 95% CI 1.055 to 1.226), LV mass index (Odds Ratio 1.307, 95% CI 1.1055 to 1.620) and DWS PW (Odds Ratio 0.848, 95% CI 0.750 to 0.959) independently predict the presence of HFpEF.

**Conclusion:** DWS and VFT are simple parameters in evaluation of diastolic func- tion and can be useful in the diagnosis and prognosis of HFpEF.

**Acknowledgement/Funding:** Governmental Grant IGA MZ ČR 14087-3/2013 and Specific University Research Grant MUNI/A/1270/2015.

**P3594 | BENCH**

A dipeptidyl peptidase-IV inhibitor attenuates cardiac fibrosis and improves diastolic dysfunction in Dahl salt-sensitive rats

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**Background:** The prevalence of heart failure with preserved ejection fraction (HFpEF) has been steadily increasing, and to date there is no established treatment to improve clinical outcomes of the patients with HFpEF. Dipeptidyl peptidase-IV (DPP-IV) inhibitors reportedly improve not only diabetes mellitus, but also heart failure with systolic dysfunction in experimental models. We investigated the echocardiogram of 460 community-dwelling sub- jects without obvious heart diseases (mean age, 67±7 years; 177 men, 283 women) in a rural community as a part of Arita epidemiological study at Saga, Japan. RV systolic function was estimated by tricuspid annular plane systolic excursion (TAPSE): LV systolic and diastolic dysfunctions were determined by ejection fraction (EF) and E/e' obtained from waves of transmural flow and mitral annular velocity, respectively.

**Results:** The average LVEF and E/e' were 55.2±3.6 and 8.2±1.95, respectively, both of which were within normal ranges and well preserved. The average of TAPSE was increased to 22.2±3.6mm, which is not linked to LV systolic or diastolic func- tion, but linked to both LV mass index and LA volume. Multivariate linear regress- ion analyses including age, sex, body surface area, LV mass, and left atrial (LA) volume, demonstrated that increases in LA volume was solely associated with increased in TAPSE.

**Conclusion**

**LV diastolic function**

**Conclusions:** In the community-based population, left and right ventricular func- tions are considerably preserved in the subjects without overt heart disease. Left ventricular remodeling characterized as left ventricular hypertrophy causes left atrium overloading, which is compensated by RV function, rather than LV mass. The increase in LA volume was associated with the acceleration of RV function, which might be caused by the subclinical volume retention caused by LV hypertrophy.

**P3595 | BEDSIDE**

Reverse remodeling and improvement in diastolic dysfunction: an echocardiographic study

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**Background:** Reverse remodeling (RR) is defined as the improvement in left ven- tricular (LV) geometry and systolic function following optimal heart failure pharma- cological and/or device therapy. Currently used criteria for the assessment of RR rely on LV volumes and ejection fraction, while clear data are lacking with respect to changes in diastolic function.

**Purpose:** We aimed to test whether RR could be compared with an improvement in diastolic function.

**Methods:** We retrospectively assessed 593 patients, aged 68±11 years, under- going two transthoracic echocardiograms over 12±2 months. Baseline LV ejection fraction was ~55% in all cases; systolic dysfunction had an ischemic etiolog- y in 70% of patients. LV volumes were calculated with the biplane apog- enon method. RR was defined as ≥10% reduction in LV end-systolic volume (LVESV) or a ≥10% increase in LV ejection fraction (LVEF). The following pa- rameters were considered in order to evaluate diastolic function: mean E/E' ratio,
mean sepal E’ value, mean lateral E’ value, deceleration time, grade of diastolic dysfunction.

Results: When using the first criterion to define RR (i.e., ≥10% reduction in LVEF), 180 patients (30.4%) underwent RR. The E/E’ ratio was more frequently reduced at follow-up echocardiogram in patients with RR compared to those without RR (P<0.011); similarly, the grade of diastolic dysfunction was more frequently improved in patients undergoing RR (P<0.001). When the second criterion (namely, ≥10% increase in LVEF) was applied, 99 patients (16.7%) experienced RR. The grade of diastolic dysfunction improved more frequently in patients undergoing RR (P<0.001), as well as deceleration time (P=0.004) and in- tense E’ (P=0.046), and deceleration time (P=0.001).

Cystatin C: A prospective, observational study was performed on consecutive patients with acute heart failure. The aim of this study was to demonstrate the usefulness of cystatin C cut off point of 1.6 mg/dl as predictor of WRF in patients with acute heart failure.

Background: The development of renal dysfunction in patients hospitalized for acute heart failure is known as cardio renal syndrome type 1 (CRS). Worsening renal function (WRF) during hospitalization is associated with poor prognosis. Cystatin C has emerged as an alternative renal function marker to creatinine.

Methods: The primary endpoint was WRF defined as an increase in admission serum creatinine >1.6 mg/dl on admission compared with the first day of hospitalization. The secondary endpoint was WRF 29.7% 28.2%

Characteristics of derivation and validation cohorts

Derivation cohort (N=166) Validation cohort (N=78)

<table>
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<th>Characteristic</th>
<th>N=166</th>
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<td>EF &lt;45%</td>
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<td>GFR, ml/min/1.73m²</td>
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<td>WRF</td>
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</tbody>
</table>

P5398 | BENCH

Antiarrhythmic effects of dantrolene in human cardiomyocytes from patients with atrial fibrillation or heart failure

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Introduction: Heart failure (HF) is often associated with lethal cardiac arrhythmias and sudden cardiac death (SCD). Therefore pharmacological treatment of arrhythmias in patients with HF is limited. It is known, that increased ryanodine receptor (RyR2)-mediated diastolic sarcoplasmic reticulum (SR) Ca2+ release in HF and atrial fibrillation (AF) triggers arrhythmias. Dantrolene (Dan), known as a drug that significantly mitigates the arrhythmogenicity of the RyR2, has been shown to improve Ca2+-homeostasis. We thus aimed to investigate the effects of Dan on arrhythmogenic triggers and contractility in human AF and HF cardiomyocytes.

Methods/Results: Human left ventricular (LV) cardiomyocytes (CM) were isolated from explanted hearts of 7 patients with HF (NYHA IV) and atrial CM from left atrial appendages of 7 patients with permanent AF. Functional measurements of diastolic SR Ca2+ sparks were performed by confocal microscopy using Flu-3 AM. In LV HF CM dantrolene (10 μM) caused a reduction of the Ca2+-spark-frequency by 33±16% (p<0.05, n=83 cells/8 patients dantrolene vs. 94 cells/6 patients control) leading to a reduced calculated diastolic SR Ca2+ leak (frequency × width × duration × amplitude) by 76±12% (p<0.05, n=83/6 vs. 94/6).

Conclusion: Our electrophysiological measurements show that Dantrolene significantly reduces the frequency of arrhythmogenic SR Ca2+ leak in HF and AF CM. Moreover, dantrolene decreased the frequency of proarrhythmic Ca2+ waves and spontaneous Ca2+ transients by 52±24% (p<0.05, n=10/26 vs. 10/9/6). The reduction in the arrhythmogenic SR Ca2+ leak was further observed in AF CM from patients with AF. Exposure of dantrolene to AF CM reduced the spark-frequency by 50±19% (p<0.05, n=122/7 vs. 120/7) and the diastolic SR Ca2+ leak by 56±21% (p<0.05, n=122/7 vs. 120/7). Patch clamp experiments revealed that dantrolene significantly abolishes delayed afterdepolarizations (DADs) in HF and in AF. Importantly, dantrolene had no effect on cardiomyocyte action potential duration in AF and HF. The investigation of the effect of dantrolene on isometrically twitching muscle strips from 5 human failing hearts (NYHA IV) showed no significant alterations of systolic and diastolic twitch force. Mean data of systolic twitch force after drug-incubation was 5.6±1.7 vs. 6.4±2.8 mN/mm² for dantrolene and vehicle control, respectively (n=5 each).

Conclusion: Our electrophysiological measurements show that Dantrolene significantly reduces the frequency of arrhythmogenic SR Ca2+ leak due to stabilized RyR2 and thereby abolished DADs. The unchanged APD and contractility in the human failing heart suggests safety of Dantrolene. Therefore, Dantrolene as an already clinically approved compound may be a promising treatment option for arrhythmias in heart failure which merits direct clinical investigation.

P5399 | BENCH

Metoprolol induces cardiac beta-3AR and S1PR1 signals to prevent LV remodeling and dysfunction after myocardial infarction

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Background: 3ARs levels and activity, and this receptor in adipocytes is responsible for S1P secretion, we measured basal and Meto-stimulated cardiac forskolin) leading to a reduced calculated diastolic SR Ca2+ leak (frequency × width × duration × amplitude) by 76±12% (p<0.05, n=83/6 vs. 94/6). Moreover, dantrolene decreased the frequency of proarrhythmic Ca2+ waves and spontaneous Ca2+ transients by 52±24% (p<0.05, n=10/26 vs. 10/9/6). The reduction in the arrhythmogenic SR Ca2+ leak was further observed in AF CM from patients with AF. Exposure of dantrolene to AF CM reduced the spark-frequency by 50±19% (p<0.05, n=122/7 vs. 120/7) and the diastolic SR Ca2+ leak by 56±21% (p<0.05, n=122/7 vs. 120/7). Patch clamp experiments revealed that dantrolene significantly abolishes delayed afterdepolarizations (DADs) in HF and in AF. Importantly, dantrolene had no effect on cardiomyocyte action potential duration in AF and HF. The investigation of the effect of dantrolene on isometrically twitching muscle strips from 5 human failing hearts (NYHA IV) showed no significant alterations of systolic and diastolic twitch force. Mean data of systolic twitch force after drug-incubation was 5.6±1.7 vs. 6.4±2.8 mN/mm² for dantrolene and vehicle control, respectively (n=5 each).

Conclusion: Our electrophysiological measurements show that Dantrolene significantly reduces the frequency of arrhythmogenic SR Ca2+ leak due to stabilized RyR2 and thereby abolished DADs. The unchanged APD and contractility in the human failing heart suggests safety of Dantrolene. Therefore, Dantrolene as an already clinically approved compound may be a promising treatment option for arrhythmias in heart failure which merits direct clinical investigation.
represent a previously unrecognized mechanism whereby tAR blockers prevent post-MI decompensation and adverse remodelling.

Acknowledgement/Funding: Ministero della salute-Ricerca Finalizzata e Giovani Ricercatori GR-2011-02346878

P360 | BENCH
Human ischemic cardiomyopathy shows cardiac NOS1 translocation and its increase maintains Ca\textsuperscript{2+} myocardial homeostasis and preserves ventricular performance
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Background: The role of nitric oxide synthase 1 (NOS1) as a major modulator of cardiac function has been extensively studied in experimental models; however, its role in human ischemic cardiomyopathy (ICM) has never been analyzed.

Purpose: To study NOS1 and NOS-related counterparts involved in regulating physiological function of myocyte, NOS1 dimerization, activity, and localization of NOS1 in cardiomyocytes.

Methods: Using isolated cardiomyocytes, we identified the histological status of 250 samples (Figure).

Results: The mRNA levels of NOS1 and NOS-related genes—XDH, NOS1AP, DYNLL1, NOSIP, CALM2, CALM3, SRP, ATP2A3, and RyR3—were upregulated in ICM, while GCH1, HSP90AA1, ATP2A2, PLN, PFKM, and PRKG1 were decreased. Although NOS1 protein levels were increased in ICM, its activity and dimer/monomer ratio were unaltered. We observed partial translocation of NOS1 from the sarcoplasmic reticulum to the sarcomere in ICM hearts, and significant correlation between left ventricular ejection fraction and NOS1 protein levels (P < 0.01).

Conclusions: We demonstrate that the upregulation of cardiac NOS1 is not accompanied by an increase in NOS activity. We observed partial translocation of NOS1 to the sarcomere in ischemic hearts, and a direct relationship between its protein levels and systolic ventricular function. NOS1 can be a significant component in the pathophysiology of human ischemic heart disease with a preservative role in myocardial ischemic Ca\textsuperscript{2+} homeostasis.

Acknowledgement/Funding: National Institute of Health [PI13/00100 and PI14/01506], RETICs, RD12/042/0003, and co-financed by European Regional Development Fund (FEDER)

P3601 | BENCH
Gene expression profiling to predict and identify cardiac allograft acute cellular rejection: the GETstudy
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Background: The role of nitric oxide synthase 1 (NOS1) as a major modulator of cardiac function has been extensively studied in experimental models; however, its role in human ischemic cardiomyopathy (ICM) has never been analyzed.

Purpose: To study NOS1 and NOS-related counterparts involved in regulating physiological function of myocyte, NOS1 dimerization, activity, and localization of NOS1 in cardiomyocytes.

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Results: The mRNA levels of NOS1 and NOS-related genes—XDH, NOS1AP, DYNLL1, NOSIP, CALM2, CALM3, SRP, ATP2A3, and RyR3—were upregulated in ICM, while GCH1, HSP90AA1, ATP2A2, PLN, PFKM, and PRKG1 were decreased. Although NOS1 protein levels were increased in ICM, its activity and dimer/monomer ratio were unaltered. We observed partial translocation of NOS1 from the sarcoplasmic reticulum to the sarcomere in ICM hearts, and significant correlation between left ventricular ejection fraction and NOS1 protein levels (P < 0.01).

Conclusions: We demonstrate that the upregulation of cardiac NOS1 is not accompanied by an increase in NOS activity. We observed partial translocation of NOS1 to the sarcomere in ischemic hearts, and a direct relationship between its protein levels and systolic ventricular function. NOS1 can be a significant component in the pathophysiology of human ischemic heart disease with a preservative role in myocardial ischemic Ca\textsuperscript{2+} homeostasis.

Acknowledgement/Funding: National Institute of Health [PI13/00100 and PI14/01506], RETICs, RD12/042/0003, and co-financed by European Regional Development Fund (FEDER)

P3602 | BEDSIDE
Potential mechanisms and reversibility of heart failure in type 2 diabetes: cardiovascular magnetic resonance assessment of diffuse cardiac fibrosis
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Objective: Patients with type 2 diabetes and elevated urinary albumin creatinine ratio (ACR) are at the highest risk of heart failure. We aimed to establish the distribution of cardiac fibrosis in those at the highest risk of heart failure and whether it is reversible after treatment with an ACE inhibitor.

Methods: We carried out cardiovascular magnetic resonance in 100 asymptomatic patients with type 2 diabetes and 30 age and gender matched controls. 50 patients had persistent microalbuminuria (ACR>ve) yet to start an ACE inhibitor and 30 had normal ACR. The protocol included T1 mapping using Modified Look-Locker Inversion (MOLLI) to assess for diffuse fibrosis and late gadolinium enhancement imaging to assess for focal fibrosis caused by prior myocardial infarction. 30 ACR>ve patients had repeat imaging 1 year after treatment with an ACE inhibitor (equivalent to ramipril 4.5±2.9mg daily).

Results: Myocardial extracellular volume fraction (ECV), a measure of diffuse fibrosis, was higher in ACR>ve than ACR-ve patients (N=100, 27.2±1 and 25.1±2%, p=0.004), see Figure. The rate of silent myocardial infarction was 17%, which was not influenced by ACR status. After one year treatment with an ACE inhibitor there was a significant reduction in left ventricular end diastolic volume (148±38.7 to 138±17.3ml, p=0.001) and ECV (26.5±3.6 to 25.2±3, p=0.01), see Figure. There was no significant change in 24 hour blood pressure or left ventricular mass.

Conclusions: Patients with type 2 diabetes and persistent microalbuminuria, at
increased risk of heart failure, had ECV expansion suggesting diffuse cardiac fibrosis. Treatment with an ACE inhibitor was associated with reduction in cavity size of the left ventricle and regression of ECV. These findings suggest ECV might be a suitable biomarker to identify patients with diabetes at increased risk of heart failure and that blockade of the renin-angiotensin system may be a potential therapeutic target.

Acknowledgement/Funding: British Heart Foundation

P3603 | BENCH
The contribution of the myocardial fiber orientation to asymmetric ischemic mitral regurgitation

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Background: Two echocardiographic phenotypes of tenting in ischemic mitral regurgitation have been identified as asymmetric and symmetric type. Little is known about how each myocardial fiber orientation affects mitral valve especially in the asymmetric type. In a previous study, we demonstrated that the longitudinal strain (LS) was lower in a left anterior descending artery (LAD) infarction than in a left circumflex artery (LCX) infarction. Our aim in this study is to investigate whether the infarction of a diagonal branch (DB), as the branch of LAD affected the LS, exacerbates IMR in an inferior myocardial infarction (MI) in pig.

Methods: An MI was induced by occluding the LCX and/or the DB with a balloon and/or a coil in Yorkshire pigs. One month after the MI induction, mitral valve deformation (valve tenting, annular length and annular function) and LV global (systolic and diastolic volumes, function) and LV strains were assessed with echocardiography (E33; Philips) and compared between the two groups (LCX only and LCX+DB).

Results: A total of 12 pigs were included in the study (LCX only n=6, LCX+DB n=6). The incidence of severe MR (grade III-IV) in the LCX+DB group was higher than in the LCX only group (66.6% vs. 0%, P=0.038). There were no significant differences between the two groups in left ventricular systolic function, valve tenting and annular length, however the ratio of posterior to anterior leaflet tethering angle was significantly decreased in the LCX+DB group (2.06±0.42% vs. 1.16±0.30%, P=0.0008, LCX+DB vs LCX only). At the papillary muscle level, echocardiographic strain analysis revealed no statistically significant differences in radial and circumferential strain between the two groups. However, in contrast with LCX only, the LCX+DB group resulted in significantly decreased LS at the mid-lateral wall (0.3±4.9% vs -21.0±3.8%, P=0.0249) compared with the ratio of tethering angle (r=0.70, P=0.0008).

Conclusion: These data indicate that the loss of LS at the mid-lateral wall may contribute to IMR in inferior MI. Understanding the underlying mechanisms of MR progression could lead to new therapeutic approaches in preventing IMR.

P3604 | BEDSIDE
Influence of left atrial function on exercise capacity and left ventricular function in patients with heart failure and preserved ejection fraction


Background: Left atrial (LA) dilatation and dysfunction are frequent in heart failure with preserved ejection fraction (HFrEF). Data are lacking regarding the specific influence of LA function in HFrEF physiology using comprehensive techniques including cardiac MRI and invasive pressure volume loops. Cardiovacular magnetic resonance myocardial feature tracking (CMR-FT) is a novel tool measuring atrial strain and phasic performance from routine cine CMR images. Aim of the current study was to investigate LA function and its influence on exercise capacity and LV function in HFrEF patients.

Methods: We performed CMR-FT in 20 patients with HFrEF and 10 patients without heart failure symptoms. LA function was analyzed using 2- and 4-chamber views for assessment of LA reservoir function (total strain [εs]), LA conduit function (longitudinal strain [εL] and LA booster pump function (active strain [εa]). Invasive pressure-volume-loops were obtained with a conductance catheter during baseline conditions, transient preload reduction and handgrip exercise to evaluate LV diastolic properties. LV stiffness constant Beta was extrapolated during transient preload reduction and isovolumetric relaxation time Tau was measured during maximal handgrip exercise. Peak oxygen uptake (VO2max max kg/m2) was determined by upright bicycle cardiopulmonary exercise testing. Time-volume curves of the LV were determined on CMR short axis stacks and the degree of LV early filling calculated, as defined by the extent of LV filling during the first 1/3 of total LV filling period.

Results: Patients with HFrEF showed greater left atrial volumes (LAV max 49±10 vs. 34±9 ml/m², P<0.01) and lower oxygen uptake (17±6 vs. 29±8 ml/kg/min, P<0.01). LA reservoir and conduit function were significantly lower in HFrEF patients as LV+DB vs. LCX only (εs: 22±6 vs. 28±6%, P=0.05, εL: -9±5 vs. -15±5%, P<0.01). HFrEF patients had a higher intrinsic stiffness constant Beta (0.036±0.006 vs. 0.021±0.008, P<0.01). Beta showed a moderate correlation with VO2max (r=-0.51, P<0.01). Strain measurement for LA conduit function showed the best correlation with VO2max (r=-0.80, P<0.001). Multivariate regression analysis to predict maximal oxygen uptake including Beta, Tau and LA conduit function (εL) revealed εL as the only predictor of VO2max (R2=0.80, R2=0.64, P<0.001). Patients with impaired conduit function (εL = median) had longer isovolumetric relaxation time Tau (40±6 vs. 34±4 ms, P<0.01) and reduced early LV filling volume as % of LV stroke volume (31±13 vs. 52±15%, P<0.01).

Conclusion: LA dysfunction is present in HFrEF and can be quantified using CMR-FT. Our results propose LA dysfunction as another important contributor to exercise intolerance in HFrEF, which is independent of load-independent LV stiffness and associated with impaired early LV filling.

Acknowledgement/Funding: Research grant Heart Center Leipzig, Germany

P3605 | BEDSIDE
Impact of hemodilution on left ventricular diastolic properties: noninvasive analysis by speckle tracking echocardiography

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Introduction: Most patients with dialysis have left ventricular (LV) hypertrophy and fibrosis due to pressure and volume overload. This may result in heart failure. Some patients with dialysis have low output and hypotension due to excessive water removal after dialysis session. Thus, the evaluation of LV function is helpful to treat the patients with dialysis. However, noninvasive assessment of LV diastolic function and the effect of dialysis on LV diastolic function have not yet been established. We reported that pulmonary capillary wedge pressure (PCWP) is accurately estimated using left atrial (LA) emptying function and volume (LAV) by speckle tracking echocardiography (STE).

Purpose: The aim of this study was to noninvasively examine LV diastolic function such as LV relaxation and stiffness and PCWP just before and after dialysis using STE and to evaluate the impact of dialysis on LV diastolic function.

Methods: Phasic LAV and LA emptying function were measured in 118 patients with dialysis (age: 66±11, 73 men) just before and after hemodilysis by 2-dimensional STE. PCWP was estimated as 10.8 – 12.4 x log (LA active emptying function/minimum LAV index). LV ejection fraction (EF) as a shortening parameter and E/e' as an index of LV filling pressure were measured just before and after hemodilysis. Moreover, we estimated time constant of LV pressure decline (Tau) as an index of LV relaxation, LV stiffness and LV diastolic stress. Isovolumetric relaxation (IVR) time was measured as the time between the end of LV outflow wave and the beginning of LV inflow wave by Doppler echo. Tau was estimated as IVR time (in 0.8 x systolic blood pressure – PCWP), LV stiffness was estimated as LV diastolic stress / LV strain by STE. LV diastolic stress was calculated as 0.334 x PCWP x LV end-diastolic dimension / (end-diastolic thickness x end-diastolic dimension).

Results: Patients with dialysis had LV hypertrophy (LV mass index: 141±34 g/m²). Systolic blood pressure and LV end-diastolic dimension were significantly decreased after dialysis (152±24 vs 140±24 mmHg and 49±6 vs 47±6 mm, respectively) associated with water removal during dialysis session. UFEW was increased after dialysis (63±8 vs 65±9%). PCWP and E/e' were decreased after dialysis.
dialysis (10.0±2.3 vs 8.0±3.1 mmHg and 15.6±4.5 vs 14.4±3.8, respectively). Tau and LV stiffness were improved after dialysis (481±8 vs 46±1 msec and −0.9±0.7 vs −0.6±0.5, respectively) associated with reduction of LV diastolic stress through dialysis (12.1±1.5 vs 9.1±4.3 dyne/cm²).

Conclusions: LV relaxation assessed by Tau using STE was improved and LV stiffness assessed by the LV-EF were also improved just after dialysis accompanied with decreased PCWP and diastolic stress. LV diastolic properties in dialysis patients could be noninvasively assessed by Tau and the assessment of diastolic function may have an incremental value in the treatment in dialysis patients.

P3606 | BEDSIDE
Comparison of the clinical course of Chagas cardiomyopathy with that of Chagas cardiomyopathy associated with chronic obstructive coronary artery disease
A.P. Otaviano, A. Cardinalli-Neto, A.M.S. Rodrigues, M.A. Nakazone, R. Bestetti. Hospital de Base, Faculty of Medicine of São José do Rio Preto, São José do Rio Preto, Brazil

Background: Chagas cardiomyopathy (ChCM) affects about 20% of patients with chronic Chagas disease. Chronic heart failure (CHF) may affect from 14% to 76% of patients with ChCM. The coronary arteries in ChCM patients are usually free of obstructive coronary artery disease (OCAD). In areas where the disease is endemic, however, ChCM and OCAD may coexist in a same patient with CHF. The clinical course of patients with CHF due to ChCM associated with OCAD (ChCM-OCAD) is not known.

Purpose: Accordingly, the aim of this study was to compare the clinical course of ChCM-OCAD patients with that of ChCM with CHF.

Methods: The study population comprised 217 patients with the diagnosis of CHF (ChCM, ChCM-OCAD, and ChCM patients with CHF due to ChCM-OCAD). All patients had a positive serology for Chagas disease, a left ventricular ejection fraction >55% on 2-dimensional echocardiogram, and were followed from January, 2000 to January, 2010. Patients underwent coronary angiography because of precordial chest pain or major risk factors for OCAD. A luminal narrowing >70% was diagnostic of OCAD. Patients received standard treatment for CHF.

Results: Mean age was 57±14 years in patients with ChCM and 68±8 years in those with ChCM-OCAD (p<0.05). On admission, mean systolic blood pressure was 106±7±61 in ChCM patients and 118±2±5.9 mmHg in those with ChCM-OCAD (p<0.005), whereas diastolic blood pressure was 70±10±18 ChCM patients, and 75.7±12.3 mmHg in those with ChCM-OCAD (p=0.01). Pacemaker wear was seen in 116 out of 217 (53%) patients of the ChCM group, and in 9 out of 28 (32%) patients in the ChCM-OCAD group (p=0.04). Ventricular premature contractions were detected in 103 of 217 (47%) ChCM patients, and in 6 of 28 (21%) ChCM-OCAD patients (p=0.009). Segmental wall motion abnormalities on echocardiogram were observed in 78 out of 217 (36%) CHM patients, and in 17 of 28 (61%) ChCM-OCAD patients (p=0.001). Mean left ventricular diastolic diameter (LVDd) was 64.6±8 mm ChCM patients and 61±±7.8 mm ChCM-OCAD patients (p=0.05). Median follow up was 27 (9, 48) months. There were 138 deaths (64%) in ChCM group, and 10 deaths (36%) in ChCM-OCAD group (p=0.005). A Cox-proportional hazards model established that the LVDd was the only independent predictor of mortality for this patient population (Wald coefficient=32, Hazard Ratio: 1.05 (95% Confidence Interval from 1.03 to 1.07; p=0.005)). Survival probability by Kaplan-Meier at 12, 24, 36, and 48 months were 78%, 61%, 51%, and 40% in ChCM patients, and 96%, 80%, 71%, and 66%, in ChCM-OCAD patients, respectively (p=0.02).

Conclusions: Therefore, patients with ChCM patients with CHF have a poor prognosis in comparison with patients with ChCM-OCAD patients. This fact can probably be ascribed to the more intense left ventricular remodeling process and poor hemodynamic profile on admission, observed in ChCM patients in comparison to those seen in ChCM-OCAD patients.

P3607 | BEDSIDE
Nursing intervention is more effective for the elderly with acute heart failure

Background: It is being happening heart failure pandemic in the world. It is important that the patients with acute heart failure (AHF) prevent recurrence of heart failure. They need to understand clinical state on heart failure, medicines and notes of daily life. Nursing intervention is a basic coaching on heart failure by medical staff during admission. Nursing intervention is effective for preventing recurrence of heart failure. But, it is well unknown the effectiveness of nursing intervention for elderly patients who have generally a low understanding.

Objective: We investigate retrospectively the effectiveness of nursing intervention for the elderly.

Methods and results: 660 consecutive patients were enrolled who were admitted by AHF in our hospital. We evaluated the incident rate of clinical events by the presence or absence nursing intervention. The clinical events were defined as all-cause death and readmission by worsening of acute heart failure. Follow up period was 2 years. The median age of the subjects was 80 years old. They were divided into two groups in the 80-years-old. In all subjects, Kaplan-Meyer Methods and Cox proportional hazard analysis showed that nursing intervention decreased significantly the incident rate of clinical events for the patients with AHF (Hazard Ratio (HR)=0.668, 95% Confidence Interval (CI): 0.530–0.843: p=0.001). But in less than 80-years-old, nursing intervention was not effective for prevent clinical events (HR=0.814, 95% CI: 0.579–1.144: p=0.236). On the other hand, in over 80-years old, it was more effective (HR=0.561, 95% CI: 0.461–0.785: p=0.001), although their nursing intervention rate was clearly lower than that in less than 80-years old (55.5% vs. 44.5%; p=0.004).

Multivariate analysis for clinical event

<table>
<thead>
<tr>
<th>Factor</th>
<th>HR</th>
<th>95% CI</th>
<th>p</th>
</tr>
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<tbody>
<tr>
<td>NYHA</td>
<td>1.171</td>
<td>1.003–1.367</td>
<td>0.046</td>
</tr>
<tr>
<td>BNP (100 increase)</td>
<td>1.014</td>
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<td>0.708</td>
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HR, Hazard ratio; CI, Confidence interval; NYHA, New York Heart Association; BNP, B-type natriuretic peptide.

Conclusions: Nursing intervention is more effective for the elderly with AHF. Aggressive intervention needs to prevent recurrence of heart failure for the elderly who are shunned it by medical staff.

P3608 | BEDSIDE
MicroRNA-21 and microRNA-133 levels in peripheral blood mononuclear cells are associated with functional capacity in patients with heart failure preserved ejection fraction
M. Marketou1, J. Kontaraki1, F. Parthenakis1, S. Maragkoudakis1, H. Nakou1, A. Patrianakos1, M. Touloupaki1, J. Konstantinou2, M. Vernardou1, P. Vardas2
1. Heraklion University Hospital, Heraklion, Greece; 2. Boston University School of Medicine, Boston, United States of America

Purpose: MicroRNAs (miRNAs) are essential regulators of gene expression implicated in cardiovascular function and disease. miRNA-21 and miRNA-133 have been shown to play a role in ventricular and vascular remodeling. However, there are limited data regarding their role in heart failure with preserved ejection fraction (HFpEF). The aim of this study is to investigate the association between miRNA-21 and miRNA-133 levels in peripheral blood mononuclear cells (PBMCs) and exercise capacity in patients with HFpEF.

Methods: We included patients with symptoms and signs of heart failure who underwent a complete echocardiographic study and a cardiopulmonary exercise test. PBMCs were isolated and microRNA levels were determined by quantitative real-time reverse transcription PCR (arbitrary units).

Multivariate analysis for clinical event

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Conclusions: Nursing intervention is more effective for the elderly with AHF. Aggressive intervention needs to prevent recurrence of heart failure for the elderly who are shunned it by medical staff.

Kaplan-Meier curve for clinical events

![Kaplan-Meier curve for clinical events](https://academic.oup.com/eurheartj/article-abstract/37/suppl_1/599/2197552/15992197552)
Results: Twenty-five patients (10 males, aged 58±16 years) were analyzed. The mean miRNA-21 levels were 4.1±0.51, mean miRNA-133 levels were 11.2±4.4, mean peak VO2 22.7±5.9 ml/kg/min. Multivariable regression analysis revealed a positive association between miRNA-21 levels and peak VO2 (p=0.004, r=0.51) and a negative association between miRNA-133 levels and peak VO2 (p=0.002, r=-0.53).

Conclusions: miRNA-21 and miRNA-133 may be an important marker or modulator of functional capacity in patients with HFpEF. Further studies are needed to assess their role as therapeutic targets in those patients.

**P3609 | BEDSIDE**

**Psychological characteristics and adherence to treatment in patients with chronic heart failure**

E.V. Eremerova, A.M. Shutov, M.V. Menzerov. Ulyanovsk State University, Ulyanovsk, Russian Federation

**Introduction:** Low adherence to medical treatment is a widely extended problem among patients with chronic heart failure (CHF). There are a lot of social and pharmacoeconomic factors of nonadherence. However, influence of psychological characteristics on adherence to treatment in patients with CHF have not been studied yet. The aim of this study was to investigate influence of psychological characteristics on adherence to treatment in patients with CHF.

**Methods:** 203 patients with CHF (130 males and 73 females, mean age was 62±10 years) were studied. CHF was defined according to ESC Clinical Practice Guidelines of Acute and Chronic Heart Failure, 2012. The main causes of CHF were coronary artery disease and arterial hypertension. CHF severity index was calculated. Psychological state, relation to disease and quality of life were estimated using MMPI, characterological questionnaire K. Leonhard, SF-36 Health Status Survey. Level of adherence to treatment of patients with CHF was studied, using Morisky Medication Adherence Scales (MMAS-4). Patients were followed up for 1 year.

**Results:** Only 61 (30%) patients were full adherence to medication treatment, and 37 (18.2%) - to non-medication therapy (recommendations for self-care and lifestyle changes). The sensitive (38.4%), paranoiac (36.9%), neurotic (27.8%) types of relation to disease were dominated in the internal structure of the disease. Age adjusted Charlson comorbidity index was 5.0±2.1 scores. Patients with high comorbidity (Charlson comorbidity index > 4 scores) had higher T-score with baroreflex activation therapy (BART) characterized by hypochondriac syndrome (78.3±15.3 and 62.7±10.6 resp. p=0.01), dysthymic character accentuation (13.6±3.7 and 11.0±4.5 scores resp. p=0.006), which indicated weakness of energy resources, reducing emotional background. Patients with high comorbidity had decreased of quality of life, both in the physical and the psychological aspects.

**Conclusions:** Nonadherence to treatment in patients with CHF is associated with desadaptive type of relation to disease, which is more common in patients with high comorbidity. Patients with desadaptive type of relation to disease should be included into group of risk for nonadherence to treatment and need more intensive observation.

**P3610 | BEDSIDE**

**The impact of rhythm control by catheter ablation on reduction of heart failure hospitalization in patients with HFPEF and AF**

T. Machino, Y. See, T. Ishizu, M. Yamamoto, Y. Hamada-Harimura, K. Aonuma. University of Tsukuba, Tsukuba, Japan

**Background:** Atrial fibrillation (AF) is common, precipitating factor for clinical deterioration of heart failure with preserved ejection fraction (HFpEF). The clinical impact of rhythm control on prognosis of patients with HFpEF is unknown.

**Purpose:** This study compared HF events of patients achieved rhythm control versus those of propensity score (PS) matched patients with heart rate control.

**Methods:** Consecutive 329 patients with HFpEF comitant AF were enrolled. Of these, 141 patients achieved maintenance of sinus rhythm by catheter ablation disease (CA) and/or antiarrhythmic drugs (AAD) and 188 had rate control. PS for each patient in both treatment groups were estimated, allowing selectively matched subgroups of 68 patients each. The covariates used in PS model were sex, age, type of AF, NYHA functional classification, LVEF, and left atrial volume (LAV). Differences were assessed by log-rank test for hospitalization-free survival.

**Results:** Matched patients had mean ages of 70 years, mean LVEF of 64%, and mean LAV of 48 ml/m². There were 33% female, 57% non-paroxysmal AF and 20% patients with NYHA class III in matched patients. Of 68 patients with rhythm control, 28 underwent CA and continued AAD, 20 underwent CA and stopped AAD, and 20 underwent AAD therapy only. During a average follow-up of 28 months, all-cause death or HF hospitalization occurred in 8 of 68 patients in the rhythm control group (12%) and 24 patients in the rate control group (35%).

**Table:** The shows the impact of treatment strategy for AF on clinical outcomes in PS-matched HFPEF cohort.

<table>
<thead>
<tr>
<th>Post-match (n=136)</th>
<th>Events (%)</th>
<th>Hazard ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rhythm control (n=68)</td>
<td>Rate control (n=68)</td>
<td>Rhythm control</td>
<td>Rate control</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>2 (3%)</td>
<td>6 (9%)</td>
<td>0.33 (0.07–1.65)</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>1 (2%)</td>
<td>5 (7%)</td>
<td>0.20 (0.02–1.2)</td>
</tr>
<tr>
<td>Non-cardiovascular</td>
<td>1 (2%)</td>
<td>2 (3%)</td>
<td>0.97 (0.06–15.46)</td>
</tr>
<tr>
<td>HF hospitalization</td>
<td>4 (6%)</td>
<td>12 (18%)</td>
<td>0.31 (0.10–0.98)</td>
</tr>
</tbody>
</table>

**Conclusion:** The PS-adjusted multivariate Cox hazard model based on 329 pre-match patients also revealed that rhythm control associated with the reduction of HF hospitalization-free survival rate and result of log-rank test in matched patients. The PS-adjusted multivariate Cox hazard model based on 329 pre-match patients also revealed that rhythm control associated with the reduction of HF hospitalization-free survival rate and result of log-rank test in matched patients.

**P3611 | BEDSIDE**

**Are NT-proBNP plasma levels useful in the management of Friedreich ataxia patients?**

L. Legrand1, C. Maupain1, M.L. Monin2, A. Tatara2, A. Durr2, R. Isnard2, F. Pousset1.


**Background:** Friedreich ataxia (FRDA), due to mitochondrial dysfunction, is the most common genetic sensory ataxia. The causal mutation is an expanded trinucleotide repeat (GAA) in the frataxin gene. Moderate hypotrophic cardiomyopathy is associated with FRDA and is the major cause of early death before 40 years old. NT-proBNP is a cardiac biomarker which could be useful to screen FRDA patients before heart failure occurred.

**Methods:** From December 2012 to November 2015, 86 genetically confirmed FRDA patients (shorter GAA repeats: 2,450±78 Kb) were included. Mean age was 39±12y, 52% were male, age at onset of the disease was 17±11y and age of wheelchair use 26±10y. 5 patients had previous atrial fibrillation and 2 previous heart failure. Echocardiographic parameters were Left Ventricular Ejection Fraction,LVEF; 64±5%, Septal Wall Thickness (SWT); 11±2mm, Posterior WT; 10±2mm, LV diastolic diameter; 45±5mm, indexed Left Ventricular Mass (LVM) 97±22g/m² and transmural E wave/DI E ratio; 6.2±2.2. Plasma levels of NT-proBNP were: 99±184 ng/L and of Hs troponin T: 15±18ng/L. In multivariate analysis, plasma levels of NT-proBNP are positively associated with age p=0.007, PWT p=0.006, LVM, p=0.003 and negatively associated with LVEF, p=0.001. Patients were divided in 2 groups according to NT-proBNP levels. Patients with NT-proBNP>125ng/L (n=15), had higher SWT (12.8±3 vs 10.8±2 mm, p=0.002), higher LVM (101±18 vs 95±22 g/m², p=0.003), lower LVEF (59±4 vs 64±4%, p=0.001) and significant longer GAA repeats on the shorter allele, (1,9±0.6 vs 1,5±0.7kb, p=0.02). NT-proBNP->125ng/L seems to be a marker of severity of the cardiopathy.

**Conclusion:** NT-proBNP plasma levels could be included in the routine evaluation of FRDA patients with preserved LVEF. It could help physicians to identify high risk patients, who will require closer cardiologic management.

**P3612 | BEDSIDE**

**Baroreflex activation therapy for the treatment of heart failure with reduced ejection fraction in patients with and without coronary artery disease**

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**Background:** Baroreflex activation therapy for the treatment of heart failure with reduced ejection fraction (HFpEF) is promoted...
Hydrogen consumption is a newly oxidative stress marker predicting the severity in patients with chronic heart failure

A. Shibata1, Y. Sugano1, A. Shimouchi2, T. Yokokawa1, N. Jinno2, H. Kanzaki1, T. Alba1, K. Kusano1, M. Shirai1, S. Yasuda1, H. Ogawa1, T. Anza1, N. Cerebral and Cardiovascular Center, Department of Cardiovascular Medicine, Osaka, Japan; 2National Cerebral and Cardiovascular Center, Department of Cerebral and Cardiovascular Center, Department of Cardiovascular Medicine, Osaka, Japan

Background: Reactive oxygen species (ROS) play some important roles in the development and progression of heart failure. Chronic exposure to ROS causes the oxidation of membrane phospholipids, proteins, and DNA. In contrast, many antioxidant stress systems exist in the living body. Previous studies have shown that hydrogen (H2) selectively reduces the hydroxyl radical (OH), known as the most cytotoxic form of ROS, in cultured cells.

Purpose: We investigated whether H2 consumption in the body during the night, estimated by overnight decrease in exhaled H2 concentration, could be a surrogate of ROS production, thus a marker for heart failure severity.

Methods: We recruited 108 patients with chronic heart failure (CHF) and 15 control subjects without CHF. All patients were put on a hospital heart failure diet of 1,600 kcal energy with 245 g carbohydrates, 60 g protein, and 40 g fat. Exhaled breath was collected before sleep and in the morning after overnight fast to measure H2 concentration by gas chromatograph. H2 consumption in the body during the night was estimated by overnight decrease in H2 concentration, which was calculated by subtracting the exhaled H2 level in morning from that before sleep. Haemodynamic profiles were evaluated by using cardiac catheterization to measure cardiac output index (CI).

Results: H2 consumption was significantly increased in patients with CHF compared with control subjects (4.3±0.7 vs. 2.0±0.9 ppm, p<0.02). H2 consumption was positively correlated with plasma brain natriuretic peptide (r=0.436, p<0.001) and serum high-sensitivity troponin T (r=0.248, p=0.012), and negatively correlated with CI (r=−0.292, p=0.002) (Fig. 1) and mixed venous oxygen saturation (r=−0.282, p=0.004). Receiver operating characteristic (ROC) curve was used to detect the optimal cut-off point of H2 consumption levels to estimate CHF. Patients were divided into two groups by the cut-off value of H2 consumption (0.6 ppm), and CI was lower in the high H2 consumption group compared to that of low H2 consumption group (2.8±0.61 vs. 3.21±0.64 L/min/m², Fig. 2).

Conclusions: This study demonstrated that H2 consumption was associated with the severity in patients with CHF, suggesting that H2 consumption could be a useful oxidative stress marker.

Hydrogen consumption was a newly oxidative stress marker predicting the severity in patients with chronic heart failure

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P3616 | BEDSIDE
Pulsatile hemodynamics is associated with cardioenal syndrome in patients with acute heart failure syndrome
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Background: The presence of cardioenal syndrome (CRS) may increase post-discharge events in patients hospitalized for acute heart failure (AHF). The present study investigated how pulsatile hemodynamics modulates CRS and its impact on post-discharge outcomes in patients with AHF.

Methods: A total of 237 AHF patients (65±15.4 years, 76.4% men) were enrolled and followed up for up to 3 years after discharge. Measures of the renal function and the pulsatile hemodynamics, including carotid systolic blood pressure (SBPc) and pulse pressure (PPc), carotid-femoral pulse wave velocity (cf-PWV), carotid augmented pressure (cAP), the amplitude of reflected wave (Pb), aortic characteristic impedance (Zc) were obtained within 24 hours of admission before discharge. CRS was defined by an estimated glomerular filtration rate (eGFR) of < 60 mL/min/1.73m².

Results: On admission, 155 patients (76.4%) presented with CRS, who were older and more likely to have hypertension, diabetes, and increased on-admission SBPc, PPc, cf-PWV and Pb, compared with those without CRS. Pre-discharge eGFR improved in 136 patients (57.4%) who had lower on-admission eGFR, left ventricular ejection fraction (LVEF), and Pb. With adjustments for age, sex, LVEF, and eGFR, lower on-admission Pb and Pb remained significantly predictive of improvement in eGFR (HR and 95% CI per-1SD decrease: 1.60, 1.16–2.22; 1.65, 1.61–2.36; and 1.72, 1.22–2.43, respectively). Before discharge, CRS left in 34 patients and new CRS developed in 10 patients. During a mean follow-up duration of 703±400 days, 121 subjects incurred their first clinical events of either re-hospitalization for AHF or mortality. Either on-admission or at-discharge CRS significantly predicted post-discharge clinical events (Figure). After accounting for age, sex, LVEF, and NT-proBNP, patients who presented with CRS on-admission and at-discharge had higher rate of post-discharge clinical events (HR and 95% CI: 2.18, 1.24–3.85), compared with those who never developed CRS. The association remained significant with further adjustment for at-discharge PpC, cAP, Pb or cf-PWV.

Conclusions: Pulsatile hemodynamics, excessive wave reflections in particular, may contribute to the development of CRS in patients with AHF. However, the presence of persistent CRS during the hospitalization is a strong predictor of post-discharge clinical events, independent of the pulsatile hemodynamics and other risk factors.

Acknowledgement/Funding: Ministry of Science and Technology, Taiwan (MOST 103-2314-B-010-050-MY2)

P3617 | BEDSIDE
Serum potassium levels and clinical outcome in patients with chronic heart failure
S. Hoss, Y. Elizur, D. Luria, A. Keren, C. Lotan, I. Gotsman. Hadassah University Medical Center, Heart Institute, Jerusalem, Israel

Background: Potassium levels are often abnormal in patients with heart failure (HF) and have a detrimental effect on clinical outcome. We evaluated potassium levels in a real world cohort of patients with HF and its effect on mortality.

Methods: All patients with a diagnosis of HF at a health maintenance organization were evaluated and followed for cardiac related hospitalizations and death.

Results: The cohort consisted of 6,073 HF patients. Mean potassium levels were 4.57±0.53 mmol/L. The majority of patients (68%) had potassium levels in the normal range (4.0–5.0 mmol/L). High-normal potassium levels (5.0–5.5) were present in 17% of the patients, low potassium levels (<4.0) in 11% and hyperkalemia (K>5.5) in 4%. Mean follow-up was 576 days. The overall mortality rate during this period was 14%. Survival rate by Kaplan-Meier analysis demonstrated that hypokalemia was associated with the lowest survival rate. Survival was highest in patients with high-normal potassium levels. Cox regression analysis showed that adjustment for significant predictors including comorbidities and standard HF drug therapies demonstrated that high-normal potassium levels was independently associated with reduced mortality compared to normal reference levels, hazard ratio (HR) 0.78, 95% confidence interval (CI) 0.64–0.95, P=0.01. Sub-group analysis showed improved outcome with high-normal potassium levels in patients with reduced renal function, spironolactone and loop diuretic therapy. High-normal potassium levels was also independently associated with reduced out-of-hospital mortality (HR 0.73, 95% CI 0.55–0.96, P=0.03).

Conclusions: Potassium levels in the high-normal range appear to be safe and are associated with an improved outcome in patients with HF.

P3618 | BEDSIDE
Impact of ventricular tachyarrhythmias in advanced non-ischemic heart failure patients who referred for heart transplant evaluation
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Background: In advanced heart failure (HF) patients, the associated conditions of refractory life-threatening ventricular arrhythmias (VAs) dominate clinical compromise and risk. In INTERMACS classification, revised modifer A defined as VAs, includes frequent ICD shock or requirement for external defibrillator, more frequent ICD therapies, weekly, or on-demand. However, available standard and standard HF drug therapies demonstrated that high-normal potassium levels was independently associated with reduced mortality compared to normal reference levels, hazard ratio (HR) 0.78, 95% confidence interval (CI) 0.64–0.95, P<0.01. Sub-group analysis showed improved outcome with high-normal potassium levels in patients with reduced renal function, spironolactone and loop diuretic therapy. High-normal potassium levels was also independently associated with reduced out-of-hospital mortality (HR 0.73, 95% CI 0.55–0.96, P=0.03).

Methods and results: We retrospectively studied 90 non-ischemicHF patients who referred to our institution between 1997 and 2014 for evaluation of heart transplantation. Electrical storm (ES) was defined as ≥3 episodes of sustained ventricular tachycardia (sVT) or ventricular fibrillation (VF) in 24 hours. 33 (37%) patients had episodes of sVT/VF, 16 (18%) patients were defined as modifier A, and 14 (16%) patients had ES. Of the patients who experienced sVT/VF, ICD was in place in 29 (88%) patients and 29 (88%) patients received left ventricular assist device (LVAD) or died after the median time of 24days [interquartile range, 5 to 397 days] after the last sVT/VF. 15 (52%) patients of those received LVAD or died within 30 days after the last sVT/VF. The patients who experienced sVT/VF had a significantly higher risk of death than those who did not experience sVT/VF (HR 3.08, 95% CI 1.28–7.65, p<0.01).

Conclusions: In advanced non-ischemic HF patients, VAs are associated with poor prognosis. There is a need to consider early implantation LVAD in advanced non-ischemic HF patients with revised modifier A.

P3619 | BEDSIDE
Prevalence of thyroid disease in HFREF and HFPEF and prognostic importance of TSH in clinical outcomes
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Purpose: We investigated the prevalence and the prognostic importance of thy-
roid dysfunction in patients with heart failure due to either reduced (HFrEF) or preserved ejection fraction (HFpEF) in an epidemiologically representative population.

Method: Consecutive patients with suspected HF referred to and followed up in a single HF clinic serving a population of ~500,000 people were enrolled. A clinical diagnosis of HF was confirmed by echocardiographic or biochemical evidence of cardiac dysfunction (LVEF <50% for HFrEF and NTproBNP >220 ng/L for HFpEF). Patients were classified using plasma concentrations of thyroid stimulating hormone (TSH) as euthyroid (TSH: 0.3–5.0 μU/ml), low-TSH (TSH: <0.3–5.0 μU/ml) or hypothyroid (TSH >5.0 μU/ml) and by thyroxine (T4) prescription. Outcome of interest was all-cause mortality.

Results: Of 6131 patients enrolled, 4658 [median age 73 (65–59) years; 1850 (40%) women] had a baseline measurement of TSH of whom 1182 (25%) had no expected heart failure (10% v 7%). However, thyroid status was generally not expected (91%) and 1680 (93%) were euthyroid. In univariable analysis, a higher TSH was associated with increased mortality compared to euthyroid patients (HR: 1.02 (91%)). Amongst patients not taking T4, 33 (3%), 34 (2%) and 43 (2%) were hypothyroid, 23 (2%), 98 (7%) and 91 (5%) had a low-TSH and 1088 (95%), 1381 (91%) and 1880 (93%) were euthyroid. In a higher analysis, a TSH was associated with increased mortality compared to euthyroid patients (HR: 1.02 (1.01–1.03), χ²=16, p<0.001) for patients with HFrEF (3-year mortality 41% v 30%) and HFpEF (37% v 30%) with similar trends for those who were considered not to have heart failure (0.3–5.0 μU/ml). The potential for an unexpected thyroid status was generally not an independent predictor in multivariable models.

Conclusions: The prevalence of thyroid dysfunction in patients referred with suspected heart failure is substantial. Patients with biochemical evidence of hypothyroidism may have a worse prognosis but these findings may reflect age and complex co-morbidity of this population.

THE WIDE WORLD OF CARDIOVASCULAR RESEARCH AND PRACTICE

P3620 | BEDSIDE
Device acceptance in ICD patients: shock anxiety, insomnia or both?
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Background: The degree to which cardiac patients adjust to life with an implantable cardioverter defibrillator (ICD) is largely influenced by psychosocial factors. “Device acceptance” refers to the psychological accommodation and understanding of the ICD and its associated benefits. However, little is known regarding the extent to which device acceptance is affected by other psychosocial factors associated with adjustment to the ICD. The potential for an unexpected ICD shock has been shown to be a particular focus of anxiety, and this population is also vulnerable to developing insomnia due to the increased risk of their device firing at night.

Purpose: The present study sought to investigate the dual impact of shock anxiety and insomnia on device acceptance in a sample of cardiac patients implanted with an ICD.

Methods: A cross-sectional design was employed examining symptoms of shock anxiety, insomnia and device acceptance in a sample of 256 patients living with an implantable cardioverter defibrillator (82% male; mean age 67.78 years, SD = 12.18). The majority of patients had a history of coronary artery disease, and ischaemic heart disease was the most common pathology leading to ICD implantation. The Florida Shock Anxiety Survey (FASAS) and Patient Acceptance Survey (FPAS) (Burns et al., 2005) were used to measure shock anxiety and device acceptance respectively. The Sleep Condition Indicator (SCI) questionnaire (Espie et al., 2005) was used to measure sleep quality, and allowed evaluation of symptoms against DSM-5 criteria for insomnia disorder (ID).

Results: 13.2% (34/257) of ICD patients screened positively for insomnia. Although no gender differences were observed for sleep disturbance (p=0.7), women were significantly more likely than men to report device-related shock anxiety (p=0.015). After controlling for age and gender in a hierarchical regression, both shock anxiety (beta=0.209, p<0.001) and insomnia (beta=0.202, p<0.002) independently predicted device acceptance in this sample.

Conclusions: Both shock anxiety and sleep disturbance adversely impact the adjustment of cardiac patients living with an ICD. Assessment for shock anxiety and insomnia may identify patients at risk of poorer device acceptance. Where possible, programmes of care should encompass cardiac rehabilitation and/or proven behavioural treatments for shock anxiety and insomnia (e.g. cognitive-behavioural therapy).

P3621 | BEDSIDE
Psychosocial adjustment of patients living with an internal cardioverter defibrillator
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Background: The implantable cardioverter defibrillator (ICD) is a cornerstone of the treatment for life-threatening arrhythmias and prevention of sudden cardiac death. The proportion of ICD recipients reporting device anxiety and/or depression, which has the potential to affect overall psycho social adjustment.

Purpose: To explore the association of anxiety and depression with psycho-social adjustment of patients living with an ICD.

Methods: A cross-sectional correlation study was conducted among participants recruited from Australia and the United States. Eligibility criteria were: ICD insertion >12 month; English speaking; not severely cognitively impaired; and not awaiting urgent heart transplant. A composite variable was developed, from three validated instruments, to capture all participants who reported symptoms of anxiety and/or depression (anxious/depressed). Patients who were anxious/depressed, and those without symptoms, were compared on: clinical and sociodemographic variables; concerns about living with an ICD (ICD-C); perception of control (Control Attitudes Scale: CAS-R) related to heart disease; social support (Multidimensional Scale of Perceived Social Support: MSPSS); and cognitive function (Montreal Cognitive Assessment: MoCA). Mean, standard deviation (SD); median, interquartile range (IQR); or proportions were compared using t-tests, Mann Whitney U test, or Chi square as appropriate.

Results: In total 213 patients (mean age 62, SD13 years; 74% male) were included; 99 (47%) were classified anxious/depressed. Anxious/depressed patients were younger (58 SD±14 years vs 65 SD±12 years, p<0.01) and more likely to rate their overall health as poor (31% vs 10%, p<0.01). They were more worried about living with their ICD on 19 out of 20 ICD-C items and had higher ICD-C scores (19, IQR 6–30 vs 6, IQR 2–12, p<0.01); felt less control over their heart disease (CAS-R: 31, IQR 26–35 vs 33, IQR 29–38, p<0.01); reported more problems with self-care (19% vs 5%, p<0.01) performing usual activities (62% vs 36%, p<0.01); and lower social support (MSPSS: 71, IQR 50–81 vs 82, IQR 70–84, p<0.01). Anxious/depressed patients were more likely to indicate their device was implanted due to a high risk of sudden cardiac arrest (39% vs 24%, p<0.03) and to think about end of life (42% vs 22%, p<0.01).

Conclusion: Nearly one in two ICD recipients reported symptoms of anxiety or depression and these common psychological issues were associated with poorer overall health and higher levels of concern about living with the ICD. Cognitive behavioural strategies to address worries, build coping strategies and reduce feelings of helplessness may be an important first step towards improving the psycho-social adjustment of this patient group.

Acknowledgement/Funding: ACU Faculty Research Grant

P3622 | BEDSIDE
Post-discharge text messaging intervention improved clinical outcomes in patients with heart failure
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Background: Self-care improves heart failure (HF) outcome after discharge. The effectiveness of short message service (SMS) in improving HF self-care and clinical outcome is still to be established.

Methods: Patients who HF were included and equally randomized into 3 groups. The SMS group regularly received batched SMS education and reminders, while the phone group received structured telephones on HF self-care. Contents included: understanding HF, medication, weight monitoring, exercises, HF diet, etc.
P3623 | BEDSIDE
Return to work after endomyocardial biopsy in patients with suspected viral myocarditis
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Introduction: In younger patients systolic heart failure is predominantly caused by viral myocarditis. A reliable classification of myocarditis requires endomyocardial catheter biopsy (EMB) for histological, immunohistochemical and molecular biological- virological examination. To date, no recommendations for physical activity resulting from the work (RTW) after EMB availability are available. We aimed to evaluate biopic findings as additional predictors for RTW at discharge after CR.

Patients and methods: In 1.153 patients (48.9±12.4 years, 66.2% male), who were hospitalized due to systolic left heart failure between 2005-2012, an EMB was performed. Routine clinical and laboratory data, sociodemographic parameters, medication, noninvasive (2D echo, exercise ECG) as well invasive cardiac informations (right and left cardiac catheterization) were registered. EMB data and clinical records were merged with RTW data from the German statutory pension insurance program (work intensity, unemployment days, retirement) and analyzed for prognostic ability by Cox regression.

Results: A total of 391 patients had a complete data set of hospital and insurance information and gave a positive consent for data query. Active myocarditis was diagnosed in 2.6%, borderline myocarditis in 23.5% and dilative cardiomyopathy in 26.1%. In 47.8% no biopathic pathways were observed. Three quarters of patients were virus-positive (56.7% parovirus B19, other or mixed infection 17.9%). Mean invasive LVEF was 44.8±18.6% (LVEF ≤ 45% in 46.4%), RTW was achieved after a mean interval of 168.8±347.7 days in 220 patients (after 6, 12 and 24 months in the other third). The model results revealed no additional impact for RTW probability. Thus, socio-medical evaluation interventions based primarily on clinical and functional parameters.

Conclusion: We identified 4 groups of CAD-patients sharing similar patterns of IP. Our result corresponds largely to recent findings in patients with COPD and chronic muscle disease thereby indicating parallels of IP in patients with different kinds of chronic illness. Further research is needed to explore if stratification of patients according patterns of IP can help to inform targeted psychosomatic interventions.

P3625 | BENCH
Anti tumor necrosis factor alpha treatment restores endothelial function and improves outcome in rheumatoid arthritis mice
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Background: Chronic inflammatory diseases such as rheumatoid arthritis (RA) are not only associated with pain and joint destruction, but also with increased cardiovascular risk beyond that of classical risk factors. Rheumatoid arthritis patients independent on all other risk factors are exposed to a high risk of cardiovascular complications. In patients with RA, endothelium dependent responses are impaired even in the absence or in presence of only few CV risk factors suggesting that RA involves alteration in endothelium. However, RA molecular mechanisms causing endothelial dysfunction are poorly understood.

Purpose: The aim of the present study is to confirm the presence of endothelial dysfunction in two animal transgenic models of RA and to address the molecular mechanisms which lead to the development of the disease. Anti Tumor Necrosis Factor alpha treatment was used to assess the disease progression and potential to restore endothelial function in the rheumatoid arthritis impaired endothelium.

Methods: Human Tumor Necrosis Factor (TNF) alpha transgenic mice (Line TG 3647 and Line TG 197) at the age of 4 and 8 weeks, develop a stronger and milder form of arthritis, respectively. To assess the disease progression, endothelial function on TNF alpha transgenic mice was studied for both transgenic lines at different time points. Functional studies were performed in aortc rings using organ chamber experiments; responses to acetylcholine were recorded during submaximal contraction to norepinephrine and relaxations were expressed as percentages of precontraction to norepinephrine. Once when the exact time point of endothelial dysfunction was determined, a week posterior of detected endothelial dysfunction, animals were randomly assigned to receive either anti TNF alpha antibody (Remicade) or placebo for 4 weeks. Agarose Activity was measured in plasma of wild types and transgenic mice lines.

Results: Acetylcholine induced vasorelaxation was impaired at week 8 and 12 for lines 197 and 3647, respectively. Chronic Remicade treatment improved vasorelaxation in both lines ex vivo, which was paralleled with the increased arginine activity in both RA transgenic mice lines.

Conclusion: We demonstrated a reduction in nitric oxide (NO) bioavailability through the impaired vasorelaxation in isolated aortic rings of RA mice. Chronic...
anti TNF alpha treatment improved endothelial function and increase arginase activity in serum of RA mice. This highlights the importance of NO mediated changes in inflammatory conditions outside of the classical cardiovascular environment.

Acknowledgement/Funding: Swiss National Science Foundation (SNF)

P3626 | BEDSIDE
Cardiovascular outcomes in renal transplant recipients: feasibility and clinical role of 2d speckle tracking to assess myocardial function

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Introduction: Left ventricular (LV) function is normally improved after renal transplant, however cardiovascular mortality remains elevated. Despite the recognition about the positive influence of a regular and moderate physical activity on myocardial function after a period of a supervised programme, few quantitative data obtained by 2D echocardiography (2DE) and 2D Speckle Tracking echocardiography (2DSTE) are nowadays available about the specific role and effects of the physical activity on renal transplant recipients (RTR).

Purpose: The study aims to evaluate the feasibility and eventual role of the deformation parameters in them.

Methods: From a large cohort of renal transplant recipients (RTR) submitted to a supervised exercise as prescription program, 10 subjects regularly trained, have been studied since January 2013. At the beginning of the study, after 6 months of exercise, they underwent an echo evaluation, Cardiopulmonary Test (CPT), and stress test for the lower and upper limbs. The LV function study was completed with the analysis of Lo Strain calculated by a dedicated software for the speckle tracking Strain analysis, at sixth month.

Results: All the echocardiographic parameters were normal during the protocol. The EF increased significantly (from 62.7±4.0 to 67.2±2.3 with p<0.05) with associated increase of the anaerobic threshold (15.3±6.8 to 20.5±1.1 p<0.05). Particularly the Global Longitudinal Strain (GLS) values was within the normal range (−19.2% ±5.1) maintaining the physiological gradient from the basal (−13.2±4.1; t, particularly the Global Longitudinal Strain (GLS) values was within the normal range

Conclusions: The assessment of LV Chamber mechanics by 2D Speckle Tracking echocardiography (2DSTE) can be effectively used to confirm the presence of myocardial strain in RTR submitted to a physical training.

P3628 | BEDSIDE
Long-term outcomes following acute coronary syndrome: results of the five-year follow up


Objective: To evaluate long-term adherence to the therapy, clinical outcomes and mortality after acute coronary syndrome (ACS).

Data and methodology: The study is based on 255 patients under the age of 65 who were admitted to a regional vascular center following acute coronary syndrome. The average age of the study population was 52.3±7.04 years. Male patients dominated in the group and comprised 203 patients, or 80.2%. After five years adherence to the therapy, long-term outcomes and mortality rate were assessed.

Results: In the study group 46.3% of the patients were diagnosed with Q wave myocardial infarction (MI), 22.8% - non-Q-MI, 29.8% - unstable angina, and in 47.3% of the patients urgent myocardial reperfusion was carried out. After five years of observation information on 126 patients was collected and analyzed. The results reveal that 71.9% of the patients have continued ambulatory monitoring, and 49% of them have been followed up by a cardiologist, and 22.9% - by a general practitioner. Evaluation of results related to adherence to medication shows that 80.2% of the patients have continued taking Aspirin, 12.5% - Clopidogrel, 66.7% - ACE-inhibitors or Angiotensin-receptor blockers, 64.6% - Statins, 68.8% - Beta blockers, and 18.8% - Nitrates. The target blood pressure has been achieved in 77.9% of the cases, and heart rate in 35.4% of the cases. Furthermore, 49% of the patients have been unaware of their cholesterol level, 3.3% have not tested cholesterol level after hospital discharge, and only 12.5% of the patients have achieved their target cholesterol level. The analysis of the long-term outcomes following the ACS also shows that significant number of patients had non-fatal atherothrombotic events: 10.4% of the patients had myocardial infarction, 3.1% -stroke, and 1% - thromboembolic events. More than one-third of the patients had no revascularization, 29.2% PCI, 10.4% - CABG. However, 59.4% of the patients currently have symptoms of stable angina, and 53.1% - chronic cardiac failure. Five-year mortality rate reached 23.8% (30 patients), of which in 30% of the cases (9 patients) the death was due to AMI or stroke, in 6.7% - due to other coronary, and 28% in control group. Average decrease in Hb in study group is 0.9 and experiment group is 1.2 g/dl. 6% of the study group and 28% in control group. Increase in Lymphocyte increase in study group was +28% in supplement group and reduces the ICU and Hospital stay in electric cardiac surgery.

Conclusions: Preoperative L-Glutamine supplementation decreases the risk of infection and reduces the ICU and Hospital stay in electric cardiac surgery.

P3629 | BENCH
Continuous and interval aerobic training associated with L-arginine supplementation improve exercise capacity and hemodynamic parameters


Background: Chronic heart failure (CHF) is characterized by the incapacity of the heart to supply sufficient myocardial oxygen demand. Continuous aerobic exercise training has been shown to improve exercise capacity in CHF patients. Consequently, endothelial dysfunction, exercise intolerance and early fatigue can be observed. Aerobic exercise training is a well-known non-pharmacological intervention to CHF treatment. However, the efficacy of high intensity interval training,
well as the supplementation of L-Arginine (Arg) to improve the treatment outcomes, remains not well elucidated.

**Purpose:** To evaluate the effect of 8 weeks of Arg supplementation associated to aerobic continuous training (ACT) or aerobic interval training (AIT) on hemodynamic parameters and exercise test capacity (ETC) in CHF rats.

**Methods:** Thirty-eight CHF male Wistar rats post myocardial infarction (MI) surgery were randomly assigned into six groups: Sedentary (SED, n=6); SED+Arg (n=7); ACT (n=8); ACT+Arg (n=5); AIT (n=7); AIT+Arg (n=5). The protocol began six weeks after MI and it was conducted over eight weeks. Supplemented rats received L-Arginine (1g/kg) by gavage twice seven times a week. Treadmill exercise training was performed five times (week: 7x 3min at 85% of maximum ETC velocity with 4-min active recovery at 60% of maximum ETC velocity; and ACT: 60% maximum ETC velocity until reach the same distance of AIT). MI was induced with intracoronary injection of 85% stenosis.

**Results:** Myocardial infarct area was similar in all groups 41±2%, p>0.05. Left ventricular end-diastolic pressure (LVEDP) was higher in the SED and TAC group compared to AIT-Arg, and SED vs. AIT (p<0.05). Left ventricular systolic pressure was lower in the sedentary groups compared to AIT-Arg (p<0.05). All trained groups showed higher distance and time of ETC values post intervention compared to sedentary groups (p<0.001), however, the L-Arginine supplementation was not able to improve ETC parameters compared to training only.

**Conclusions:** Both, interval and continuous aerobic training were able to enhance ETC and hemodynamic parameters. In accordance with combination of AIT and L-Arginine supplementation, suggesting a synergistic effect of interventions.

**Acknowledgement/Funding:** CAPES

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**P3630 | BEDSIDE**

**Differences in symptoms in relation to myocardial infarction type**

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In myocardial infarction (MI) rapid diagnosis and treatment is crucial for prognosis. Previous research has found that symptom presentation influence pre hospital delay times but studies about differences in MI symptoms between patients with ST-elevation myocardial infarction (STEMI) and non-ST-elevation myocardial infarction (NSTEMI) are sparse and inconclusive. To enhance the understanding of symptom presentation in relation to MI type, we aimed to describe symptoms in relation to MI type and to find predictors of STEMI versus NSTEMI in patients with MI.

**Methods:** Patients with MI (n=694) from the SimTime Study were included. SymTime was a multicentre cross-sectional study of symptoms and actions in the prehospital phase of MI and data were collected using a previously validated questionnaire administered to MI patients within 24 h of admission to hospital.

**Results:** Patients with STEMI were younger, more often men and smokers. Patients with STEMI were more likely to have a history of hypertension, MI and stroke. Chest pain was the most common symptom in both groups. Pain, discomfort, or pressure located in the jaw or teeth, vertigo/pre-syncope, cold sweat and nausea/vomiting were significantly more frequent in patients with STEMI (Table 1). In a multivariate logistic regression model patients with STEMI were more likely to present with cold sweat (OR 4.13, 95% CI 2.71–6.29) jaw pain (OR 2.14, 95% CI 1.30–3.54), nervousness (OR 0.35, 95% CI 0.15–0.84), anxiety (OR 0.54, 95% CI 0.36–0.83) and nausea/vomiting (OR 0.54, 95% CI 0.32–0.92) compared to patients with NSTEMI.

**Table 1. Symptoms in MI**

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Patients with STEMI</th>
<th>Patients with NSTEMI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain location, n (%)</td>
<td>472 (88.7)</td>
<td>141 (87.0)</td>
<td>0.60</td>
</tr>
<tr>
<td>Chest or throat</td>
<td>115 (21.6)</td>
<td>26 (16.0)</td>
<td>0.23</td>
</tr>
<tr>
<td>Jaw or teeth</td>
<td>10 (1.8)</td>
<td>17 (10.5)</td>
<td>0.015</td>
</tr>
<tr>
<td>Back</td>
<td>85 (15.0)</td>
<td>32 (19.8)</td>
<td>0.26</td>
</tr>
<tr>
<td>Stomach</td>
<td>43 (8.1)</td>
<td>18 (11.0)</td>
<td>0.64</td>
</tr>
<tr>
<td>Shoulders</td>
<td>120 (21.2)</td>
<td>42 (25.9)</td>
<td>0.06</td>
</tr>
<tr>
<td>Arms/hands</td>
<td>256 (46.6)</td>
<td>85 (52.5)</td>
<td>0.48</td>
</tr>
</tbody>
</table>

**Other symptoms, n (%)**

| Numbnesses in arms/hands | 157 (29.5) | 50 (30.9) | 0.74 |
| Tinnitus                | 139 (25.5) | 52 (32.0) | 0.45 |
| Weakness                | 211 (39.7) | 60 (37.0) | 0.55 |
| Weakness of breath      | 171 (31.2) | 53 (32.7) | 0.89 |
| Vertigo/cold sweat      | 137 (25.2) | 56 (34.6) | 0.015 |
| Nausea/vomiting         | 179 (33.6) | 28 (17.3) | <0.001 |
| Cold sweat              | 329 (61.8) | 44 (27.2) | <0.001 |
| Annoyance               | 63 (11.8)  | 28 (17.3) | 0.07  |
| Fear                    | 108 (20.3) | 42 (25.9) | 0.13  |
| General sick feeling    | 83 (15.6)  | 21 (13.0) | 0.41  |
| Other                   | 37 (7.0)   | 13 (8.0)  | 0.64  |

**Conclusion:** Patients with STEMI differed significantly from those with NSTEMI regarding symptom presentation. This knowledge is important for health care personnel to recognize symptoms alarming for STEMI when evaluating patients with MI symptoms.

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**P3631 | BEDSIDE**

**Job distress and satisfaction among young cardiologists in Italy. Insights from the IANUS survey**

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**Background:** Since physician burn-out adversely affects quality of care, prevention of job-related distress, a life-long priority should start from early career stages. To assess prevalence of job distress and protective factors among young cardiologists (YC), we analysed data from the nationwide IANUS survey (IANUS cardiologists Undetected distress Study).

**Results:** The YC sample was representative of the 1200 cardiologists of the same age range registered in the ANMCO database for age, sex, geographic area of work. Mean YC age was 35±4 years, in cardiology practice average aged 8±4, 50% were women; 62% held a permanent work contract. Main area of activity was general cardiology, second was coronary care or heart failure unit for 49%, outpatient clinic/diagnostic area for 20% and interventional cardiology for 31%. When compared to the older cohort (mean age 55±7, years in cardiology practice average 16±4), 50% were women; 62% held a permanent work contract. Main area of activity was general cardiology, second was coronary care or heart failure unit for 49%, outpatient clinic/diagnostic area for 20% and interventional cardiology for 31%. Compared to the older cohort (mean age 55±7, women 23%), YC reported a similar prevalence of factors indicative of job strain (loss of enthusiasm (33% vs 37%), helplessness (36% vs 39%), work-life imbalance (34% vs 34%), frustration due to organizational problems (71% vs 71%) or lack of control over their work (36% vs 36%). Likewise comparable between YC and older responders were issues of emotional fatigue in dealing with chronically ill (21% vs 23%) end-stage patients (15% vs 20%) and feelings of personal vulnerability (17% vs 19%). No difference was found in the prevalence of relational difficulties defined as worries about malpractice suits (50% vs 47%), cynical feelings towards patients (11% vs 14%) and difficulties in recalibrating patients’ and caregivers’ expectations (31% vs 30%).

**Conclusions:** Within a generation lapse, although socio-demographic of Italy cardiologists has markedly shifted, job distress does not differ. The high prevalence among YC of distress factors connected to the burnout core constructs (loss of enthusiasm and cynicism, helplessness and personal vulnerability) markers of resilience when compared to older responders are particularly alarming and call for educational and organizational actions targeted to YC needs.

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**P3632 | BEDSIDE**

**Economic evaluation of sacubitril/valsartan for the treatment of heart failure with reduced ejection fraction**

St. Patyolas1, D. Farmakis2, G. Giamouzis3, M. Hatzikou4, G. Kourlaba5, I. Papoutsouma6, N. Maniadakis7

**Purpose:** To estimate the cost-effectiveness of sacubitril/valsartan (LCZ696) compared with enalapril for the treatment of patients who had heart failure with a reduced ejection fraction (HF/EF).

**Methods:** A two-stage Markov model has been produced with regression models used to predict events within the alive health state. Clinical outcomes have been extracted from the PARADIGM-HF study. Cost outcomes were evaluated over lifetime (30 years), discounted at 3.5% with 2015 as reference year from the perspective of the Greek health care payer. We have assumed a daily cost of activity of €50.40 and an annual cost of €3,860/€4,513 for hospitalization costs. Incremental cost-effectiveness ratios were calculated for the incremental cost of new drug (€1219). Incremental cost-effectiveness ratios were calculated for the incremental cost of new drug (€1219) and the threshold of cost-effectiveness was based on the gross domestic product (GDP) per capita that has been adopted. In accordance with this approach, an incremental cost per QALY gained lower than €16,451 was considered as highly cost-effective for the Greek setting.
and lower than €49,353 as cost-effective. One-way and probabilistic sensitivity analyses on clinical and economic data were performed.

**Results:** Sacubitril/valsartan was associated with an incremental cost per QALY gained of approximately €15,992 and an incremental cost per LYG of €13,107. Moreover, it was predicted to improve patient survival by 0.75 years and lead to a 0.61 additional quality-adjusted life years and 5.83% fewer hospitalisations (0.10/year absolute reduction; 7.67% reduction in discounted lifetime hospitalisation costs). The results were robust in probabilistic analysis and one-way sensitivity analyses.

**Conclusions:** The study suggested that sacubitril/valsartan was superior to enalapril in long-term survival and quality of life but also proved to be a cost-effective choice for the treatment of patients with heart failure and reduced ejection fraction in the Greek setting assuming a low willingness-to-pay threshold.

**Acknowledgement/Funding:** This study was funded by Novartis (Hellas) S.A.G.I.

### P3633 | BEDSIDE

**Circulating long-chain ceramides and dihydroyceramides predict outcomes in acute coronary syndromes**

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**Background:** Acute coronary syndromes (ACS) cause much morbidity and mortality. Ceramides are non-cholesterol (NC) lipids implicated in atherosclerosis and cardiomyocyte death.

**Purpose:** We quantified 68 ceramide species in ACS patients to assess their prediction of 12-month major adverse cardiovascular and cerebrovascular events (MACCE).

**Methods:** We performed targeted profiling of ceramides (Cer) and dihydroyceramides (DHCer), using hydrophilic interaction-liquid chromatography tandem mass spectrometry in plasma from ACS patients (n=349). The topmost predictive species were identified using a statistically weighted voting analysis.

**Results:** A signature of 7 Cers and 4 DHCers (table 1) predicted MACCE (composite P=8.6×10^{-10}) with greater confidence than the GRACE risk score (P=0.003). In a 4-country validation cohort (n=474), Cer(d18:1/20:4, Cer(d18:1/28:0). DHCer(d18:0:24:0) and DHCer(d18:0:24:1/152) remained independently predictive (P=6.4×10^{-7}).

### Table 1. Predictive ceramides

<table>
<thead>
<tr>
<th>Ceramide species</th>
<th>12-month MACCE no</th>
<th>12-month MACCE adjusted mean ceramide value (pmol/mL)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cer d18:1/16:0</td>
<td>36.9</td>
<td>19.51</td>
<td>5×10^{-3}</td>
</tr>
<tr>
<td>Cer d18:0/22:0</td>
<td>14.43</td>
<td>6.24</td>
<td>5×10^{-3}</td>
</tr>
<tr>
<td>Cer d18:1/18:1 (9Z)</td>
<td>0.42</td>
<td>0.12</td>
<td>0.006</td>
</tr>
<tr>
<td>Cer d18:20:0</td>
<td>10.15</td>
<td>4.65</td>
<td>8×10^{-3}</td>
</tr>
<tr>
<td>Cer d18:0:24:0</td>
<td>0.54</td>
<td>0.18</td>
<td>0.003</td>
</tr>
<tr>
<td>Cer d22:0:22:0</td>
<td>52.35</td>
<td>24.28</td>
<td>0.006</td>
</tr>
<tr>
<td>Cer d18:1/22:1</td>
<td>2.8</td>
<td>1.09</td>
<td>6×10^{-3}</td>
</tr>
<tr>
<td>Cer d18:24:0</td>
<td>236.38</td>
<td>93.23</td>
<td>0.018</td>
</tr>
<tr>
<td>Cer d18:24:1 (152)</td>
<td>98.79</td>
<td>39.1</td>
<td>1×10^{-4}</td>
</tr>
<tr>
<td>Cer d18:26:0</td>
<td>1.5</td>
<td>0.59</td>
<td>0.001</td>
</tr>
<tr>
<td>Cer d18:26:1 (172)</td>
<td>0.7</td>
<td>0.23</td>
<td>6×10^{-3}</td>
</tr>
<tr>
<td>DHCer d18:0:16:0</td>
<td>1.58</td>
<td>0.61</td>
<td>3×10^{-4}</td>
</tr>
<tr>
<td>DHCer d18:0:22:0</td>
<td>6.96</td>
<td>2.33</td>
<td>0.004</td>
</tr>
<tr>
<td>DHCer d20:0:24:0</td>
<td>9.9</td>
<td>4.19</td>
<td>6×10^{-3}</td>
</tr>
<tr>
<td>DHCer d24:0:24:1 (152)</td>
<td>15.03</td>
<td>5.49</td>
<td>1×10^{-4}</td>
</tr>
</tbody>
</table>

**MACCE** = major adverse cardiovascular or cerebrovascular event; **FDR** = false discovery rate.

**Conclusion:** Circulating long-chain ceramides and dihydroyceramides predict MACCE in ACS patients, highlighting the prognostic potential of NC lipids.

**Acknowledgement/Funding:** National Medical Research Council, Singapore

### P3634 | BEDSIDE

**Increased recurrent coronary heart disease and mortality risk among intensive medically managed patients following myocardial infarction**

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**Background:** Among US adult Medicare beneficiaries, rehospitalisation following myocardial infarction (MI) is common. The effect of statins in recurrent MI patients receiving intensive medical management is unknown.

**Methods:** We performed an administrative claims-based population-based study on Medicare fee-for-service beneficiaries from 2007 to 2011. MIs were defined by a hospitalisation with an ICD-9 discharge diagnosis code (ICD-9) of 410.xx (except 410.x2) in the primary discharge diagnosis position. MI patients were matched 1:2 by age to a random sample of adults who had Medicare health insurance coverage in the same calendar year (n=47,924). Both groups of patients followed through administrative claims and the incidence of MI, CHD events (recurrent MI or coronary revascularisation) and all-cause mortality were identified using validated algorithms.

**Results:** The mean age of the MI patients receiving intensive medical management and population-based controls was 75 years. Over a mean follow-up of 2.8 years, there were 4,919 recurrent MIs, 8,200 CHD events and 12,971 deaths. For MI patients receiving intensive medical management and population-based controls, the incidence per 1,000 person-years was 52.5 (95% CI 50.7, 54.4) and 12.8 (95% CI 12.2, 13.4) for MI, respectively; 96.7 (94.2, 99.4) and 21.2 (20.4, 21.9) for CHD events, respectively; and 78.8 (76.7, 81.0) and 56.8 (55.6, 58.1) for all-cause mortality, respectively. After multivariable adjustment for demographics and co-morbid conditions, the hazard ratio comparing patients receiving intensive medical management to age-calendar year matched population controls was 3.25 (95% CI 3.07, 3.46) for MI, 3.67 (95% CI 3.54, 3.84) for CHD events, and 1.20 (95% CI 1.16, 1.25) for all-cause mortality.

**Conclusion:** Despite intensive medical management with high intensity statins, renin-angiotensin system inhibitors, beta-blockers and antplatelet agents, substantial residual risk remains present for individuals following MI.

**Acknowledgement/Funding:** Amgen, Inc

### P3635 | BEDSIDE

**The effect of statins in erectile dysfunction**

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**Introduction:** The term erectile dysfunction (ED), which replaced the emotive word “impotence”, is the inability to start and maintain an erection sufficient to achieve sexual intercourse. The etiology of this condition is multifactorial but it is usually attributed to vascular lesions caused by endothelial dysfunction.

**Purpose:** This study aims to investigate the relationship of erectile dysfunction with dyslipidemia and the possible impact of statins on erectile dysfunction (not receiving phosphodiesterase inhibitors).

**Methods:** The study included 100 male patients (aged 40-70 years) with unique risk factor dyslipidemia (none of them was receiving lipid-lowering treatment) and erectile dysfunction. The diagnosis of erectile dysfunction and its extent were assessed using the international questionnaire erectile function (IIEF). The lowest 10-20% of the international questionnaire indicates significant erectile dysfunction. Total cholesterol (CHOL), low (LDL) and high (HDL) density lipoproteins and triglycerides (TRG) were assessed in all participants. The study group was divided in two subgroups each consisting of 50 patients. In the first subgroup patients received a statin (atorvastatin) while the second subgroup received no treatment (control group). All the participants were re-examined using the same processes (completion questionnaire IIEF-determination in blood levels of CHOL, LDL, HDL, TRG) after three months.

**Results:** The results of the study demonstrated at the following Table 1

<table>
<thead>
<tr>
<th>Table 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before treatment</td>
</tr>
<tr>
<td>After treatment</td>
</tr>
</tbody>
</table>

*Mean (average) score IIEF (International Index of Erectile Dysfunction) – p<0.05.

**Patients receiving lipid-lowering therapy for 3 months significantly improved both lipid profile and ED.**

**Conclusions:** Patients receiving lipid-lowering therapy for 3 months significantly improved both lipid profile and erectile function. This study demonstrates that positive effects may be achieved with statins in patients with ED.
loss interventions have been shown to decrease circulating Angptl2 levels in over-weight subjects. Angptl2 response to bariatric surgery-induced weight loss in severe obesity is unknown.

**Purpose:** To assess the impact of the biliopancreatic diversion with duodenal switch (BPD-DS) bariatric surgery on plasma Angptl2 levels before, and in the acute (day 1 and 5) and late post-operative (6 and 12 months) phases.

**Methods:** A total of 73 severe obese patients (age, 41.2±10.9 years; BMI, 49.8±7.1 kg/m²) underwent BPD-DS. Plasma metabolic parameters and anthropometric measures were obtained.

**Results:** A significant rise in Angptl2 levels, fasting plasma glucose (FPG), plasma insulin, and IL-6 levels was observed early post-operatively (day 1) followed by a progressive decline at day 5 (p < 0.01). Beside weight loss following BPD-DS at 6 months (BMI, -15.3±3.4 kg/m²; visceral adipose tissue (AT), -90 356 ±50 cm³) and at 12 months (BMI, -17.2±4.7 kg/m²; visceral AT, 1347.0±673.8 cm³) (p < 0.0001), Angptl2 levels were significantly reduced at 12-month follow-up (14.0±3.9 vs. 11.5±4.7 ng/ml, p < 0.001), and overall survival increased (figure A; Log-rank p<0.001; HR=0.5 0.85 CI 0.36–0.89, p<0.001). BMI per kg/m² increase was associated with post-operative survival. Obese had better survival than NW and the combination NW/OW. These associations remained significant after adjustment (table).

**Conclusion:** BMI increase had no effect on the survival (figure B) in some subgroups: younger <70 years, diabetics, hypertensive etiology, preserved renal function and those in whom protein intake ≥1.0 g/day. BMI paradox was significant according to sex, nyha class, Na-ProBNP (median=1485) and the combination therapy. The subgroups analysis was adjusted as the global model. No subgroup of patients had a negative association with BMI.

**Acknowledgement/Funding:** Quebec Heart and Lung Foundation.

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**P3637 | BEDSIDE**

Increased basal coronary blood flow and obesity: what are the characteristics of patients with coronary hyperflow?

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**Background:** A decreased coronary flow reserve (CFR) in normal coronary arteries is driven by two different mechanisms: coronary microvascular dysfunction (CMD), and increased basal coronary blood flow.

**Purpose:** The purpose of this study was to evaluate the characteristics of patients exhibiting increased basal coronary blood flow.

**Methods:** In 134 consecutive patients with angiographically normal coronary arteries, CFR and a novel index of microcirculatory resistance (IMR) were simultaneously measured using a pressure/temperature-sensing coronary wire. Eighty patients with lower CFR and a lower IMR, suggesting an increased basal coronary flow, were assigned to group A. Twenty-five patients with a lower CFR and a lower IMR, suggesting CMD, were assigned to group B.

**Results:** (1) The mean blood flow transit time in the coronary arteries was significantly shorter in group A than in group B (0.37 vs. 0.70 s, P < 0.001). (2) The mean blood flow velocity was significantly higher in group A than in group B (8.57±3.20 vs. 5.17±2.40 cm/s, P < 0.001). (3) The body mass index was significantly higher in group A than in group B (24.2 vs. 22.1, P < 0.05).

**Conclusions:** Diabetic patients reportedly exhibit increased basal coronary flow, since they have a higher oxygen demand as a result of impaired cellular metabolism. Our findings suggest that obesity might also be accompanied by coronary hyperflow.
The effect of moderate wine intake on carotid atherosclerosis in type 2 diabetes: a 2-year intervention study

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Background: Despite observations of an inverse association between moderate alcohol consumption and cardiovascular mortality, evidence for the effects of alcohol consumption on atherosclerosis in randomized studies is lacking. 

Purpose: To assess the effect of initiating moderate alcohol intake on progression of carotid atherosclerosis in alcohol-abstaining adults with well-controlled T2DM.

Methods: In the 2-year CASCADE (Cardiovascular Drunk Alcohol & Ethanol) trial, patients were randomly assigned to 150mL of mineral-water, white wine, or red wine for 2 years. Wines and water were provided. All groups followed a Mediterranean-diet without caloric restriction. Carotid-total-plaque-volume (carotid-TPV) and vessel-wall-volume (VWW), were assessed using three-dimensional-ultrasound at baseline and after 2-years.

Results: Two-year repeated, high-quality, paired carotid images were available from 174 participants (age = 59 years; 67% men; HbA1C = 6.6%). Baseline detectable plaque was found in 55% of the participants. Mean TPV did not change significantly in the entire cohort (mean change = -1.3 mm³±17.6), or in individual intervention groups (red wine: -1.3±17.6, white wine: 1.1±16.9, mineral water: -1.3±17.7, p>0.05). However, in a post-hoc analysis of the 78 (45%) patients who had detectable plaque at baseline, amongst participants in the top tertile of baseline carotid TPV levels, wine consumption was associated with a greater reduction in TPV (white wine: -20.4 mm³ vs. water: -5.5 mm³, p=0.002, compared to baseline).

Data on VWW were available from 160 participants. After 2 years, no significant changes were observed in VWW (619.7mm³ vs. 610.9mm³ after 2-years, p=0.09) with no differences between intervention groups (p>0.05). Two-year changes in systolic-blood-pressure remained an independent predictor of greater regression in VWW (beta=-0.187, p=0.029) adjusting for intervention-group, baseline VWW, age, statin use and 2-year changes in BMI.

Conclusions: In a 2-year randomized study we were unable to detect a significant effect of wine consumption on carotid plaque volume or vessel wall volume in the entire group. The weak signal of greater TPV reduction by wine in those patients with highest baseline plaque volume should be further evaluated in larger randomized studies.

Acknowledgement/Funding: European Foundation for the Study of Diabetes EFSD

FIGHTING AGAINST DIABETES EPIDEMIC

P3641 | BEDSIDE

Angiopoietin-like 2 is associated with increased risk of death in diabetic patients

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Introduction: High serum angiopoietin-like 2 (Angpt2) concentration is an independent risk factor for developing diabetes (T2DM) and is associated with insulin resistance and atherosclerosis. In this work we have examined the impact of serum Angpt2 on improving risk stratification in patients with T2DM.

Methods: A prospective monocentric cohort of consecutive French T2DM patients (SURDIAGENE: total of 1535 T2DM patients (58% men), aged of 64±11 years) was followed up for a median of 6.0 years for death as primary end-point. Patients were stratified according to quartiles (Q) of Angpt2 concentrations at inclusion: Q1≤11.2, Q2=11.2–19.5, Q3=19.5–48 mmol/mL.

Results: During follow-up, 367 patients (4.5% person-year, PY) died, and 290 patients (3.2% PY) presented a MACE. Both survival and MACE-free survival rates were significantly different between Angpt2 quartiles (log-log rank: 82.12 p=0.0001, log-log rank: 65.14 p<0.0001, respectively for death and MACE). Patients with Angpt2 concentrations >19.5 mmol/L (Q4) had a significantly increased risk of death and MACE as compared to those with Angpt2≤19.5 mmol/L (Q1–3; HR: 2.44, 95% CI: 1.98–3.00, p<0.0001; HR: 2.43 95% CI: 1.92–3.06, p<0.0001 respectively) after adjustment for sex, age, and established CV risk factors. Using Angpt2 prediction of the risk of mortality as assessed by integrated discriminaiton testing, the model significantly improved (0.0062 p=0.0026) and correctly classified 73% of deaths.

Conclusion: In T2DM, serum Angpt2 concentrations were independently associated with death and MACE. Therefore, Angpt2 is a promising candidate biomarker for improving risk stratification in T2DM patients.

Figure 1. Long-term mortality (%) by HbA1c in patients with and without diabetes.

Conclusions: According to criteria based on HbA1c, 15% of the patients with heart failure had previously undetected and further 30% were at high risk for diabetes. In these patients long-term mortality deteriorated with increasing HbA1c. In contrast HbA1c did not predict mortality in patients with known diabetes. This emphasizes the importance of screening for dysglycaemia in populations with heart failure and favours the assumption that glucose control should be initiated early in the development of dysglycaemia.

Acknowledgement/Funding: PHRC-Poitiers 2004, PHRC-IR 2008; Association Française des Diabétiques; GEMMS Poitiers,Canadian Institutes of Health Research, Montreal Heart Instit.
Epicardial adipose tissue and cardiovascular disease in type 2 diabetes


Background: Epicardial adipose tissue (EAT) is the visceral fat of the heart. Observational studies indicate that patients with type 2 diabetes (T2D) have more and inflamed EAT compared to non-diabetic individuals, and EAT excretes biologically active substances that may provoke coronary atherosclerosis. Whether EAT promotes cardiovascular disease (CVD) in diabetic patients is currently unknown.

Purpose: To evaluate the amount of EAT and its association with the composite endpoint comprising incident CVD and all-cause mortality in patients with T2D, and to investigate the association between EAT and markers of low-grade inflammation and coronary artery calcium score (CAC).

Methods: The study was a prospective study including 200 T2D patients without known coronary artery disease (CAD). EAT was measured from baseline echocardiography as the echo-free space at the free wall of the right ventricle in the parasternal long axis view averaged from two cardiac cycles. Baseline EAT was available for 194 patients. Coronary artery calcium score (CAC) and markers of low-grade inflammation (IL-1α, IL-6, IL-8, TNFα and hsCRP) were measured at baseline. Follow-up was performed after 6.1 years (6th to 95th percentile 2.9–7.1) with no lost to follow-up. Descriptive data was expressed as means±SD. EAT was investigated both as a continuous variable and split in quartiles (the highest vs. the three lowest). Time-to-event data were analysed by Kaplan-Meier survival plots and Cox regression models. Adjustment was performed for traditional risk factors of CVD (sex, age, LDL-cholesterol, smoking, HbA1C, and systolic blood pressure).

Results: 152 (76%) were men, with an age average of 59±9 years, and known diabetes duration of 13±7 years. Mean EAT was 3.5±1.7 mm. EAT in the highest quartile was 5.6±1.2 mm vs. 2.4±0.9 mm EAT in the three lower quartile groups. Median CAC (IQR) was 107 (3;547). During the follow-up period 66 patients had experienced a CVD event or died. In Cox regression analysis EAT was not associated with the composite endpoint (HR 1.09, 95% CI 0.91–1.00) and all-cause mortality (HR 0.96, 95% CI 0.93–1.00).

Conclusion: Increased arterial stiffness, as measured by pulse pressure, normal range ABI and carotid artery distensibility coefficient, is independently related to increased risk of cardiovascular events and all-cause mortality in patients with type 2 diabetes.

Background: Increased arterial stiffness is a risk factor for cardiovascular events and all-cause mortality in the general population. The vasculature in patients with type 2 diabetes is characterized by increased arterial stiffness which is in turn related to microvascular complications. However, current literature on the relation between arterial stiffness and macrovascular disease in patients with type 2 diabetes is scarce.

Purpose: To evaluate the relationship between arterial stiffness and the risk of cardiovascular events and all-cause mortality in patients with type 2 diabetes.

Methods: Prospective cohort study of 1829 patients with type 2 diabetes included in the Second Manifestations of ARterial disease (SMART) cohort. Arterial stiffness was measured by brachial artery pulse pressure, normal range (≥0.9) ankle-brachial index (ABI) and carotid artery distension. Cox proportional-hazard models were used to evaluate the risk of arterial stiffness on cardiovascular events (composite of myocardial infarction, stroke and vascular mortality) and all-cause mortality. Analyses were adjusted for age, sex, diastolic blood pressure, renal function, non-HDL cholesterol, and current smoking.

Results: 338 new cardiovascular events and 390 deaths occurred during a median follow-up of 7.0 years (IQR 3.9–10.5). A 10 mmHg increase in pulse pressure was related to higher risk of cardiovascular events (HR 1.09, 95% CI 1.02–1.17) and all-cause mortality (HR 1.09, 95% CI 1.03–1.16). A 0.1 increase in ABI was related to a lower risk of vascular mortality (HR 0.81, 95% CI 0.68–0.96) and all-cause mortality (HR 0.85, 95% CI 0.75–0.96). Absolute carotid artery distension was not related to cardiovascular events (HR 1.02, 95% CI 0.91–1.15) and all-cause mortality (HR 0.99, 95% CI 0.89–1.10), but the derived carotid artery distensibility coefficient was related to a lower risk of vascular mortality (HR 0.95, 95% CI 0.91–1.00) and all-cause mortality (HR 0.96, 95% CI 0.93–1.00).

Conclusion: Increased arterial stiffness, as measured by pulse pressure, normal range ABI and carotid artery distensibility coefficient, is independently related to increased risk of cardiovascular events and all-cause mortality in patients with type 2 diabetes.

Plasma dehydroepiandrosterone levels are inversely associated with the risk of type 2 diabetes: the Rotterdam Study

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Background: Dehydroepiandrosterone (DHEA) is the most abundant circulating steroid hormone in healthy individuals. Other than its role as precursor of sex steroid hormones, recent data from animal studies show that DHEA modulates glucose utilization, implicating it in the development of diabetes. However, little data is available in humans on the role of DHEA in type 2 diabetes (T2D) and to date, no observational study has examined prospectively the association between DHEA and incident T2D.

Purpose: To assess the relationships between DHEA and its main derivatives dehydroepiandrosterone sulfate (DHEAS) and androstenedione, with the risk of incident T2D.

Methods: We measured serum levels of DHEA, DHEAS and androstenedione in 5533 subjects, participating in the prospective population-based Rotterdam Study. All hormone variables were naturally log-transformed to approximate normal distribution. Hazard ratios (HRs) and 95% Confidence Intervals (CI) were calculated using Cox proportional-hazard models.

Results: During a median follow-up time of 10.9 years, 688 incident T2D cases were identified. After adjusting for age, glucose, insulin, body mass index, lifestyle factors, prevalent cardiovascular diseases, serum total cholesterol, systolic blood pressure, and traditional risk factors, DHEA, DHEAS and androstenedione were inversely associated with the risk of incident T2D.

Conclusion: Plasma dehydroepiandrosterone levels are inversely associated with the risk of type 2 diabetes.
pressure and C-reactive protein, both DHEA (per 1 unit, HR = 0.76, 95% CI: 0.67–0.88) and DHEAS (per 1 unit, HR = 0.76, 95% CI: 0.67–0.88) were inversely associated with the risk of T2D in the total population. Further adjustment for sex hormones for each other, including estradiol and testosterone, did not materially affect the association between DHEA and incident T2D, but abolished the association between DHEAS and T2D. Androstenedione was not associated with the risk of T2D. Also, no sex-differences were observed for any of these associations.

Conclusions: This is the first prospective population-based cohort study to show that DHEA serum levels may be an independent marker for T2D. However, it is not clear whether medications or lifestyle factors that alter DHEA metabolism can be effectively used in prevention of T2D. Also, further investigation is needed to clarify the underlying mechanisms.

P3646 | BEDSIDE
Are the LDL-cholesterol targets from the ESC/EASD guidelines achievable in diabetic patients?
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Background: Dyslipidemia is a major risk factor for cardiovascular diseases, particularly in diabetic patients. Lowering LDL-cholesterol (LDL-C) prevents cardiovascular morbidity and mortality. The ESC/EASD guidelines for the management of dyslipidemia in Type 2 diabetes mellitus (T2DM) have been updated in 2013. Objectives of guidelines are difficult to reach in daily practice.

Purpose: Our study aimed to assess the proportion of T2DM patients reaching the ESC/EASD LDL-C targets: LDL-C target of <2.5 mmol/L (<1g/L) in patients with T2DM at high risk (without any other CV risk factor and free of target organ damage) and LDL-C targets (<1 mmol/L (<0.39g/L)) in T2DM patients with established cardiovascular disease (CVD) or with diabetic nephropathy.

Methods: We analyzed the prospective cohort of diabetic patients followed by the university center for study of diabetes and cardiovascular complications (CUDC cohort). The CUDC allows a multidisciplinary ambulatory care of diabetic patients on the same location. Our database included 5760 patients who attended our center at least once between September 2014 and August 2015. Each patient record is common to different specialists and computerized in a structured way. Clinical data, complications status and lipid profile were available for 3539 patients after excluding patients with triglycerides above 4g/l or missing data.

Results: As a whole, our cohort was at very high risk for cardiovascular diseases (data are expressed in median and quartiles): men 57.8%; age 58 y.o. (18–80); 3539 patients after excluding patients with triglycerides above 4g/L or missing data. Our database included 5760 patients who attended our center at least once between September 2014 and August 2015. Each patient record is common to different specialists and computerized in a structured way.

Clinical demographics

<table>
<thead>
<tr>
<th>TG/HDL-C ratio</th>
<th>Clinical demographics</th>
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<tr>
<td>First tertile</td>
<td>Second tertile</td>
</tr>
<tr>
<td>HDL-C (mg/dL)</td>
<td>23.6 ± 3.2</td>
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<tr>
<td>HDL-C (%)</td>
<td>7.3 ± 1.5</td>
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P3648 | BEDSIDE
Triglyceride to HDL-C ratio is associated with high risk coronary plaques characterized with coronary CT angiography in patients with suspected coronary artery disease

Background: For the prevention of future cardiovascular events, control of residual risks such as triglyceride rich lipoproteins and HDL-cholesterol is an emerging problem beyond LDL-cholesterol. Triglyceride to HDL-cholesterol ratio (TG/HDL ratio) has been reported to be a good maker for risk classification of cardiovascular diseases. Meanwhile, recent studies showed that lesion characteristics which evaluated with coronary CT angiography is associated with the incidence of acute coronary syndrome.

Purpose: We evaluated the association between the TG/HDL ratio and lesion characteristics evaluated with coronary CT angiography.

Methods: A total of 457 patients with suspected coronary artery diseases (mean age 64 years, 266 men) were evaluated by 64-slice CT. Coronary high risk plaques were defined as a plaque with all three component; low attenuation plaque (>50H.U.), positive remodeling (>1.05), and spotty calcification. Blood sampling was performed within one week before coronary CT angiography.

Results: The TG/HDL ratio was significantly associated with body mass index (r = 0.24, p < 0.01), waist circumference (r = 0.11, p < 0.02), HDL-C (r = 0.10, p < 0.04), uric acid (r = 0.13, p < 0.01), and ALT (r = 0.16, p < 0.01), but not with LDL-cholesterol (r = -0.08, p = 0.10). The ROC curve analysis demonstrated TG/HDL ratio had specificity 76% and sensitivity 38% at a cut-off value of 0.32 for discriminating patients with high risk plaque. When patients were divided into two groups according to cut-off value of TG/HDL ratio, the prevalence of calcified plaque, non-calcified plaques, coronary plaques with low attenuation plaque, positive remodeling, spotty calcification in the higher group were greater than those in the lower group (Figure). Of note, the difference in high risk plaque between two groups was significant (35.8% vs. 18.6%, p = 0.017). Multivariate logistic analysis revealed that the higher TG/HDL ratio was an independent predictor of high risk plaque (OR, 1.86; 95% CI, 1.07–3.24; p = 0.03), along with age > 65 years (OR, 2.60; 95% CI, 1.47–4.61; p < 0.001), diabetes mellitus (OR, 2.23; 95% CI, 1.30–3.83; p < 0.003) and smoking (OR, 2.27; 95% CI, 1.28–3.99; p = 0.005). However, the TG/HDL ratio was not associated with the presence of significant coronary stenosis after adjustment of conventional risk factors.

Conclusion: The TG/HDL ratio could be a good marker for risk stratification and therapeutic indicator for preventing cardiovascular events.
P3649 | BEDSIDE
Ethnic and regional variation in diabetes among Asian patients with heart failure
Methods: Quantitative data synthesis was performed using a random-effects model with weighted mean difference (WMD) and 95% confidence interval (CI) as summary statistics.
Results: In 30 studies (43 study arms) with 2953 participants a significant increase in plasma adiponectin levels was observed after statin therapy (WMD: 0.57, 95% CI: 0.35–0.79, p<0.004) (figure). In subgroup analysis, atorvas-
tatin, simvastatin, rosvastatin, pravastatin and pitavastatin were found to change plasma adiponectin concentrations by 0.70 μg/mL (95% CI: −0.26, 1.65), 0.50 μg/mL (95% CI: −0.44, 1.45), −0.70 μg/mL (95% CI: −1.08, −0.33), 0.62 μg/mL (95% CI: −0.12, 1.35), and 0.51 μg/mL (95% CI: 0.30, 0.72), respectively. With respect to duration of treatment, there was a significant increase in the subset of trials lasting ≥12 weeks (WMD: 0.88 μg/mL, 95% CI: 0.19, 1.57, p=0.012) but not in the subset of <12 weeks of duration (WMD: 0.18 μg/mL, 95% CI: −0.23, 0.59, p=0.390). Random-effects meta-regression suggested a significant association between statin-induced elevation of plasma adiponectin and changes in plasma low density lipoprotein cholesterol levels (slope: 0.04; 95% CI: 0.01, 0.06; p=0.002).

Conclusions: The meta-analysis showed a significant increase in plasma adiponectin levels following statin therapy. Although statins are known to increase the risk for new onset diabetes mellitus, our data suggest that the mechanism for this is unlikely to be due to a reduction in adiponectin expression.

P3651 | BEDSIDE
Sildenafil does not improve VO2max in subjects with diabetes mellitus despite augmenting non-invasively assessed central hemodynamics
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Background: Exercise capacity is reduced in people with diabetes mellitus (DM) but the pathophysiological mechanisms remain incompletely understood. We hypothesised that (1) pulmonary microangiopathy and resultant right ventricular dysfunction may contribute and that (2) Sildenafil will therefore improve central hemodynamics and maximal oxygen consumption (VO2max).
Methods: Forty subjects with DM and 20 matched controls (C) were recruited in a double blind cross-over study randomised to placebo or a single dose of oral Sildenafil (50mg) in randomised order. The DM group was equally divided into Type 1 (T1DM) and Type 2 (T2DM) subjects as well as the presence/absence of microvascular complications. On each treatment, participants performed a VO2max test and a semi-supine bicycle ergometer five-stage exercise echocardiography protocol.
Results: DM and C subjects were of similar age (DM: 44±13 yrs vs. C: 43±13 yrs, p=0.87), gender (70% vs. 65% male, p=0.7) and reported similar weekly ex-
tercise participation. However, DM subjects had greater body mass index (28±4 vs. 25±3 kg/m², P=0.005). The mean duration of diabetes was 16±10 yrs and gly-
caemic control was moderate (HbA1c: 7.7±1.3%). Resting left ventricular ejection fraction (LVEF), right ventricular fractional area change (RVFAC) and pulmonary artery systolic pressure (PASP) were similar amongst DM and C (LVEF: 59.7% vs. 60.0%, P=0.87; RVFAC: 45.5% vs. 45.8%, P=0.87; PASP: 26.7 vs. 26.4 mmHg, P=0.83). Exercise capacity was reduced in DM as compared with C (VO2max: 21.1 ml/kg/min vs. 40.1 ml/kg/min, P<0.001).
In DM subjects, Sildenafil did not improve exercise capacity or ventilatory effi-
ciency when compared with placebo (VO2max: 31.8 vs. 32.1 ml/min/kg, p=0.42; and VE/VCO2: 25.2 vs. 24.3, P=0.41). However, Sildenafil did cause signifi-
cant augmentation of all measures of central hemodynamics and maximal oxygen consumption (VO2max).

Conclusions: DM and C subjects were of similar age (DM: 44±13 yrs vs. C: 43±13 yrs, p=0.87), gender (70% vs. 65% male, p=0.7) and reported similar weekly exercise participation. However, DM subjects had greater body mass index (28±4 vs. 25±3 kg/m², P=0.005). The mean duration of diabetes was 16±10 yrs and glycaemic control was moderate (HbA1c: 7.7±1.3%). Resting left ventricular ejection fraction (LVEF), right ventricular fractional area change (RVFAC) and pulmonary artery systolic pressure (PASP) were similar amongst DM and C (LVEF: 59.7% vs. 60.0%, P=0.87; RVFAC: 45.5% vs. 45.8%, P=0.87; PASP: 26.7 vs. 26.4 mmHg, P=0.83). Exercise capacity was reduced in DM as compared with C (VO2max: 21.1 ml/kg/min vs. 40.1 ml/kg/min, P<0.001).
In DM subjects, Sildenafil did not improve exercise capacity or ventilatory efficiency when compared with placebo (VO2max: 31.8 vs. 32.1 ml/min/kg, p=0.42; and VE/VCO2: 25.2 vs. 24.3, P=0.41). However, Sildenafil did cause significant augmentation of all measures of central hemodynamics and maximal oxygen consumption (VO2max).
was lower (see Figure 1) and RVFAC increased (+2.4%, P < 0.001) with Sildenafil as compared with placebo. Significant augmentation of hemodynamic and cardiac function with Sildenafil was not observed in the Control group: cardiac output augmentation (+193mL/min, P = 0.36), heart rate (+0.73bpm, P = 0.55) and stroke volume (+1.25mL, P = 0.43).

Conclusion: Consistent with the novel mechanistic hypothesis that pulmonary microangiopathy may limit exercise capacity in DM, Sildenafil resulted in improved pulmonary vascular resistance, RV function and cardiac output. However, VO2max did not improve with cardiac output suggesting that peripheral oxygen extraction may be adversely affected by Sildenafil.

P3652 | BENCH
Blood circulating microRNA-15a and microRNA-16 in diabetic patients: preliminary results of the DIAPASON study
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Background: microRNAs (miRs) are small non coding RNAs that regulate gene expression at the post-transcriptional level. They have been shown to regulate important cellular processes in health and their altered expression has been associated with pathological conditions, including diabetes and its vascular complications. Our group and others previously demonstrated that miR-15a and miR-16 inhibit angiogenesis via targeting VEGF-A and thus may play a pivotal role in post-ischemic vasculogenesis. We have also shown that miR-15a/16 are increased in serum in a cohort of 122 patients with Type 2 diabetes mellitus (T2DM) and will be conducted in a later stage. Prevention of the complications is the primary objective of treating people with diabetes and thus miR-15a/16 represent highly relevant potential biomarkers.

Aim: Analyze whether the quantification of blood circulating miR-15a/16 is able to provide with useful information about diabetes progression in the early phase of disease and on endothelial damage.

Methods: Subjects were selected among those enrolled in a clinical study conducted at IRCCS Multimedica for the prediction and early diagnosis of diabetes mellitus (DIAPASON-DIAbetes Prediction And Screening Observational study). The study is ongoing and will enroll a total of 755 subjects with high risk for diabetes, that according to diagnostic procedures are being divided in 3 groups: 1) newly diagnosed T2DM; 2) patients with altered glucose metabolism (IFG, IGT e HbA1c >6.0%); and 3) subjects with normal glycemic values. At this stage, miR-15a/16 levels have been measured in both serum and plasma by Real Time PCR of 75 subjects, 25 in each of the 3 groups. In the same patients, endothelial function has been measured via Endopath technology and ABI-Ankle Brachial Index and fundus oculi examination have been conducted as additional vascular function parameters. MiR levels have been compared among groups using the analysis of variance.

Results: We have found that miR-15a is significantly increased in plasma (p = 0.0254) and miR-16 in serum (p = 0.0062) of patients with newly diagnosed T2DM and with prediabetes compared to normal subjects. The analysis of the association with endothelial function has not reached enough statistical power and will be conducted in a later stage.

Conclusion(s): Our data suggest a potential association of blood circulating miR-15a/16 with early and asymptomatic phases of diabetic vasculopathy and thus strongly support the relevance of extending the analysis of these two miRs in the entire cohort of the DIAPASON study.

Acknowledgement/Funding: Fondazione Invernizzi/University of Milan and Cariplo Foundation p n: 2013-0887

P3653 | BENCH
Impact of serum 1,5-anhydro-d-glucitol level on prediction of major adverse cardiac and cerebrovascular events in non-diabetic patients without coronary artery disease
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Background: Increasing evidence has demonstrated that postprandial hyperglycemia and fluctuation of glucose level affect cardiovascular events. The serum 1,5-anhydro-d-glucitol (1,5-AG) level rapidly decreases concomitantly with urinary glucose excretion in hyperglycemia and is an important and feasible clinical marker of short-term glycemic status. However, there is currently no established evidence regarding the predictive value of 1,5-AG for cardiovascular events, especially in individuals without diabetes mellitus (DM).

Purpose: The aim of this study was to prove the predictive value of 1,5-AG for major adverse cardiac and cerebrovascular events (MACCE) in non-DM patients.

Methods: Serum 1,5-AG values and coronary angiograms of consecutive 889 patients who consented to the study were evaluated. The study patients were divided into two groups (the 1,5-AG >10.0 μg/ml group and the 1,5-AG ≤10.0 μg/ml group) by their measured 1,5-AG values. They were followed up and information regarding MACCE was collected. MACCE consists of all causes of death, stroke, non-fatal myocardial infarction and cardiovascular hospitalization.

Results: During the follow up period (757±357 days), 216 patients presented with MACCE. In all patients (n=889), the 1,5-AG >10.0 μg/ml group demonstrated a significantly higher risk of MACCE (adjusted hazard ratio 1.62, p = 0.001). Even in non-DM patients without coronary artery disease (n=368), the 1,5-AG >10.0 μg/ml group showed significantly higher risk of MACCE (adjusted hazard ratio 2.28, p = 0.032). Similar results were found even if the events were limited to [All cause death, Non-fatal myocardial infarction and Stroke (adjusted hazard ratio 3.99, p = 0.005)] or [All cause death (adjusted hazard ratio 3.82, p = 0.018)].
contrast to normal cells. We have found that M1-cell CM exert a decrease of p-Akt-Thr308 while increasing p-Akt-Ser473 in ST31L adipocytes; these effects were not observed if M2 cell CM was used for adipocyte treatment. On the contrary, M2 Mph CM induced the increase of p-Akt-Thr308 and decrease in p-Akt-Ser473. The decline of Thr-308 phosphorylation in inflammatory conditions may be due to regulatory inhibitory Ser/Thr phosphorylation of IRS-1 by IKK.

**Conclusion:** We have demonstrated the possibility of adipocyte insulin sensitivity regulation via modulation of inflammatory status of macrophages. The proposed mechanism of p-Akt-Ser473 increase in inflammatory conditions may be associated with IKK-dependent activation of mTORC2, the possibility of which is shown in some studies. Thus, possible mechanism mediating the influence of M1/M2-polarized Mphs on insulin-dependent Akt-phosphorylation may be associated with divergent regulation of IKK-kinase in target cells. It may be realized in latent inflammation, insulin resistance and metabolic syndrome.

**Acknowledgement/Funding:** This work was supported by RFR grants No. 16-34-00282, No. 15-04-07840.

P3655 | BEDSIDE
Impact of high-density lipoprotein cholesterol increase on long-term clinical outcomes in patients following percutaneous coronary intervention
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**Background:** Residual cardiovascular risk persists despite the achievement of target low-density lipoprotein cholesterol levels with statin. High-density lipoprotein cholesterol (HDL-C) is an established coronary risk factor that is independent of LDL-C levels.

**Purpose:** We evaluate the impact of HDL-C increase on long-term clinical outcomes in patients following percutaneous coronary intervention (PCI).

**Methods:** We prospectively enrolled 3037 consecutive patients with coronary artery disease who were treated by PCI at our institution between 2000 and 2011. Among these 2,486, we collected HDL-C at the registration and after 6 to 9 months. We divided the patients to HDL-C increase group and non-increase group and assessed the association of HDL-C increase with adverse cardiac events. The primary endpoint was composite of MACE (all-cause mortality and acute coronary syndrome).

**Results:** The mean follow up duration was 8.1 years. LDL-C level and systolic blood pressure at baseline were significantly higher in HDL-C increase group than non-increase group. HDL-C increase was associated with better long-term clinical outcomes including overall mortality (HR 0.80, 95% CI 0.67–0.96, p=0.02).

**Conclusion:** HDL-C increase was associated with better long-term clinical outcomes among patients who underwent PCI.

P3665 | BEDSIDE
Insulin resistance is associated with impaired endothelial glyocalyx and LV myocardial deformation, twisting-untwisting in dysglycaemics and first-degree relatives of diabetic patients

**Background:** Insulin resistance is associated with endothelial dysfunction and impaired LV myocardial deformation. We investigated whether first-degree relatives of type-2 diabetes patients (FDR) present differences in glyocalyx thickness and LV function at baseline and during postprandial hyperglycemia compared to dysglycaemic or normoglycaemic subjects.

**Methods:** We studied 40 FDR with normal oral glucose test (OGTT), 40 sub-

**Conclusion:** All measured additional anthropometric parameters have shown a highly significant direct positive correlation for overall mortality, rendering them useful tools in the comprehensive practice helping predictor fatal outcomes in the setting of the metabolic syndrome.
Background: Circulating endothelial progenitor cells (EPCs), which have the ability to differentiate into mature endothelial cells, elicit angiogenesis, vasculogenesis, and vessel repair in cardiac ischaemia, vascular injuries and diabetic vasculopathy caused by endothelial damage. Serum 1.5-anhydro-D-glucitol (1.5-AG), which is a useful clinical marker of postprandial hyperglycemia, n-3 polyunsaturated fatty acids, and the plasma fatty acid profile (eicosapentaenoic acid [EPA] and arachidonic acid [AA]), are reported to improve the endothelial function in coronary artery disease (CAD). However, no previous study has reported the association between EPCs and the serum 1.5-AG, EPA and AA levels in CAD patients with type 2 diabetes mellitus (DM).

Purpose: To evaluate the association of the EPC numbers and serum 1.5-AG and EPA/AA values, we conducted a cross-sectional study to assess the correlation between EPCs and 1.5-AG and other clinical variables, including EPA, which is an omega-3 fatty acid and has a cardioprotective effect.

Methods: The peripheral EPCs assessed both as CD34+ cells co-expressing CD45dim, CD133, and vascular endothelial growth factor receptor-2, were studied in 76 CAD patients (mean age, 69 ±11.3 years) with DM. The serum 1.5-AG, EPA and AA levels were also measured.

Results: EPC numbers showed a significant association with 1.5-AG and HbA1c (r = 0.290; p = 0.007 and r = 0.328; p = 0.011, respectively). In addition, there were significant associations between EPC numbers and EPA and body mass index (BMI) (r = 0.354; p = 0.027 and r = 0.402; p = 0.002, respectively) and no relevance to the AA level was found. In multiple linear regression analysis, HbA1c, BMI and EPA values were significant predictors of EPC numbers (β = 0.316, 95% confidence interval (CI) -0.256 to –0.008, p = 0.037; β = 0.413, 95% CI -0.099 to –0.017, p = 0.007; and β = 0.400, 95% CI 0.004 to 0.020, p = 0.010, respectively).

Conclusions: The EPC number was associated with the HbA1c, 1.5-AG, EPA and body mass index values, suggesting that postprandial hyperglycemia and n-3 polyunsaturated fatty acids, especially the EPA levels, contribute to the diabetic vasculopathy and endothelial dysfunction via EPCs in CAD patients with type 2 DM.

LIVING LONGER WITH CARDIOVASCULAR DISEASE - BUT LIVING WELL?

P3658 | BEDSIDE

Heart rate range and all-cause mortality in the elderly


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Introduction: Heart rate is a well-known predictor of outcomes. The prognostic value of parameters assessing heart rate variability has also been well established. Heart rate range (HRR) over a 24-hour period is simpler and easier to estimate than heart rate variability parameters, and has been shown to predict mortality beyond baseline heart rate in these subjects or whether sex has any influence on these associations. Hence, our aim was to assess the effect of HRR on all-cause mortality in elderly individuals.

Methods: A total of 12,097 community-based individuals aged 65 years or older who underwent 24-hour Holter monitoring between March 1, 2000 and December 2014 were initially considered for inclusion in the study. Exclusion criteria were a history of pacemaker implantation, treatment with any negative chronotropic or antiarrhythmic drugs, or any rhythm other than normal sinus rhythm during Holter monitoring. Thus, the final study population consisted of 7,999 individuals. For each Holter recording, maximal, minimal and mean heart rate over the 24-hour period were recorded. Heart rate range (HRR) was estimated as the difference between maximal and minimal heart rate over that period.

Results: Overall, 3,994 subjects were male (49.9%), and mean age was 75 ±8.6 years. Mean heart rate and HRR were, respectively, 68 ±11 and 65 ±19 beats per minute (bpm) and found in multiple linear regression analysis. However, there was no significant interaction between HRR and sex.

Conclusion: We observed a significant association between HRR, as assessed by 24-hour Holter monitoring, and all-cause mortality in an elderly cohort, which was independent of age, sex, and mean heart rate. Further prospective studies are warranted to confirm these findings and to ascertain their generalizability to other populations.

P3659 | BEDSIDE

Time-trend analysis of heart failure mortality by gender in the elderly in Brazil from 1996 to 2012

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Introduction: Heart failure (HF) presents epidemiological characteristics with considerable impact on morbidity and mortality, especially among the elderly. In Brazil, HF is responsible for high mortality rates.

Hypothesis: To evaluate the variation trend of HF gross mortality rates by gender in the elderly in Brazil, comparing with the variability of population growth by age and cardiac mortality rate.

Methods: Information was obtained from data published by Datasus (Source: Hospital Universitario A Coruña, A Coruña, Spain). Kaplan-Meier survival curves were used to construct probability of survival for CVD. Hazard ratios (HR) and 95% confidence intervals (CI) for CVD mortality were calculated using Cox models. Two models were performed: Model 1 - adjusted for age; Model 2 - adjusted for age, education, marital status, parenthood, working status, deprivation, social activity, participation in social organization, smoking status, alcohol intake, physical activity, body mass index, arterial hypertension, lipids and glucose levels.

Results: Survival curves ascertained that survival over eight years is influenced by CF among 45–72 years population according to their gender. Respondents with good CF had higher survival rates compared to participants with a lower level of CF (in men Log Rank=5.4, p=0.02, in women Long Rank=6.1, p=0.01). After adjustment for age (Model 1) good CF predicts lower CVD mortality risk in men (HR=0.64, 95% CI 0.40–1.02; in women HR=0.52, 95% CI 0.28–0.98). After additional adjustment (Model 2), good CF significantly related with lower mortality risk for CVD only in women (HR=0.38 95% CI 0.17–0.84, but not in men,HR=0.91 95% CI 0.53–1.56).

Conclusion: Good CF was related with lower risk for CVD mortality only in women aged 45–72 years.

Acknowledgement/Funding: Wellcome Trust (grant no. 081081/Z/06/Z), the US National Institute on Aging (grant no. 1R01 AG23552), Research Council of Lithuania (No SEN-02/2015)
P3662 | BEDSIDE
Lower carotid flow velocities were associated with impaired cognitive function in a community-based elderly population
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Background: Carotid atherosclerosis (high intima-media thickness) was recognized to associate with stroke and cognitive function impairment. However, few studies investigated the association between carotid flow velocities and cognitive function. This study investigated the association between carotid flow velocities and cognitive function.
Materials and methods: A total of 1684 seniors aged more than 65 years and without dementia was recruited for this aging study. All seniors were receiving the physical and mental examinations and drawing fasting blood sample for testing biochemical markers. The Mini-Mental State Examination (MMSE) was used to evaluate cognitive function. We classified the subjects with poor (MMSE<24), normal (MMSE: 24–27) and well (MMSE ≥ 28) cognitive function. We used the linear regression and logistic regression to evaluate the association between carotid flow velocity and cognitive function. Multivariate linear regression and ordinal logistic regression were used to evaluate the association between carotid flow velocities and cognitive function.
Results: Old age, women gender, low education and high systolic blood pressure, poor nutritional status, worse glucose control and inflammation status were associated with cognitive function. We also found that the peak systolic velocity (PSV) in common carotid artery (CCA) and in internal carotid artery (ICA), and end-diastolic velocity in the ICA were positively associated with well cognitive function. The multivariate linear regression showed low systolic blood pressure (beta=−0.010, p-value=0.0145) and high CCA PSV (beta=0.025, p-value=0.026, p-value=0.014) were significantly associated with altered MMSE, after controlling the age, sex, education, nutritional status and smoking. Compared to the referent group with higher CCA PSV (>=68 cm/sec), the group with lower CCA PSV (<=60 cm/sec) significantly increased 54% risk (OR=1.54; 95% CI: 1.14–2.07), and those seniors with middle CCA PSV slightly increased 27% risk (OR=1.28; 95% CI: 0.988–1.63) for impaired cognitive function in the multivariate logistic regression.
Conclusion: Low carotid flow velocities were significantly associated with impaired cognitive function and this relationship needs further prospective studies to confirm.

P3663 | BEDSIDE
The development and validation of predictive model of perioperative cardiac risk optimized for geriatric patients – The Geriatric Cardiac Risk Calculator (GRCR)
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Background: Geriatrics Patients have characteristic, progressive constriction of homestatic reserve that occurs with aging in every organ system. The decreased physiologic reserve makes them more prone to complications. Previous cardiac risk models, such as RCRI and Gupta NSQIP, have not considered this distinction in their analysis and developed models that do not discriminate between Geriatric and Non-Geriatric population. This could lead to decreased performance and prediction discrimination in these models in geriatric patients.
Hypothesis: Using subgroup analysis on patients (age ≥65), we could develop more calibrated coefficients for the model variables, resulting in a final model with higher performance and improved calibration in geriatric patients.
Methods: We investigated the performance of the RCRI and Gupta NSQIP models in a geriatric subset (age ≥65) of the NSQIP 2012 (N=489,133) for predicting the perioperative cardiac risk of MICA (Myocardial Infarction/Cardiac Arrest). We then developed our model based upon a multivariable logistic regression model using subgroup analysis. Parameter estimates from the NSQIP 2012 were then applied to the NSQIP 2013 (N=587,956) in order to determine model performance when generalized to a novel sample. The Area Under the Curve (AUC) for these models was then compared. Additionally, a gradient boosting machine learning model was developed and tested to compare for maximum prediction potential in improving the model using the available data.
Results: Testing the Gupta Model with the published coefficients on patients 65 had an AUC of 0.703, a significant deterioration (<17%) from previously published performance in the NSQIP 2007. RCRI also showed poor performance (AUC=0.683) in geriatric patients. Our model had the best performance with an AUC of 0.772 in the 2013 validation dataset.

Table 1. Examination of Performance of Models in NSQIP 2012-Training Set Model AUCs presented

<table>
<thead>
<tr>
<th>Age ≥ 65 AUC</th>
<th>AUC Model</th>
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<tbody>
<tr>
<td>RCRI Model</td>
<td>0.653</td>
</tr>
<tr>
<td>Gupta Model-Using Published Coefficients</td>
<td>0.699</td>
</tr>
<tr>
<td>Geriatric GRCR Model</td>
<td>0.776</td>
</tr>
<tr>
<td>GMB Model</td>
<td>0.796</td>
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</table>

Models Comparison and Validation Tables
Conclusion: This model has optimized performance in geriatric patients. Based on these analyses, it outperforms the Gupta Model by 7% and the RCRI by 12% in improving the prediction discrimination. This model is the first of its kind, and is designed with optimal performance for use solely in Geriatric Patients and out-performs all current models.

P3664 | BEDSIDE
Predictive value of serum albumin in addition to traditional risk factors as risk of cardiovascular events and all-caused death in elderly and middle-aged persons: a population-based cohort study
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Background: It has been reported that serum albumin concentrations are associated with the risk of cardiovascular disease and mortality. However, it remains unclear whether this association differs between elderly and middle-aged persons, and this finding provides an additional information on the prediction for cardiovascular and mortality risk by traditional risk factors.
Methods: A population-based prospective cohort study was performed in 12,214 subjects aged 40 years or older with no urinary protein and no history of atherosclerotic cardiovascular events (CVE). A multivariate Cox regression analysis was performed to examine the relationship between tertiles of serum albumin levels and CVE in individuals who were younger than 65 and who were over 65 years of age. The net reclassification improvement (NRI) and the integrated discrimination improvement (IDI) were calculated to compare predictive models.
Results: There were 839 CVE, which was defined as stroke or acute myocardial infarction/sudden cardiac death, and a total of 1,083 death during a mean follow-up period of 9.2 years. In participants older than 65 years, serum albumin levels...
of 2.7 to 4.2 g/dL (the lowest tertile) had increased risk of CVE (HR, 1.30; 95% CI, 1.07–1.58) and all-caused death (HR, 1.37; 95% CI, 1.16–1.61) compared with those with levels of 4.5 to 5.5 g/dL (the top tertile; reference). Furthermore, among those participants, adding the serum albumin levels to Framingham risk score improved the accuracy of risk prediction in CVE (NRI = 5.4%, p < 0.01; IDI = 0.2%, p < 0.01) and all-caused death (NRI = 22.7%, p < 0.001; IDI = 1.2%, p < 0.01). In contrast, participants younger than 65 years of age did not have a significant relationship between the serum albumin levels and outcomes.

**Conclusions:** In elderly persons, not in middle-aged persons, there is an association between the serum albumin levels and outcomes. In contrast, participants younger than 65 years of age did not have a significant relationship between serum albumin levels and outcomes.

**Acknowledgement/Funding:** This research was supported in part by grants-in-aid for scientific research fund of the Ministry of Education, Science, and Culture of Japan.

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**P3665 | BEDSIDE**

**Undernutrition, a novel marker of peripheral artery disease in African elderly: the EPIDEMICA study**

I. Desmoulin1, V. Aboyans2, M. Guercel5, B. Ndamba-Bandouzi4, P. Mblessoss3, PM. Preux4, P.H. Lacroux1 on behalf of EPIDEMICA study.

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**Introduction:** While the debate regarding the association between obesity and cardiovascular disease in elderly: the EPIDEMICA study.

**Methods:** Study design used data from 2007 to 2012 from the Singapore Myocardial Infarction Registry (SMIR), a mandatory national registry in Singapore. Patients were divided into 3 age groups with young patients defined as <45 years of age, octogenarian patients defined as 80 years of age and middle-aged-to-old (MAO) defined as 45–80 years of age. The primary outcome of the study was one year mortality and secondary outcomes include two year mortality and inpatient complications such as heart failure, arrhythmias and stroke.

**Results:** There were 12,409 STEM1 patients in total. Of these, there were 1,109 (8.9%) young patients, 10,093 (81.3%) MAO patients and 1,207 (9.7%) octogenarian patients. Octogenarian patients had overall more cardiovascular risk factors compared to MAO and young patients such as hypertension (70.9% vs 56.3% vs 36.4%, p < 0.0001) and previous myocardial infarction (16.2% vs 10.9% vs 5.7% p < 0.0001). They had lower rates of smoking (26.4 vs 56.8 vs 75.2%, p < 0.0001) as well as lower body mass index (21.7 ± 25.4 vs 26.6 ± 0.0001). Treatment, octogenarian patients had the highest rate of medical therapy (72.0% vs 23.7% vs 11.5%, p < 0.0001). They also had higher rates of in-hospital complications such as heart failure (27.4% vs 15.5% vs 7.1%, p < 0.0001), atrial fibrillation (24.9% vs 10.7% vs 4.2%, p < 0.0001), acute renal failure (16.0% vs 6.8% vs 2.0%, p < 0.001) and stroke (2.4% vs 1.7% vs 0.6%, p = 0.004). For mortality, octogenarians had the highest in-hospital mortality (38.5% vs 11.2% vs 2.7%, p < 0.001, one year (60.6% vs 16.4% vs 4.1%, p < 0.0001) and two year mortality (66.7% vs 20.5% vs 4.9%, p < 0.001). Multi-variant predictors of one year mortality in MAO patients include age, hypertension, diabetes mellitus, raised creatinine, as well as Killip class III/IV heart failure. Multivariate predictors of one year mortality in octogenarians include hypertension, diabetes mellitus, raised creatinine and Killip Class II heart failure and raised creatinine.

**Conclusions:** Patients at the extreme of ages make up a significant proportion of STEMI patients and present with different risk factor profiles with different outcomes. Octogenarian patients have worse in-hospital and long term outcomes as compared to MAO and young patients.

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**P3666 | BEDSIDE**

**Greater visit-to-visit variability was associated with cognitive function impairment in an elderly population: prospective study**


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**Background:** Increased visit-to-visit systolic blood pressure (SBP) has been associated with increased stroke risk. The role of visit-to-visit BPV in the development of cognitive dysfunction remains unestablished. We aimed to investigate the association between visit-to-visit blood pressure variability (BPV) and future cognitive performance.

**Methods:** CVDFACTS study was a longitudinal cohort study and the first wave survey was established during 1989–1991 and four waves of survey were carried out between 1992 and 2002. The on-going sixth wave survey was started in 2015. Among the 3200 seniors aged 60 years and older, we had hyperbolic left ventricles with normal or even hyperkinetic systolic function. The diastolic function was just slightly impaired. Critical aortic stenosis prevailed in centenarians.
standard deviation of measurements of brachial SBP and diastolic blood pressure (DBP) from each wave of survey. The first quartiles of SBP and DBP for BPV were defined as the high variability group and others as the normal variability group. The general linear regression and the logistic regression were used to evaluate the associations between visit-to-visit BPV and MMSE and cognitive dysfunction (MMSE<24), respectively. Results: Both SBP and DBP BPV were significantly associated with cognitive function. The correlation coefficients between DBP and MMSE were -0.132 (p-value=0.0182) for SBP and -0.158 (p-value=0.0047) for DBP. However, the association DBP and MMSE remained significant only for DBP (r=0.39, p-value=0.01) but not for SBP (r=-0.09, p-value=0.153) when age and sex were accounted for. DBP BPV remained significantly associated with MMSE and cognitive dysfunction in the multivariate models with adjustment for DBP, history of other confounders in the logistic regression (β=-0.11, p-value=0.0347) and the logistic regression (odds ratio = 1.17, 95% CI: 1.03–1.32). Subjects with high visit-to-visit DBP BPV had significantly lower MMSE and higher prevalence of cognitive dysfunction. Conclusion: High visit-to-visit DBP BPV was associated with future cognitive dysfunction.

P3669 | BEDSIDE
Cognitive function and muscle strength: Additive significant indicators of hospital-to-home discharge in the elderly inpatients with heart failure

Background: Cognitive decline and heart failure (HF) frequently coexist in the elderly. Handgrip strength is used as a measure of whole-body muscular strength in the elderly. We hypothesized that higher cognitive function might be associated with hospital-to-home discharge in the elderly inpatients with HF. In addition, we investigated whether muscle strength moderates the relationship or not.

Purpose: To explore the relationships among cognitive function, muscle strength and hospital-to-home discharge in the elderly patients with HF.

Methods: Cognitive function was evaluated using mini-mental state examination (MMSE) in 261 elderly inpatients in stable phase of HF (83±5.9 years old, male 47%). Standing isometric relative handgrip strength was calculated as the average level of maximal absolute handgrip strengths from both hands.

Results: In the HF patients with outcome of hospital-to-home discharge (n=216), MMSE score and prevalence of the highest tertile of MMSE score (23.2 vs 18.9, p<0.001 and 36.6 vs 13.9%, p<0.001, respectively) as well as handgrip strength and prevalence of the highest tertile of handgrip strength (17.0 vs 10.3kg, p<0.001 and 36.6 vs 18.0%, p<0.001, respectively) were significantly different with those in the HF patients with outcome of inpatient rehabilitation or other institutionalized care (n=65). In the logistic regression analysis adjusting for the confounding factors including age, gender, body weight, left ventricular ejection fraction, log brain natriuretic peptide, clinical scenario classification, Barthel Index and length of hospital stay, the highest tertile of MMSE score (β=3.12, 95% CI:1.05 to 9.26, p<0.05) as well as that of handgrip strength (β=6.17, 95% CI:1.85 to 10.5, p<0.01) were significantly associated with hospital-to-home discharge. The interaction term of the highest tertile of MMSE score by that of handgrip strength had no significant association with hospital-to-home discharge in the regression model.

Conclusions: In the elderly inpatients with HF, higher MMSE score and higher handgrip strength were significantly associated with hospital-to-home discharge. Cognitive function and muscle strength were serve as additive indicators for the discharge outcome. Preservation of cognitive function and muscle strength might be key factors for prevention of inpatient rehabilitation or other institutionalized care in the elderly with HF.

P3670 | BEDSIDE
Prevalence of multimorbidity of cardio-metabolic disease in the United Kingdom

Background: The prevalence of cardio-metabolic conditions is increasing globally, and is expected to continue to rise, driven by an ageing population. However, little is known on vulnerable groups with multiple conditions, despite multimorbidity being associated with worse health care utilisation and health care costs. There are few studies providing prevalence estimates of multimorbidity in the UK.

Purpose: To estimate the prevalence of multimorbidity defined by twelve chronic cardio-metabolic conditions in the UK, and determine the association between multimorbidity and age, sex & socioeconomic status (SES).

Methods: Data was obtained from the Clinical Practice Research Datalink (CPRD), a database of routinely-collected primary care data in the UK that is broadly representative of the UK population for key factors including age and sex. We performed a cross-sectional analysis of all patients over 30 years of age with a valid CPRD record on 1 Jan 2013. We looked back at patient records to 1st Jan 1990 to identify cases with prior history of any of the following twelve chronic conditions: ischaemic heart disease (IHD), cerebrovascular disease, diabetes, chronic kidney disease (CKD), peripheral arterial disease, aortic aneurysm, atrial fibrillation, heart failure, deep vein thrombosis, pulmonary embolus, valvular heart disease and dementia. Multimorbidity was defined as having two or more conditions. Prevalence rates were calculated for each individual condition and for multimorbidity. We used multivariable logistic regression (OR [95% CI]) to examine the association between multimorbidity and age group, sex and SES.

Results: Analysis of 4.1 million patients showed the most common conditions were IHD (8.4%, n=349,128), diabetes (8.3%, n=343,812), and CKD (5.5%, n=227,604), with 9.6% (n=398,692) of the population having multimorbidity. The most common multimorbidity combination was diabetes and IHD (n=29,903). The odds of multimorbidity was significantly higher in the elderly; patients aged ≥91 years were fifty times more likely to have multimorbidity than those aged 30–40 years (4.5 [3.6–5.8] vs 0.09 [0.01]). The odds of multimorbidity for males, compared with females, was almost double (1.96 [1.72–2.23], p<0.001) and the odds of multimorbidity in patients from the most deprived quintile of deprivation was a third higher than those from least deprived areas (1.30 [1.05–1.59], p<0.001).

Conclusion: Using a national representative sample we estimate 10% of the UK population over 30 years old is affected by cardio-metabolic multimorbidity. Increasing age, male sex and deprivation are predictive of chronic cardio-metabolic multimorbidity in the UK. These indicative results provide the basis for further work into the determinants of multimorbidity, in order to better understand and manage this vulnerable group in the UK healthcare system.
P3673 | BEDSIDE
Geriatric patients have non-linear increase of perioperative risk of MICA (myocardial infarction/cardiac arrest). Counterintuitively, age has decreased odds ratio for MICA in geriatric patients

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Background: Increased age is often used as risk factor for perioperative cardiac risk. However, the age often treated in predictive model as linear in regression theory-driven selection of covariates to study the age as risk factor. We conducted fit and Lowess fit. We proceeded to multivariate logistic regression analysis with submitted by 374 participating hospitals. We studied the association of age with improvement Program NSQIP 2012 prospective dataset, which has 543,885 cases

Methods: We used American College of Surgeons National Surgical Quality Improvement Program NSQIP 2012 prospective dataset, which has 543,885 cases submitted by 374 participating hospitals. We studied the association of age with MICA using logistic regression, and then we concurrently plotted the best linear fit and Lowess fit. We proceeded to multivariate logistic regression analysis with theory-driven selection of covariates to study the age as risk factor. We conducted the analysis on all the patients, patients >65 and patients <65 separately in order to compare the adjusted odds ratio for age (1 year unit) between geriatric vs. non-geriatric patients.

Results: As expected, age association with MICA is non-linear and forcing age to fit as linear term would yield in decreased calibration in the geriatric patients. However, this increased risk with age in the univariate analysis yielded smaller odds ratio for age in the multivariate analysis, indicating that older age increased risk is mainly due to increased comorbidities rather than increased risk with age itself.

<table>
<thead>
<tr>
<th>Overall OR</th>
<th>Patients &lt;65 OR</th>
<th>Age ≥ 65 OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>p-value</td>
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</tr>
<tr>
<td>1.034</td>
<td>&lt;0.001</td>
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</tr>
<tr>
<td>N excluding emergency cases</td>
<td>489,133</td>
<td>314,001</td>
</tr>
</tbody>
</table>

Conclusion: Age has non-linear association with MICA probability with age, and to estimate the odds ratio for age in geriatric patients after controlling for potential confounders.

P3674 | BEDSIDE
Hypertension as a predictor of pattern of LV hypertrophy and geometric remodeling in elderly

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Background: Hypertension (HTN) inarguably causes remodeling of left ventricle (LV). However, the effect of awareness, treatment and control of hypertension (HTN) on LV geometry has not been established. We sought to identify the relationship between the classification of LV geometry and awareness, treatment and control of hypertension in a large elderly population.

Methods: Participants with complete echocardiographic data from the 5th survey of the Electricity Generating Authority of Thailand study were enrolled in 2012. Detailed hypertension data was retrieved from the survey in 1997, 2002, 2007 and 2012. Linear regression models adjusted for age, gender, diabetes, smoking status were used to analyze an association between awareness, percentage of controlled hypertension over 15 years and LV geometry.

Results: Complete echocardiographic data was available in 1,021 participants. A mean age was 69±5 years; 69.7% were male. Prevalence of hypertension, diabetes (DM) and current smoker were 73.4%, 29.3% and 6.8% respectively. Compared with no hypertension, hypertensive participants had higher LV septal thickness, posterior wall thickness, stroke volume index, relative wall thickness and LV mass per body surface area (BSA) (all p-value <0.05). Adjusted odds ratio for MICA in patients older than 65. This proves that advanced age is not a sole, reliable indicator for increased risk. In addition, modeling age based on linear fit would result in underestimation of the risk in geriatric patients.

Conclusion: Our results found an expected normal decline in effort capacity with advanced age groups (Vo2max (L/min); group 1 mean 2.02, 2 mean 1.59, 3 mean 1.29) with a significant decline between the first and second group (P=0.0001) and a trend for decline between the second and third group (P=0.1). There was a significant reduction in peak CO from first to second tertile (P=0.0001), but with no further decline in the third tertile. This suggests that our classification of age was not appropriate. The decline in effort capacity with age is due to an attenuated SV and HR response between the ages of 65 to 75, but in the oldest group age it is mostly because of the decline in the ability of the muscles to extract enough oxygen for the necessary effort.

P3675 | BEDSIDE
Decline in effort capacity with age: echo stress analysis

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Introduction: Aging is associated with a decline in effort capacity. It is unclear whether this decline is related to diastolic or diastolic dysfunction with reduced cardiac output (CO) or regression of peripheral muscles associated with diminished arterio-venous difference (A-V diff.).

Purpose: Evaluate elderly patients by stress echo and to assess the physiologic determinants of their effort capacity.

Methods and population: The retrospective analysis included 370 consecutive patients above the age of 65 with a normal systolic function and no ischemia who underwent a stress echo test on a treadmill between Jan 2012 until Dec 2015 in our facility. The population was divided into 3 groups of age by tertiles: 65-74, 75-82, 83-94 and stress echo parameters including diastolic parameters, stroke volume (Simpsons method SV), CO, calculated peak Vo2 (Bruce derived METS=3.5xweight) and calculated A-V diff. were compared in order to reveal the determinants of deteriorating effort capacity with age.

Results: At rest, a significant difference in relaxation was noted between the first and second tertile (lateral e’ 8.5 vs. 7.7; p=0.005) and between first and third tertile (8.5 vs. 6.9, p<0.01). No difference was observed in other rest parameters including LVEDD, LVEFD, E/A, LA volume, stroke volume or cardiac output.

Conclusion: The cardiovascular system undergoes several age-related changes. Increased age is often used as risk factor for perioperative cardiac risk. However, the age often treated in predictive model as linear in regression theory-driven selection of covariates to study the age as risk factor. We conducted fit and Lowess fit. We proceeded to multivariate logistic regression analysis with theory-driven selection of covariates to study the age as risk factor. We conducted the analysis on all the patients, patients ≥65 and patients <65 separately in order to compare the adjusted odds ratio for age (1 year unit) between geriatric vs. non-geriatric patients. However, this increased risk with age in the univariate analysis yielded smaller odds ratio for age in the multivariate analysis, indicating that older age increased risk is mainly due to increased comorbidities rather than increased risk with age itself.

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</tbody>
</table>

Conclusion: Age has non-linear association with MICA probability as the risk increase in older patients, yet the increased risk in not due to age itself. After controlling for confounders, we find age unit has lower adjusted odds ratio for MICA in patients older then 65. This proves that advanced age is not a sole, reliable indicator for increased risk. In addition, modeling age based on linear fit would result in underestimation of the risk in geriatric patients.

P3676 | BEDSIDE
Hypertension: An independent risk factor for LV hypertrophy and remodeling in elderly patients

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Background: While handgrip strength has been linked to future risk of death and cardiovascular disease, data characterizing the underlying link between cardiac remodeling and cardiac function with handgrip strength are limited, particularly among elderly participants.

Objective: We studied the association between left ventricular (LV) concentric...
ity and LV function with handgrip strength and timed-up-and-go test (for lower extremity function) among community-dwelling elderly.

Methods: Participants from the population-based Singapore Chinese Health Study cohort were longitudinally followed-up from 1993 to 2015. We studied participants who did not have self-reported physician-diagnosed cardiovascular disease, cancer or stroke. We assessed cardiac remodeling by cardiac magnetic resonance imaging (MRI) (left ventricular [LV] concentricity 0.67 and LV function by resting tissue Doppler imaging (TDI) performed at the septal and lateral mitral annulus, deriving myocardial systolic velocity (S), diastolic velocity (E) and ratio of E/A. Diastolic function was defined as normal or abnormal (Grade I, II, III).

Results: We examined 56 participants without cardiovascular disease (36 females, mean age 73.6±3.4 years), preserved LV ejection fraction (mean LVEF 70.3±6.7 %) and cardiac index (0.86±3.4). There were significant correlations between handgrip and LV concentricity (r=0.294, p=0.031), and between timed-up-and-go test and lateral S (r=0.34, p=0.018), lateral E/A (r=0.489, p=0.024). Compared to participants with abnormal diastolic function, participants with normal diastolic function were more likely to have better handgrip (p=0.037). By regression analysis, LV concentricity (r=0.086 SE 0.021, p=0.035) (with adjustment for hypertension and age) was independently associated with handgrip strength.

Conclusion: Our study provides important preliminary observations that could serve to unravel mechanistic links behind functional aging and cardiovascular alterations that occur among elderly adults. Further investigations are required to confirm these observations and to target goals that preserve health and function with age.

Acknowledgement/Funding: National Medical Research Council; Edwards Life-sciences; Hong Leong Foundation

P3676 | BEDSIDE
Correlations between geriatric nutritional risk index and peripheral artery disease in elderly coronary artery disease patients
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Aim: Malnutrition is associated with the development of atherosclerosis and an increased risk of cardiovascular mortality in elderly patients. The purpose of this study was to investigate the association between geriatric nutritional risk index (GNRI), a simple nutritional assessment tool, and the prevalence of peripheral artery disease (PAD) in elderly coronary artery disease (CAD) patients.

Methods: We evaluated 228 elderly CAD patients (mean age: 74.0±7.7 years). Ankle–brachial index (ABI) measurements were routinely performed to investigate the prevalence of lower extremity PAD. Patients showing ABI < 0.9 were defined as having PAD.

Results: Based on our findings, 20.6% study patients had PAD. The median GNRI values were significantly lower in patients with PAD than those in patients without PAD (92.8 versus 99.3, p=0.001). Even after multivariate adjustment, GNRI values were independently associated with PAD (odds ratio: 0.94, 95% CI 0.9 to 1.0; p=0.001). Even after multivariate adjustment, GNRI values showed a strong relationship with PAD in elderly CAD patients. These data reinforce the utility of GNRI as a screening tool in clinical practice.

Conclusions:

P3677 | BEDSIDE
Left ventricular diastolic function is associated with cognitive impairment in patients at risk of heart failure
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Background: Heart failure confers an increased risk of mild cognitive impairment (MCI). It is unclear whether left-ventricular (LV) dysfunction in the absence of heart failure correlates with MCI independent of concurrent vascular sequelae.

Purpose: To determine whether LV diastolic function in the setting of high heart failure risk is associated with MCI independent of its clinical correlates and established vascular risk markers.

Methods: Patients from the Nurse-led Intervention for Less Chronic Heart Failure (NIL-CHF) Study (≥45 years and ≥1 of atherosclerotic cardiovascular disease, type 2 diabetes, and/or hypertension – but excluding those with atrial fibrillation [n=290, aged 67±10 years, 71% male, 69% coronary artery disease, 13% cerebrovascular disease], completed the Montreal Cognitive Assessment (MoCA) and were classified as demonstrating MCI if their score was in the range 18–26 (out of a possible 30). LV diastolic function was assessed via echocardiography (ratio of early diastolic filling and tissue velocities; E/e'). Arterial stiffness (carotid-ankle vascular index: CAVI) and carotid intima-media thickness (IMT) – mean of left and right for both – were measured in a subgroup (n=144).

Results: MCI prevalence was significantly higher across E/e' tertiles (27% in tertile 1 vs. 44% [tertile 2] and 53% [tertile 3]; p=0.001). MoCA score showed a progressive decline across E/e' tertiles (Figure: data are estimated marginal means with standard error), even after correcting for age, sex, education, coronary artery disease, cerebrovascular disease, diabetes, body mass index, mean arterial pressure, smoking, alcohol, diet, and medications (ANCOVA; with adjustment for multiple post hoc comparisons). In multiple logistic regression adjusting for the same covariates, the highest vs. lowest tertile for E/e' was a significant predictor of MCI (odds ratio 2.3 [95% CI 1.1 to 5.0]; p=0.025), whereas the middle vs. lowest tertile was a borderline significant predictor (odds ratio 1.8 [95% CI 0.9 to 3.6]; p=0.082). In the subgroup in whom additional adjustment for CAVI and carotid IMT was possible, the highest E/e' tertile remained independently predictive of MCI (p=0.012).

Conclusions: The independent association of LV diastolic dysfunction with MCI points to potential cardiac involvement in cognitive decline.
the model testosterone levels were no longer associated with mental capacity (p=0.17), suggesting a mediating effect of Vt D.

**Conclusions:** Higher testosterone levels seem to be related with preserved mental capacity in elderly individuals. Vitamin D levels interfere in this relationship, indicating the important role of Vitamin D deficiency on cognitive function. Thus, correction of Vitamin D levels with markers of cognitive decline opens a new door for early diagnosis and even therapeutic target of cognitive impairment, beyond traditional cardiovascular risk factors.

### AORTIC VALVE DISEASE

**P3670 | BEDSIDE**

The long-term clinical outcome of patients with low gradient severe aortic stenosis

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**Background:** Although current guidelines recommend the watchful waiting for aortic valve replacement (AVR) until symptom emerge in patients with low gradient [mean aortic jet velocity (Vmax) < 4 m/s and mean aortic pressure gradient [PG] < 40mmHg and aortic valve area (AVA) < 1cm²] severe aortic stenosis (AS) except for patients who are undergoing other cardiac surgery, the management of patients with LG severe AS remains controversial.

**Purpose:** The aim of study was to evaluate the impact of initial AVR strategy on long-term clinical outcome of patients with LG severe AS.

**Methods:** The CURRENT AS registry is a multicenter retrospective registry enrolling 3,815 consecutive patients with severe AS.

**Results:** Among the entire cohort, LG severe AS was seen in 1718 patients (44.8%). Patients with LG severe AS were older (79.0±9.3 versus 76.8±10.0 years old) and more often had left ventricular dysfunction (ejection fraction < 50%) and comorbidities such as prior stroke or coronary artery disease than those with HG severe AS. Surgical AVR was more frequently performed in patients with HG than in those with LG during the follow-up (60.0% versus 28.2%, P<0.001). The cumulative 5-year incidences of all-cause death and HF hospitalization were higher in patients with LG severe AS than in those with HG (47.0% versus 39.8%, P<0.001; 35.2% versus 25.3%, P<0.001). Initial AVR strategy was chosen in 220 of patients with LG, and in 977 of patients with HG severe AS. The cumulative 5-year incidence of all-cause death was lower in the initial AVR than in the conserva-
tive strategy both in patients with LG severe AS (28.9% versus 49.5%, P<0.001) and those with HG (25.3% versus 39.8%, P<0.001).

**Conclusions:** Despite less severe gradient, the long-term clinical outcome of patients with low gradient severe AS was dismal, which might be improved by initial AVR strategy.

**P3671 | BEDSIDE**

Prognosis of paradoxical low gradient severe aortic stenosis: a network meta-analysis approach

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**Objectives:** The outcomes associated with paradoxical low gradient aortic stenosis have been variable in different studies. Using the novel network meta-analysis, we will examine the prognosis of the different gradient/flow states associated with severe aortic stenosis (SAS).

**Methods:** Studies that investigated prognosis of SAS with left ventricular ejection fraction >50% were included. The prognosis of SAS was compared to moderate aortic stenosis using network meta-analysis, according to gradient states [threshold of 40mmHg; high-gradient (HG) versus low-gradient (LG)]. Prognosis associated with LG severe AS was further stratified by flow [normal-flow (NFL) versus low-flow (LF)].

**Results:** Data from 29 publications (38,101 patients) were extracted for the network meta-analysis. Compared to moderate AS, LG SAS was associated with the worst prognosis, followed by HG SAS (hazard ratio [HR] 1.65 [1.29, 2.14] and 1.34 [1.03, 1.75], respectively). Further stratified by flow states, patients with NFLG had a similar prognosis as moderate AS (HR 1.11 [0.79, 1.54]) whilst LFLG was associated with the worst prognosis (HR 1.91 [1.45, 2.49]).

**Conclusions:** Paradoxical low gradient aortic stenosis (particularly low flow state) was associated with increased all-cause mortality compared to moderate and severe AS.

**Acknowledgement/Funding:** National Science Centre (2013/11/B/NZ5/00157 to EW)

**P3680 | BENCH**

Human aortic valve interstitial cells express coagulation factors: the impact of inflammatory stimulation

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**Background:** Endothelial dysfunction plays an important role in the pathogenesis of atherosclerosis. Local inflammatory stimulation impacts the interaction of coagulation proteins with the endothelial cells.

**Purpose:** To evaluate if human interstitial cells (VICs) from the valves of patients with congenital bicuspid aortic valve regurgitation (CBAV-AR) express coagulation factors and are able to express FII and FVII under inflammatory stimulation.

**Methods:** VICs were isolated from valve leaflets of patients with CBAV-AR and CBAV-AS and cultured for 7 days. VICs were co-cultured with monocytes and the effects of LPS were evaluated. VICs were also cultured in the presence of platelets and fibrinogen. VICs were analysed by immunofluorescence using corresponding monoclonal antibodies and visualized with the secondary antibodies conjugated with fluorochromes. Evaluation of positive cells was performed as: a number of cells presenting antigen expression/total cell number.

**Results:** VICs control cultures revealed the presence of TF (12.±1.3%), FX (76.±14.5%), PAR1 (0.±8.2%) and PAR2 (1.±6.8%) antigens. No expression of FII and FVII was observed. Exposure of VICs to TNF-α caused the up-regulated expression of TF (83.±12.1% vs. 12.±1.3%, p<0.001). Moreover, under inflammatory stimulation, 74.±10.3% of VICs revealed the expression of FVII and 29.±15.3% the expression of FII (p<0.001 and p<0.02, respectively, in comparison with the control group). The expression of FX, PAR1 and PAR2 antigens remained unaltered upon stimulation.

**Conclusions:** We showed for the first time that VICs express constantly FX, PAR1 and PAR2 and are able to express FII and FVII under inflammatory stimulation. The presence of PARs suggests a possible action of thrombin and FXα directly on the VICs. We conclude that in the diseased aortic valves, local expression of coagulation proteins derived in part from VICs might contribute to disease progression.

**Acknowledgement/Funding:** National Science Centre (2013/11/B/NZ5/00157 to EW)

**P3681 | BENCH**

Pathological investigation of congenital bicuspid aortic valve stenosis, comparing with atherosclerotic tricuspid aortic valve stenosis and congenital bicuspid aortic valve regurgitation

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**Background:** Congenital bicuspid aortic valve (CBAV) is the cause of aortic stenosis (AS). However, histopathological features of AS patients with CBAV have not been fully investigated.

**Methods:** We examined specimens of aortic valve leaflets obtained from patients who had undergone aortic valve replacement at our institute for severe AS with CBAV (n=24, CBAV-AS group), severe AS with tricuspid aortic valve (n=24, TV-AS group) and severe aortic regurgitation (AR) with CBAV (n=24, CBAV-AR group). We compared histopathological features between the three groups. Scoring of pathological features was classified using semi-quantitative methods (graded on a scale from 0 to 3) by experienced pathologists without knowledge of the patients’ backgrounds.

**Results:** Pathological features and thickness of fibrotic lesion are shown in the Table. The severity of inflammation, neovascularization, and calcium and cholesterol deposits were higher in CBAV-AS group than CBAV-AR group. Meanwhile,
the severities of these 4 parameters did not differ between CBAV-AS group and TAV-AS group. The grade of valvular fibrosis and thickness of fibrotic lesion were greater in CBAV-AS group, compared with TAV-AS and CBAV-AR group. Among AS patients, valvular fibrosis was thicker on aortic side than ventricular side (both p<0.01). Meanwhile, valvular fibrosis was comparable between aortic and ventricular sides among CBAV-AR group (p=0.35).

### Table 3

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Thickness of fibrotic lesion</th>
<th>Aortic side (mm)</th>
<th>Ventricular side (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>76.5±16.0</td>
<td>0.54±0.16</td>
<td>2.00±0.12</td>
<td></td>
</tr>
<tr>
<td>61.6±12.8</td>
<td>1.23±0.65</td>
<td>0.91±0.10</td>
<td></td>
</tr>
<tr>
<td>38.6±13.4</td>
<td>0.34±0.13</td>
<td>0.29±0.10</td>
<td></td>
</tr>
<tr>
<td>&lt;70</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>≥70</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td></td>
</tr>
</tbody>
</table>

*Compared between three groups using one-way analysis of variance. †Post hoc analysis using Tukey test, *TAV-AS vs. CBAV-AS, ‡CBAV-AS vs. CBAV-AR.

### Conclusions

Valvular fibrosis, especially on the aortic side, was significantly greater in patients with CBAV-AS than those without, suggesting the difference in the pathogenesis of AS between CBAV and TAV.

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### P3683 | BESIDE

**Aortic valve replacement with homografts: improving outcome**

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#### Introduction

Aortic valve replacement in patients with aortic valve infective endocarditis is usually performed using classical biological or mechanical prostheses. Prosthetic valve endocarditis after this operation is the most wide-spread complication. Improving postoperative outcome in this category of patients is still a matter of concern.

#### Purpose

To analyze short- and mid-term outcomes after surgical aortic valve replacement with homografts versus mechanical and biological prostheses in patients with infective and prosthetic aortic valve endocarditis.

#### Methods

Prospective single-center study was carried out conducted in the period 2009–2014. Patients with infective or prosthetic endocarditis underwent aortic valve replacement: the 1st group – 46 patients received aortic homografts (cryopreserved homografts – 36 patients (78.3%), homografts sterilized in antibiotics – 8 patients (17.4%), homovalve – 2 patients (4.3%)); the 2nd group – 56 patients received mechanical or biological aortic prostheses. The indications for the operation were the following: infective endocarditis in 24 patients (52.2%), prosthetic endocarditis in 22 patients (47.8%) in the 1st group; infective endocarditis in 48 patients (86.3%), prosthetic endocarditis in 8 patients (13.7%) in the 2nd group of patients. Survival and freedom from recurrent infections were estimated during the follow-up period of 905±546 days.

#### Results

The 30-day postoperative mortality was 10.9% (5 patients) in the homografts group, 5.3% (3 patients) in the prostheses group, which wasn't statistically different (p<0.05). In postoperative period actuarial survival was significantly higher in patients with homografts in comparison with patients with prostheses (p<0.05). The reinfection rate was significantly lower for the homograft group in comparison with the prostheses group of patients, 2.4% and 7.3% respectively (p<0.05).

#### Conclusion

Aortic valve replacement surgery with homografts has better outcomes for survival and absence of reinfection in patients with infective and prosthetic aortic valve endocarditis.

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### P3684 | BESIDE

A novel scoring system may identify high risk patients with low gradient severe aortic stenosis with preserved ejection fraction

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#### Background

Optimal management of low gradient severe aortic stenosis (LG SAS) with preserved left ventricular ejection fraction (LVEF) has not been fully determined. Prior studies showed that LG SAS consists of heterogeneous patients who vary from simple echocardiographic findings (aortic valve area [AVA] <1.0 cm²), mean aortic pressure gradient (MPG) <40 mmHg) to a cluster of clinical syndrome (a high prevalence of elderly, obesity, atrial fibrillation, congestive heart failure etc.). We hypothesized that development of a scoring system combining with clinical characteristics and echocardiographic parameters could better identify high risk patients with LG SAS.

#### Methods

A total of 307 patients with LG SAS (AVA ≤1.0 cm², MPG ≤40 mmHg and LVEF ≥50%) from January 2010 to May 2014 were enrolled at Wake Forest Baptist Medical Center. A risk score was first established by univariate and multivariate logistic regression analysis of 147 patients enrolled in the first two years, which was defined as testing group (TeG). The risk score included eight variables (age ≥75 years, BMI ≥30 kg/m², history of atrial fibrillation, congestive heart failure, chronic obstructive pulmonary disease or renal insufficiency, SVI ≤35 mL/m², and mitral valve systolic pressure [PASP] ≥50 mmHg). SVI and PASP were scored as 2 points each and others as 1 point each with the maximal points of 10. This score system was validated in the remaining cohort (validation group [VaG], n=160). One-year all-cause mortality was used as an endpoint.

#### Results

Fifty percent of patients was male with the average ages 77 years old. The mean AVA index was 0.43±0.08 cm², and mean MPG was 30±55 mmHg. Sixty-one patients (20%) died and 65 patients (21%) underwent aortic valve intervention (AVI) within one year. Echocardiographic parameters, either AVA or MPG failed to identify the patients with increased 1-year mortality. However, in the TeG, patients with a risk score ≥5 showed a 5 fold increase in 1-year mortality compared to patients with a risk score <5 (54% vs. 11%, p<0.001). The AUC of the risk score was 0.73 (95% CI: 0.62–0.84, p<0.001) with the predictive accuracy higher than any single variable. In the VaG, patients with a risk score ≥5 has significant higher 1-year mortality than those with a risk score <5 (31% vs. 14%, p<0.02). When the risk score was applied to patients without AVI in the total cohort (n=242), 1-year mortality was significantly higher in patients with a risk score ≥5 than those with a risk score <5 (45% vs. 14%, p<0.001).

#### Conclusions

Development of a scoring system can stratify high risk patients with LG SAS, suggesting that echocardiographic parameters should be integrated with clinical variables to determine the “true” severity of LG SAS. This finding would be important for patients’ selection for an early AVI.

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### P3685 | BESIDE

**Aortic valve disease**

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#### Background

Current guidelines recommend aortic valve replacement for severe aortic stenosis (AS) in symptomatic and asymptomatic patients when there is impairment of left ventricular (LV) function, defined as an ejection fraction (EF) <50% in the absence of heart failure. Patients with severe AS have a normal LVEF even when symptoms are present. Conversely, LV hypertrophy and abnormal non-invasive measures of LV diastolic function are common in these patients. Most studies reported that higher peak
and mean transaortic gradient and lower aortic valve area are associated with a higher risk of symptomatic deterioration. However, they did not include a comprehensive evaluation of LV diastolic function.

**Purpose:** The aim of the study was to determine whether tissue Doppler measures of LV diastolic function were associated with symptomatic status in patients with severe AS.

**Methods:** We studied 78 consecutive symptomatic and asymptomatic patients with severe AS (38 men, 39 women, mean age 74±7 years). Peak and mean transaortic gradient and aortic valve area (by the continuity equation using peak velocity) were determined using standard two-dimensional and Doppler techniques. Left atrial diameter, area, volume and LVEF were also measured. To assess LV diastolic function, the trans-mitral early (E) and late (A) velocities were measured by pulsed Doppler ultrasound at the mitral leaflet tips. Peak systolic (S') and early (E') diastolic velocities of the medial mitral annulus were measured by pulsed tissue Doppler imaging from the apical four-chamber view. The ratio E/E' was calculated. A value > or = 13 identified an LV-end-diastolic pressure > 15 mmHg. Data were expressed as mean ± standard deviation and compared with the Student's t test. A p<0.05 was considered statistically significant.

**Results:** The symptomatic patients were 50 and asymptomatic 28. There were no significant differences in the mean value of peak aortic gradient (74±7 versus 72±23 mmHg; p=0.5), mean value of mean aortic gradient (48±16 versus 50±10 mmHg; p=0.3), mean value of aortic valve area (0.75±2 versus 0.89±0.3 cm²; p=0.2) between the two groups. On the contrary, the mean value of left atrial diameter (48±8 versus 42±7 mm; p=0.002), mean value of left atrial area (25±8 versus 21±6 cm²; p<0.01), mean value of left atrial volume (104±47 versus 76±29 cm³; p=0.003) were significantly higher in the symptomatic than asymptomatic group. The E/E' ratio was also significantly higher in symptomatic than asymptomatic patients (19±12 versus 12±5; p=0.004). Besides, LVEF was significantly lower in the symptomatic than asymptomatic group (58±0.1% versus 65±11%; p=0.01).

**Conclusions:** In our study patients with AS, abnormal LV diastolic function and a lower LVEF, despite similar peak and mean aortic gradient and aortic valve area, were related to symptomatic status.

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**P3687 | BEDSIDE Impact of myocardial fibrosis measured by cardiac magnetic resonance imaging on reverse left ventricular remodelling after transcatheter aortic valve implantation**

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**Background:** Intertitial myocardial fibrosis is common in patients with aortic stenosis and can be visualised by delayed contrast-enhanced (DCE) cardiac magnetic resonance imaging (MRI). Previous data suggest an inverse correlation between myocardial fibrosis and an improvement of left ventricular (LV) function after aortic valve replacement. We previously observed an improvement of LV function and a decrease of LV mass after transcatheter aortic valve implantation (TAVI).

**Purpose:** The aim of the current study was to evaluate the impact of myocardial fibrosis detected by MRI on post-TAVI LV remodelling.

**Methods:** 61 patients treated with TAVI using a Sapien 3 or Lotus prosthesis between 7/14 and 8/15 who underwent post-TAVI MRI were included into the analysis. Additional interventional DCE, assessing the presence and pattern of myocardial fibrosis, was included. Patients were classified in three groups according to TTE at discharge: (i) group HVS <3 segments with DCE revealed no differences in LV remodelling.

**Results:** In this elderly TAVI cohort, no significant correlation was seen between the presence and severity of myocardial fibrosis visualised by DCE and LV functional or structural remodelling.

**Conclusions:** In this elderly TAVI cohort, no significant correlation was seen between the presence and severity of myocardial fibrosis visualised by DCE and LV functional or structural remodelling.
no differences in the follow-up periods among groups. Death or aortic valve replacement appeared in 71% (34) of group AVA < 0.75 cm², 51% (36) of group AVA 0.75–1 cm² and in 46% (12) of group AVA > 1 cm². Kaplan-Meyer analysis showed significantly difference survival curves for appearance of adverse events with p=0.012 (Figure 1).

Table 1. Baseline characteristics and echocardiographic indices

<table>
<thead>
<tr>
<th></th>
<th>AVA &lt; 0.75 cm²</th>
<th>AVA 0.75–1 cm²</th>
<th>AVA &gt; 1 cm²</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, year (mean ± SD)</td>
<td>76 ± 16</td>
<td>73 ± 15</td>
<td>74 ± 20</td>
<td>0.04</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>34 (71%)</td>
<td>44 (63%)</td>
<td>10 (38%)</td>
<td>0.022</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>38 (79%)</td>
<td>54 (77%)</td>
<td>22 (85%)</td>
<td>0.725</td>
</tr>
<tr>
<td>Dyspl哈dima, n (%)</td>
<td>28 (58%)</td>
<td>34 (49%)</td>
<td>15 (51%)</td>
<td>0.517</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>18 (37%)</td>
<td>18 (26%)</td>
<td>11 (42%)</td>
<td>0.207</td>
</tr>
<tr>
<td>Presence of symptoms, n (%)</td>
<td>21 (44%)</td>
<td>44 (64%)</td>
<td>17 (65%)</td>
<td>0.065</td>
</tr>
</tbody>
</table>

Conclusions: Despite of current guidelines recommend the use of AVA < 1 cm² to diagnose severe AS, evolution of patients with AVA between 0.75–1 cm² is similar to patients with AVA between 1–1.5 cm². Therefore, in patients with AVA between 0.75–1 cm² surgical treatment indication should be based on the integration of several parameters and not only AVA calculated by continuity equation.

P3691 | BEDSIDE

Atrial fibrillation increases short-term outcomes and 1-year mortality after transcatheter aortic valve implantation: an analysis of the brazilian multicenter TAVI registry (RIBAC)

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Introduction: Risk evaluation and patient selection for transcatheter aortic valve implantation (TAVI) are evolving and the impact of atrial fibrillation (AF) still unknown. The goal was to evaluate the impact of previous AF (PREAF) and new onset perioperative AF (NOPAF) in the short and long-term outcomes in patients who underwent TAVI.

Methods: The RIBAC enrolled 819 TAVI patients (Jan2008-Dec2014). Outcomes defined according to VARC-II included immediate mortality (72%), 30-day and 1-year complications and mortality. Groups: No-AF, PREAF and NOPAF. Univariate analysis was performed to detect variables associated with short and long-term complications and all-cause and cardiovascular mortality. Survival analysis with Kaplan-Meyer and Cox Regression.

Results: 49% male; 82±7 years. No-AF 684 patients (83.5%); PREAF 109 patients (13.3%); NOPAF 26 patients (3.2%). 96% of transmural access. PREAF group showed higher prevalence of pulmonary hypertension and NYHA Class III-IV. 30-day mortality 8.9%, immediate mortality 5% and procedural mortality 11.7%. NOPAF showed increases in hospital stay (No-AF 12±18, PREAF 14±23, NOPAF 24±70, p=0.024), and a nonsignificant trend to increased 30-day incidence of stroke, vascular complications and death. PREAF increase 1-year incidence of all-cause death (No-AF 19.6%; PREAF 35.7%; NOPAF 16.1%; p=0.001). In a fully adjusted Cox regression model, previous FA was an independent predictor of 1-year all-cause death (HR1.92; 95CI:1.31–2.81; p=0.001). Other independent predictors include age, severe HF and mitral regurgitation.

Conclusion: In TAVI patients, New Onset AF is associated with short-term morbidity and longer hospital stay. Previous AF is an independent predictor of 1-year all-cause death after TAVI. The presence of AF should be included in the preoperative risk evaluation of patients for TAVI.

P3692 | BEDSIDE

The effect of pre-procedural significant mitral regurgitation upon mortality after transcatheter aortic valve intervention for severe aortic stenosis


Background: The presence of concomitant mitral regurgitation (MR) is a common issue in patients with severe aortic stenosis and negatively affects patient outcome. Although aortic gradient reduction and left ventricular reverse remodeling can reduce MR after transcatheter aortic valve intervention (TAVI), reported data are contradictory. Our purpose was to investigate the prognostic impact of both pre-procedural and post-procedural MR in patients following TAVI with a self-expandable valve.

Methods: Patients with severe and symptomatic aortic stenosis (effective orifice area [EOA]<1 cm²) referred for TAVI with a self-expandable valve at our institution were consecutively enrolled. Prospectively collected echocardiographic data matching according to the method of annual assessment PVL was observed in 24 of 359 (6.7%) and 22 of 359 (6.1%) patients in TOE and MSCT group respectively (p=0.44). However, the rate of post balloon dilatation in the MSCT group (39/359, 10.9%) compared to TOE group (71/359, 19.8%) remained significantly higher (p=0.001). There was also significantly higher rate of post balloon dilatation in patients treated with CoreValve (p=0.0001).

Conclusion: The modality of imaging in annulus sizing (TOE vs MSCT) in TAVI patients does not have an impact on PVL at the end of the procedure.
before and after TAVI were retrospectively analyzed in all patients. Patients were stratified into two groups according to severity of MR: ≥grade 3 were defined as significant and <grade 2 as non-significant. Change in MR severity was assessed by comparison of baseline and 30-day echocardiograms. Primary clinical end-point was all-cause mortality defined according to the criteria proposed by the Valve Academic Research Consortium-2.

Results: We included 157 patients (mean age: 79.9±6.9 years) in the study and in 40 of them, significant MR (≥grade 3) was present prior to TAVI (25.4%). These patients were of higher perioperative risk (logistic EuroScore 28.2±11.0% versus 24.2±9.6%, p=0.02) had higher systolic pulmonary pressure (48.0±13.1mmHg versus 41.4±10.2mmHg, p<0.01) and were more dyspnoeic (New York Heart Association class IV: 30% versus 25.5%, p=0.001). The primary clinical end point occurred in 41 patients (26.1%) during a follow-up period of 26.8±20.7 months. Patients with significant MR prior to TAVI had a worse 30-day survival rate (37.5% versus 22.2%, p<0.01). Significant MR was independently associated with mortality [OR 2.100, 95% CI (1.491–2.906), p<0.01]. Of patients with significant MR only 30% had improvement in MR severity and appears to be independently associated with increased all-cause mortality.

Conclusions: Significant MR is a common finding in patients undergoing TAVI and appears to be independently associated with increased all-cause mortality. However, almost half also present significant improvement in MR severity and commodiation provided by the vendor specifications. A S3 valve was considered oversized when the S3 annular area was greater than the systolic MDCT annular area. The percentage of oversizing (positive percentage) or undersizing (negative percentage) was calculated using the following formula: % oversizing = (S3 annular area - MDCT area) / MDCT area × 100. Aortic valve calcium score was performed by MDCT in a subgroup of 135 S3 prosthesis (% of prosthesis length above to the annulus level) was measured. The percentage of oversizing (positive percentage) or undersizing (negative percentage) was calculated using the following formula: % oversizing = (S3 annular area - MDCT area) / MDCT area × 100. Aortic valve calcium score was performed by MDCT in a subgroup of 135 S3 prosthesis (% of prosthesis length above to the annulus level) was measured. The percentage of oversizing (positive percentage) or undersizing (negative percentage) was calculated using the following formula: % oversizing = (S3 annular area - MDCT area) / MDCT area × 100. Aortic valve calcium score was performed by MDCT in a subgroup of 135 S3 prosthesis (% of prosthesis length above to the annulus level) was measured.

Methods: The first 196 pts. treated with S3 were analyzed (182, 92.9% transcatheter aortic valve implantation with TAVI). We included 206 patients (81.6±5 years; 49% male; mean STS score of reference was 66 Km (0.2–154 Km). The 28% of the procedures were performed under general anaesthesia with full percutaneous intervention in 90%. Pre-dilatation was performed in 74% of the patients and 20% of valves were post-dilated. The success of the device was achieved in 97%. Regarding the outcomes, in-hospital mortality and at 30 days was 4.9% and 4.4% respectively (2.45% cardiovascular and 2.45% non-cardiovascular death). No annular ruptures or aortic dissections were described. There were 4 cardiac perforations and 3 coronary occlusions which were managed percutaneously. No transfers to urgent or elective surgery occurred. The incidence of major bleeding and major vascular complications was 8% and 3% respectively and 26% required a definitive pacemaker insertion.

Results: We included 206 patients (81.6±5 years; 49% male; mean STS score of reference was 66 Km (0.2–154 Km). The 28% of the procedures were performed under general anaesthesia with full percutaneous intervention in 90%. Pre-dilatation was performed in 74% of the patients and 20% of valves were post-dilated. The success of the device was achieved in 97%. Regarding the outcomes, in-hospital mortality and at 30 days was 4.9% and 4.4% respectively (2.45% cardiovascular and 2.45% non-cardiovascular death). No annular ruptures or aortic dissections were described. There were 4 cardiac perforations and 3 coronary occlusions which were managed percutaneously. No transfers to urgent or elective surgery occurred. The incidence of major bleeding and major vascular complications was 8% and 3% respectively and 26% required a definitive pacemaker insertion.

Conclusions: In this multicentre registry, survival at discharge and 30-day are similar to those published in centres with on site cardiac surgery. The few complications recorded were all managed percutaneously. Nowadays, with the improvement of self-expandable devices and the higher experience on the selection of patients, the restriction of TAVR interventions for centres without on site cardiac surgery does not seem reasonable.

P3695 | BEDSIDE
Paravalvular aortic regurgitation after transcatheter aortic valve implantation with the Sapien 3 valve: impact of valve sizing, implantation height and valve calcification

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Background: Even a mild paravalvular regurgitation (PVR) after transcatheter aortic valve implantation (TAVI) has been found to have a negative impact on outcomes. We sought to evaluate the possible role of elevated TGF-β level in the development of a mild or greater PVR (OR 0.96 [95% CI 0.92–0.99], p=0.049). By ROC curve analysis, an area oversizing of 4.91% resulted as the best cut-off for the development of a mild or greater PVR for the S3 valve (sensitivity 64%, specificity 62%, area under the curve, 64.2%).

Conclusion: Under sizing of the S3 valve based on the MDCT-measured area of the annulus seems to be a major predictor of development of a mild or greater PVR after TAVR. Valve calcification had less impact on the development of PVR in the Valve Academic Research Consortium-2.

Aims: To evaluate the the impact of implantation height, valve calcification and valve sizing on PVR after TAVI.

Methods: The first 196 pts. treated with S3 were analyzed (182, 92.9% transcatheter aortic valve implantation with TAVI). We included 206 patients (81.6±5 years; 49% male; mean STS score of reference was 66 Km (0.2–154 Km). The 28% of the procedures were performed under general anaesthesia with full percutaneous intervention in 90%. Pre-dilatation was performed in 74% of the patients and 20% of valves were post-dilated. The success of the device was achieved in 97%. Regarding the outcomes, in-hospital mortality and at 30 days was 4.9% and 4.4% respectively (2.45% cardiovascular and 2.45% non-cardiovascular death). No annular ruptures or aortic dissections were described. There were 4 cardiac perforations and 3 coronary occlusions which were managed percutaneously. No transfers to urgent or elective surgery occurred. The incidence of major bleeding and major vascular complications was 8% and 3% respectively and 26% required a definitive pacemaker insertion.

Results: We included 206 patients (81.6±5 years; 49% male; mean STS score of reference was 66 Km (0.2–154 Km). The 28% of the procedures were performed under general anaesthesia with full percutaneous intervention in 90%. Pre-dilatation was performed in 74% of the patients and 20% of valves were post-dilated. The success of the device was achieved in 97%. Regarding the outcomes, in-hospital mortality and at 30 days was 4.9% and 4.4% respectively (2.45% cardiovascular and 2.45% non-cardiovascular death). No annular ruptures or aortic dissections were described. There were 4 cardiac perforations and 3 coronary occlusions which were managed percutaneously. No transfers to urgent or elective surgery occurred. The incidence of major bleeding and major vascular complications was 8% and 3% respectively and 26% required a definitive pacemaker insertion.

Conclusions: In this multicentre registry, survival at discharge and 30-day are similar to those published in centres with on site cardiac surgery. The few complications recorded were all managed percutaneously. Nowadays, with the improve-
Conclusions: Despite the overall benign outcome, we found the obvious MVP progression in young person over long-term follow-up. Elevated TGF-β1 level may contribute to the excessive progression of the MVP and appear to be potential target in its limiting.

P3696 | BEDSIDE
Prognostic significance of right ventricular dysfunction in patients with functional mitral regurgitation and left ventricular systolic dysfunction undergoing MitraClip
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Background: Functional mitral regurgitation (MR) is commonly associated with heart failure and left ventricular (LV) dysfunction. Percutaneous edge-to-edge mitral valve repair using the MitraClip has emerged as a novel option for the treatment of severe MR patients with high surgical risk. Right ventricular (RV) dysfunction is known as an important predictor of patients with heart failure. However, the influence of RV dysfunction on clinical outcomes of functional MR and LV dysfunction after MitraClip remains unclear.

Purpose: N the present study, we aimed to clarify the prognostic significance of RV dysfunction in patients with LV dysfunction and functional MR undergoing MitraClip implantation.

Methods: We evaluated 117 severe functional MR patients with reduced LV ejection fraction (LVEF) ≤40% successfully treated by MitraClip in our institute. We defined RV dysfunction as tricuspid annular plane systolic excursion (TAPSE) ≤15mm. Responders of N-terminal pro-B-type natriuretic peptide (NT-pro BNP) were defined as patients whose NT-pro BNP levels decrease by >30%. The median follow-up period was 707±590 days.

Result: RV dysfunction was observed in 41 patients (35%). Mean age and gender were similar between two groups. Prior history of coronary artery bypass graft tended to be more common in patients with RV dysfunction (34% vs. 18%, p=0.057). Atrial fibrillation was more frequently complicated with patients with RV dysfunction (68% vs. 38%, p=0.003). Prevalence of other comorbidities including hypertension, diabetic mellitus, chronic kidney disease, and prior history of myocardial infarction was not different. Baseline New York Heart Association class and NT-pro BNP level were also comparable between patients with and without RV dysfunction. MR grade at baseline and at hospital discharge were similar between two groups. Baseline LVEF was not different between patients with and without RV dysfunction (23.8±12.7% vs. 26.7±7%, p=0.106). Six months after the procedure, NT-pro BNP levels at 6 months after the procedure tended to be higher (7.318±8.385 vs. 4.009±5.987 pg/mL, p=0.094) and responders of NT-pro BNP were less common (29% vs. 65%, p=0.005) in patients with RV dysfunction. LVEF at 6 months after the procedures was significantly lower in patients with RV dysfunction (25.5±6 vs. 30.9±5, p=0.006). Kaplan-Meier curves and the log-rank test revealed that the survival rates of patients with RV dysfunction were significantly lower than those of LV dysfunction (p=0.008). After adjustment for covariates, as well as older age (>75 years), RV dysfunction was still associated with survival (hazard ratio 1.975, p=0.042).

LV dysfunction patients undergoing MitraClip in association with sustained increasing NT-pro BNP levels and impaired improvement of LV function.

Acknowledgement/Funding: The Japan Society for the Promotion of Science

P3697 | BEDSIDE
Organic vs. functional mitral regurgitation in patients undergoing transcatheter aortic valve replacement for severe aortic stenosis
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Introduction: Many patients undergoing TAVR for severe or inoperable aortic stenosis (AS) have concomitant mitral regurgitation (MR). Prior work has suggested that MR is correlated with echocardiographic and clinical outcomes. We suggest that Organic MR confers a higher risk of cardiac complications than functional MR.

Methods: High risk or inoperable patients who underwent TAVR for AS at Emory University or Hadassah University had echocardiograms at baseline and early follow up (within 30 days) and were followed for long-term clinical outcomes. MR was graded as functional or organic, and minimal (none-mild) or significant (mod-severe).

Results: 257 patients with MR (53% functional, 47% organic) underwent TAVR reducing mean aortic valve gradients by 36 mmHg. Patients with functional MR were more likely to be male but otherwise had similar baseline characteristics and early follow-up outcomes. Significant functional MR patients (n=53) had a greater improvement in MR and pulmonary artery systolic pressure (PASP) vs. significant organic MR patients (n=55) (38% vs. 26% achieving minimal MR, p<0.001; 5.9 mmHg vs. 3.4 mmHg PASP, p=0.03). Organic MR was associated with a worse survival free of death/CHF than functional MR (mean follow up = 738 days; p=0.03). Multivariate analysis showed functional MR, an Edwards valve, and a larger mean change in AV gradient were protective against death/CHF (HR=0.49, 0.16, 0.92 P=0.002, 0.001, 0.01 respectively).

Conclusions: TAVR patients with functional MR had greater improvements PASP and MR severity, as well as increased survival free of death/CHF compared to organic MR.

P3698 | BEDSIDE
Interleukin-6 receptor gene polymorphism rs2229238 is associated with hypoxia-induced interleukin-6 blood level and bioprosthetic mitral valve calcification
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Background: Valvular calcification precedes the development of valvular stenosis and may represent an important early phenotype for valvular heart disease. Methods: Here, we have examined whether functional polymorphisms within innate immunity genes (total 30 polymorphisms of 13 genes) predict the risk of mitral valve disease and bioprosthetic mitral valve failure caused by calcification. A total of 80 consecutive Russian patients who underwent mitral valve replacement surgery due to mitral valve disease and 300 healthy age, gender, and ethnicity-matched blood donors have been recruited in the study. Genotyping has been carried out using the TaqMan SNP genotyping assay. The blood expression level of cytokines (IL-1β, -6, -8, -10, -12p40, and TNF-α) has been measured by enzyme-linked immunosorbent assay (ELISA) using the respective kits of eBioscience (CA, USA) according to manufacturer’s instructions.

Results: We found that C/C genotype of rs2228145 polymorphism within IL6R gene, C/T genotype of rs2229238 polymorphism within IL6R gene, and C/C genotype of rs2227306 polymorphism within IL6 gene are significantly associated with increased interleukin-6 and interleukin-6 blood level, respectively. Moreover, C allele of rs1800796 polymorphism within IL6 gene and C/T genotype of rs3804099 polymorphism within TLR2 gene have been associated with increased mitral valve disease risk (OR=1.96, 95% CI: 1.03–3.72, P=0.046 and OR=2.17, 95% CI: 1.28–3.67, P=0.004, respectively) whilst C/T genotype of rs2229238 polymorphism within IL6R gene has correlated with decreased mitral valve disease risk (OR=0.57, 95% CI: 0.32–1.01, P=0.047). Logistic regression analysis has shown that the C/T genotype of the rs2229238 polymorphism within the IL6R gene correlates with mitral valve failure (OR=3.81, 95% CI: 1.22–11.91, P=0.021).

Conclusions: We suggest that C/T genotype of rs2229238 polymorphism within IL6R gene may increase interleukin-6 blood level and may thus promote bioprosthetic mitral valve calcification.

Acknowledgement/Funding: Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, Russian Federation
Postoperative right ventricular dysfunction is associated with mortality and morbidity

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Background: Right ventricular (RV) dysfunction can result as a consequence of chronic mitral regurgitation (MR), and is known to adversely influence the operative outcome of mitral valve (MV) repair or replacement. Little is known about the impact of RV dysfunction on prognosis in the post-operative period.

Purpose: This study sought to determine the prevalence of RV dysfunction after MV surgery and evaluate the influence of RV dysfunction in the early and late follow-up periods on outcomes post MV surgery.

Methods: 130 patients who underwent MV surgery for moderate MR during 2008-2012 were part of a single centre retrospective study. Tissue Doppler imaging, plane systolic excursion (TAPSE ≤ 16mm) on transthoracic echocardiography was determined to indicate the presence of RV dysfunction. Pearson Chi-square test was used to analyse the relation of RV dysfunction at both 6 months and beyond 6 months post surgery to post-operative outcomes.

Results: Early RV dysfunction within 6 months of surgery was present in 76 (73.08%) patients and 50 (38.46%) patients had late RV dysfunction beyond 6 months post surgery. At 6 months follow-up, left ventricular ejection fraction (LVEF ≤ 40%) but not RV dysfunction (OR=1.79, p=0.18) was associated with cause intolerable outcome of all-cause mortality, hospital admission for congestive cardiac failure (CCF), and stroke (OR = 5.38, p=0.02). Beyond 6 months post surgery, both TAPSE ≤ 16mm (OR=13, p=0.001) and LVEF ≤ 40% (OR=17.74, p value < 0.001) were independent predictors of composite outcome. Incidence of composite outcome significantly worse in patients with late RV dysfunction (36% vs. 10%, p<0.001).

Conclusions: RV dysfunction and LVEF ≤ 40% beyond 6 months follow-up predicts for composite outcome of death, CCF, and stroke. Findings support emerging view that RV dysfunction may be considered a composite outcome, for non-invasive monitoring and for research.

P3700 | BEDSIDE
Percutaneous mitral valve repair improves exercise capacity and quality of life in patients with mitral regurgitation with and without atrial fibrillation

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Background and objective: Significant mitral regurgitation (MR) leads to exercise intolerance, reduced quality of life and recurrent rehospitalisation in patients (pts) with or without relevant reduction of left ventricular ejection fraction (LVEF). These symptoms can be aggravated by several comorbidities such as atrial fibrillation, which is common in these pts. Since percutaneous mitral valve repair has become a routine procedure in pts with MR grade 3+/4+, we sought to evaluate the effects of atrial fibrillation on procedural and clinical outcomes after MitraClip (MC) procedure.

Methods and results: A total of 624 pts with MR grade 3+/4+ (degenerative MR 328, rheumatic MR 196) underwent mitral valve surgery according to heart team decision under MC procedure at our centre from 08/2008 to 09/2015. These pts were predominantly male (61.2%), had a median age of 75±9.3 years and high surgical risk expressed by a median logEuroScore of 20.8 (11.7–32.8). The majority of pts suffered from atrial fibrillation (66.7%). These pts were older (76.4±7.39 years, p=0.0061) and had a higher logEuroScore (21.8 vs. 18.4, p=0.0017), but the presence of comorbidities e.g. coronary artery disease, COPD, chronic kidney failure and stroke did not differ significantly between both groups. Although LVEF ≥ 40% (p=0.004) and MR grade 3+/4+ (50.3/49.8% vs. 51.3/48.7%, p=0.62) were similar at baseline, pts with atrial fibrillation had worse NYHA class (60%) were frequent, being prosthesis (52%) and diabetes mellitus (27%) the most frequent. Main complications during hospitalization were heart failure (52%), persistent in-10% (37%) and renal failure (33%). The microorganisms more frequently isolated were: Escherichia coli (35%), Pseudomonas aeruginosa (12%) and Serratia (8%), with a high frequency of polymicrobial infection (29%). Vegetation appeared in 85% of patients, perianul arrhythmia complication in 19% and moderate to severe valve insufficiency in 58%. Surgery was performed in 46%, only 30% in an urgent way, being the main indications heart failure (55%), prophylaxis location (46%) and persistent infection (27%). In-hospital mortality was 38%, being the principal causes of death uncontrolled infection (35%) and heart failure (15%).

Predictors of mortality were heart failure (70 vs 41%, p=0.039); renal failure (50 vs 22%, p=0.035) and septic shock (55 vs 13%, p=0.001).

Conclusions: Non-HACEK Gram-negative bacilli causes 5% of infective endocarditis in our series. It affects patients with previous heart disease and comorbidities, leading to high in-hospital mortality. Heart failure, renal failure or septic shock are associated with higher in-hospital mortality.

P3701 | BEDSIDE
Profile of non-HACEK gram-negative bacilli infective endocarditis

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Introduction: Non-HACEK Gram-negative bacilli infective endocarditis is a very severe illness insufficiently studied. Only one small retrospective series and barely cases have been published within last years regarding this entity.

Objective: To analyse the clinical, microbiological and echocardiographic profile and the outcomes of patients with left-sided infective endocarditis due to non-HACEK Gram-negative bacilli, and to look for mortality predictors in those patients.

Methods: Among 1020 episodes of definite infective endocarditis consecutively diagnosed in three tertiary centres, between 1996 and 2014, 52 were caused by non-HACEK Gram-negative bacilli (5%). We described the clinical, microbiological, echocardiographic and outcome of those patients and performed a univariate analysis to look for mortality predictors.

Results: Mean age was 66±12 years, 42% were male and 35% noncompliant. Previous heart disease (87%), predisposing conditions (60%) and comorbidities (60%) were frequent, being prosthetic (52%) and diabetes mellitus (27%) the most frequent. Main complications during hospitalization were heart failure (52%), persistent in-10% (37%) and renal failure (33%). The microorganisms more frequently isolated were: Escherichia coli (35%), Pseudomonas aeruginosa (12%) and Serratia (8%), with a high frequency of polymicrobial infection (29%). Vegetation appeared in 85% of patients, perianul arrhythmia complication in 19% and moderate to severe valve insufficiency in 58%. Surgery was performed in 46%, only 30% in an urgent way, being the main indications heart failure (55%), prophylaxis location (46%) and persistent infection (27%). In-hospital mortality was 38%, being the principal causes of death uncontrolled infection (35%) and heart failure (15%).

Predictors of mortality were heart failure (70 vs 41%, p=0.039); renal failure (50 vs 22%, p=0.035) and septic shock (55 vs 13%, p=0.001).

Conclusions: Non-HACEK Gram-negative bacilli causes 5% of infective endocarditis in our series. It affects patients with previous heart disease and comorbidities, leading to high in-hospital mortality.
longer durability (table 1). When histological findings in OMP and IMP groups were compared, no differences were found. Glutaraldehyde treated prosthesis had less calcification (42.9 vs. 6.1%) but an increment of inflammatory markers. Calcification was greater in mitral prosthesis (35.4%) than in aortic (23.8%) or tricuspid ones (6.1%). Hypertension and diabetes were related with more calcification. In case of ascending aortic, inflammatory cells without evidence of infection were more frequent found (44% vs 16%).

Conclusions: Hyaline fibrosis and calcification are the most common histological findings in dysfunctional bioprosthesis. Inflammation appears to play an important role in tissue degeneration and active smoking is associated with increased presence of inflammatory cells. Future studies, specifically designed, will determine whether these findings can be translated to durability.

P3704 | BEDSIDE
Raised red cell distribution width as a prognostic marker in patients undergoing valve surgery

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Background: Several studies have reported that elevated red cell distribution width (RDW) levels are associated with poor outcomes in patients with cardiovascular diseases such as coronary artery disease, idiopathic pulmonary hypertension and chronic heart failure. Their prognostic utility in patients with valvular disease undergoing valve surgery is unknown.

Purpose: The aim of the study was to investigate the prognostic value of RDW in patients undergoing valve replacement or repair surgery.

Methods: A prospective study was conducted on a group of 315 consecutive patients with hemodynamically significant valvular heart disease (aortic, mitral, and/or tricuspid) who underwent elective valvular surgery. Preoperative complete blood count, data on risk factors, the course of operations and the postoperative period were assessed. The pre-defined primary endpoint at the 30-day follow-up or until the patient was discharged from the hospital was total mortality. Univariate analysis followed by multivariate regression analysis were performed.

Results: The primary endpoint occurred in 17 (5.4%) patients. At univariate analysis coronary artery disease (OR 2.805; 95% CI 1.010–7.791; p = 0.04), diabetes mellitus (OR 3.285; 95% CI 1.195–9.029; p = 0.02), red blood cell count (OR 0.112, 95% CI 0.041–0.306; p = 0.0001), hemoglobin level (OR 0.518; 95% CI 0.379–0.705; p = 0.0001), glomerular filtration rate (OR 0.972; 95% CI 0.944–1.001; p = 0.05), creatinine (OR 1.017; 95% CI 1.000–1.033; p = 0.05) and RDW (OR 1.837; 95% CI 1.345–2.508; p = 0.0001) were associated with the occurrence of the death. At multivariate analysis RDW (OR 1.451; 95% CI 0.005–2.096; p = 0.04) remained independent predictor of the primary endpoint. ROC analysis determined a cut off value of RDW for the prediction of the occurrence of the death at 14.4%. Figure 1 depicts Kaplan–Meier event-free survival curves for primary endpoint according to the cut-off value of RDW.

Conclusions: Elevated RDW is associated with a worse outcome following heart valve repair or replace independent of RBC. RDW may be helpful in selecting patients with a higher risk for postoperative complications requiring more attention while being qualified for surgery.

P3705 | BEDSIDE
Effect of infliximab treatment on QT intervals in patients with ankylosing spondylitis

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Background: Cardiovascular complications are one of the most common and the most severe extrascalar manifestations of ankylosing spondylitis (AS). Infliximab, a monoclonal antibody against tumor necrosis factor, is widely used in the treatment of AS. QT dispersion (QTD), which relates to left ventricular function and is used as an index of cardiac dysrhythmia, may be useful as a prognostic guide. Early detection of possible cardiac involvement may not be clinically evident, whereas it may be detected by electrocardiography.

Objectives: The aim of this prospective study was to assess the effect of infliximab treatment on QT intervals in patients with AS.

Methods: Twenty-one patients (17 females and 4 males) with AS who were in the active phase of disease (Bath Ankylosing Spondylitis Disease Activity Index score > 4) were enrolled in the study. Infliximab was administered intravenously at a dosage of 5 mg/kg at weeks 0, 2, and 6 and every 6 weeks thereafter. QT intervals were recorded before and after 6 months of treatment.

Results: QT corrected (QTc) for heart rate was significantly reduced in the patients with AS after 6 months of infliximab therapy (406±5.5 vs 388±6.6 milliseconds; P = 0.029). There was no difference in the QTD dispersion (34.3±11.1 vs 34.1±8.6; P = 0.171). Body mass index and lipid profile were slightly increased after the treatment, but the difference was statistically insignificant.

Conclusion: Inflammation can affect the ventricles with an unknown mechanism, and QcT may be slightly prolonged as a result in the active phase of AS. In our study, QcT was shortened under infliximab therapy by suppressing inflammation. Therefore, this effect may protect patients with AS from fatal arrhythmias and sudden cardiac death.

P3706 | BENCH
Inhibition of aortic valve calcification by local delivery of zoledronic acid. A PET/CT study

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Background: Bisphosphonates have been proven to have a beneficial effect on inhibition of aortic valve calcification in an experimental animal model of aortic stenosis.

Methods: Sixteen New Zealand rabbits were placed on vitamin D enriched alfalfa diet for 3 weeks. At that time a cardiac ultrasound was performed to assess the aortic stenosis and aortic calcification of the aortic valve by measuring aortic valve area (AVA). Subsequently half of them were treated with local delivery of a mixture containing 500 μg of zoledronate that was delivered on the cusps of the aortic valve, by a dedicated balloon catheter. A placebo mixture was administered on the rest eight animals, which were used as controls. At 28 days all animals were sacrificed. All aortic valves and proximal parts of the ascending aorta were fixed in 10% neutralized buffered formalin solution for 24 hours. The cusps were separated then embedded in paraffin waxes. Serial sections 4 μm thick were obtained and routinely stained with eosin–hematoxylin and von Cossia stain for calcium deposits. The stained slides were digitized using a light microscope (Nikon Eclipse 80i, Nikon Corp., Tokyo, Japan).
The file processed in a computer with the appropriate software (Image Pro Plus, version 5.1, MD, USA), and the calcified areas for both the aortic valve and the aorta were expressed as the percentage to the total area. The difference between the extent of calcification between the proximal part of the aorta and the cusps was calculated and assigned as ΔC. Statistical analyses were carried out with the Statistical Package for the Social Sciences (SPSS, Chicago, IL) release 13.0.

Results: At baseline, all animals developed aortic valve stenosis with severe calcification. No differences regarding the AVA were recorded between both groups. (0.21±0.17 vs 0.21±0.03, p=0.53). In all animals the local delivery of zoledronate and placebo mixtures was successful and uncomplicated. The animals treated with zoledronate had a significantly lower expression of calcium compared to the controls (16.66±0.99 vs 26.41±1.84% of the area, p<0.0001). ΔC was significantly higher in the zoledronate group compared to the control (5.38±6.24 vs -2.90±5.54, p=0.001)

Conclusions: Local delivery of zoledronate in the aortic cusps of an experimental model of aortic stenosis results in an attenuation of the progress of calcification.

ACUTE PULMONARY EMBOLISM

P3707 | BEDSIDE
New onset paroxysmal atrial fibrillation in the course of the acute pulmonary embolism
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The potential relationship between acute pulmonary embolism (PE) and atrial fibrillation (AF) is poorly investigated. Little is known about the clinical consequences of a paroxysmal AF occurring for first time during PE episodes.

Purpose: To analyze clinical characteristics and prognosis in patients with the first episode of paroxysmal AF (newAF) appearing in the course of PE.

Methods: From the cohort of 391 consecutive patients with PE 31 subjects with newAF were selected. Their characteristics including medical history, clinical course of PE incident (variables enclosed in sPESI score, laboratory and ECHO parameters), short and long-term all-cause mortality was compared with 319 patients with PE and sinus rhythm (SR) and 32 patients with PE and continuous AF (cAF).

Results: NewAF patients were older, more often had history of stroke, less often deep vein thrombosis (DVT) than patients from SR group (Table 1). Among ECHO parameters newAF patients had the highest pulmonary artery systolic pressure (sPAP) and the shortest pulmonary artery acceleration time (AcT). Compared with cAF group newAF patients had lower previous stroke history, better renal function, normal LV EF and smaller left atrial (LA) diameter. Furthermore, among newAF patients in-hospital mortality was comparable with SR patients and significantly lower than among cAF patients.

Table 1

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group</th>
<th>Mean ± SD</th>
<th>p value vs newAF</th>
<th>p value vs cAF</th>
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<tr>
<td>Age, years</td>
<td>61.9±7.1</td>
<td>75.4±10.3</td>
<td>&lt;0.001</td>
<td>72.1±12.5</td>
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<td>History of stroke</td>
<td>44</td>
<td>80</td>
<td>0.02</td>
<td>60</td>
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<td>DVT</td>
<td>55.9±16.9</td>
<td>55.8±14.9</td>
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<td>42.6±15.5</td>
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<tr>
<td>sPESI score (%)</td>
<td>5</td>
<td>13</td>
<td>0.001</td>
<td>22</td>
</tr>
<tr>
<td>LV EF, %</td>
<td>49</td>
<td>32</td>
<td>0.02</td>
<td>28</td>
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<tr>
<td>LA, mm</td>
<td>3.7±0.5</td>
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<tr>
<td>sPAP, mmHg</td>
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<td>59.2±15.6</td>
<td>0.006</td>
<td>51.6±14.7</td>
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<tr>
<td>AcT, ms</td>
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<td>61.2±20.1</td>
<td>0.035</td>
<td>71.2±23.5</td>
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<tr>
<td>In-hospital mortality</td>
<td>5</td>
<td>6.5</td>
<td>0.001</td>
<td>25</td>
</tr>
<tr>
<td>Long term mortality</td>
<td>34</td>
<td>48</td>
<td>0.001</td>
<td>59</td>
</tr>
</tbody>
</table>

Conclusions: Patients with newAF in the course of PE constitute a separate population. Further systematic impairment of the parameters reflecting right ventricle overload indicates the relation between severity of PE and newAF. NewAF has no impact on short and long-term mortality.

P3708 | BENCH
Repetitive intravenous thrombin injections result in pulmonary arterial endothelial dysfunction in a mouse model of sublethal acute pulmonary embolism
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Background: Usually, acute pulmonary embolism (PE) result from deep vein thrombosis (DVT) and undergo total or near-total resolution. However, in a considerable amount of patients, particularly after recurrent PEs, emboli are not completely resolved. Caused by yet unidentified mechanisms, a process of remodeling ultimately results in chronic thromboembolic pulmonary hypertension (CTEPH). The mechanisms that underlie the chronication of embol and ultimately the development of CTEPH remain uncertain. We therefore aimed to investigate the effect of single or repetitive sublethal experimental pulmonary embolism on the pulmonary vascular remodeling and further comparing it to the IVC (interior vena cava)-stenosis model, an established model of DVT.

Methods: C57BL/6 mice were anaesthetized with isoflurane and monitored. Sublethal experimental PEs were induced by i.v. injection of thrombin 2.5–5 Units (U) per 100 g bodyweight. Post-injection 95 to 160 Ukg bolus and 2.5 to 5 Ukg/min infusion of thrombin. Acetylcholine and H&E staining. Right ventricular dimensions and IVC-thrombi were imaged and pulmonary artery (PA)-pressure was delineated by high frequency ultrasound. PA vasoconstriction as well as endothelial dependent and –independent relaxation was analyzed by exposure to increasing concentrations to phenylephrine, acetylcholine and glyceryl trinitrate after mounting of segments of the pulmonary trunks on force transducers under physiologic conditions. ROS-burden was evaluated by L-012-derived chemiluminescence and dihydroethidium (DHE) staining of PA cryosections.

Results: PEs after injection of thrombin were confirmed by a sudden bradycardia or asystole, apnea or bradypnea and an increase in PA-pressure as observed by echocardiography. While after a single thrombin injection symptoms were generally resolved and PA-pressure normalized within minutes, the time to recovery lengthened with every injection (after 12h or repetitive thrombin injections, isometric tension studies revealed a significant endothelial dysfunction in PAs placed from embolized animals as compared to untreated animals. Importantly, no APE or PH and no PA endothelial dysfunction were detected after IVC-ligation. Further, the levels of superoxide were significantly increased in triple-embolized mice as compared to PAs from control mice or after IVC-ligation.

Conclusion: Although the subtotal IVC-ligation is an established model to study deep vein thrombosis, it does not model PEs as the most important complication of DVT. Repetitive injection of thrombin results in sublethal PE and PA endothelial dysfunction, which could initiate remodeling cascade resulting in CTEPH. Further studies are necessary to further elucidate the underlying mechanisms.

Acknowledgement/Funding: Federal Ministry of Education and Research Grant BMBF 01EO1003

P3709 | BENCH
Comparison of simplified PESI, CHA2DS2-VASc and HAS-BLED scores for the prediction of net-adverse clinical outcome in patients with pulmonary embolism
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Background: Estimation of risk for dying and bleeding is crucial for the choice of treatment strategy in patients with acute pulmonary embolism (PTE). The aim of this study is to determine the best clinical score for the prediction of major adverse outcome in patients with acute PTE.

Patients and methods: One hundred seventy one consecutive patients with acute PTE treated in a single intensive care unit during the period of 6 years were enrolled in this study. Average age of patients was 61±17 years and 87 (50.9%) were women. According to sPESI, CHA2DS2-VASc and HAS-BLED scores determined at admission, patients were divided into groups with low-risk scores (0 and 1 point) and high-risk score (score ≥ 2), for all scores separately. Cox regression model was used to determine hazard ratios (HR) for all subgroups of patients according to risk stratification for the net-adverse clinical outcome of death, major bleeding and use of mechanical ventilation during six months follow-up. We used the hierarchical end-point calculation; death (the first), major bleeding (the second) and use of mechanical ventilation (the third) whatever come first during six-month follow-up.

Results: The number and proportion of high-risk patients for sPESI, CHA2DS2-VASc and HAS-BLED scores were 66 (38.6%), 93 (54.4%) and 57 (33.3%) of all patients, respectively. The net-adverse clinical end-point was registered in 47 (27.5%) of patients, and among them 26 (15.2%) patients died, 7 (9.9%) patients had major bleeding and 4 (2.3%) patients was on mechanical ventilation. Six-month net-adverse clinical outcome was presented in 24 (51.1%), 43 (72.3%) and 29 (61.7%) of patients in high-risk score groups of sPESI, SHA2DS2-VASc and HAS-BLED score, respectively. In the multivariate Cox regression model, HAS-BLED score was the independent predictor of net-adverse clinical end-point at six months with HR 3.284 (95% CI 1.717–6.283, p<0.001). HAS-BLED score had low sensitivity (50.88%, 95% CI 37.29–64.37%) and positive predictive value (41.70%, 95% CI 41.70–67.49%) for the prediction of net-adverse clinical outcome, however, it had high specificity (84.21%, 95% CI 76.20–93.37%) and negative predictive value (77.42%, 95% CI 60.04–84.44%).

Conclusion: HAS-BLED score had better predictive value for the prediction of net-adverse clinical outcome in patients with acute PTE than sPESI and CHA2DS2-VASc score.
Re-admission for VTE in same or subsequent Clostridium difficile infection 0 (0) 7 (0.6) 0.01
Catheter-associated vascular infection 0 (0) 0 (0) –
Catheter-associated UTI 0 (0) 0 (0) –
Poor glycemic control 0 (0) 2 (0.2) 0.16
Falls/Trauma 43 (3.9) 36 (3.3) 0.42

Total hospital costs, 2015 US$ (mean ± SD) 3,228±2,000 7,618±7,278

Length-of-stay (mean ± SD) 2.3±1.3 4.9±3.0 <0.001
Encounter lasting ≥2 midnights 326 (29.5) 938 (84.9) <0.001
Total hospital costs, 2015 US$ (mean ± SD) 3,228±2,000 7,618±7,278 <0.001
Any hospital-acquired condition 64 (5.8) 136 (12.3) <0.001
Air embolism 0 (0) 0 (0) –
Pressure ulcer 0 (0) 2 (0.2) 0.16
Falls/fracture 43 (3.9) 36 (3.3) 0.42
Poor glycemic control 0 (0) 2 (0.2) 0.16
Catheter-associated UTI 0 (0) 0 (0) –
Catheter-associated vascular infection 0 (0) 0 (0) –
Hospital-acquired bacterial pneumonia 23 (2.1) 100 (9.0) <0.001
Clostridium difficile infection 0 (0) 7 (0.6) 0.01
In-hospital death or thrombosis ≥2 days after presentation 1 (0.1) 5 (0.5) 0.10
Re-admission for VTE in same or subsequent 2 months 13 (1.2) 13 (1.2) <0.99
Re-admission for major bleed in same or subsequent 2 months 2 (0.2) 0 (0) 0.16

Conclusion: Compared to inpatient stays, observation stays were associated with reduced LOS, costs and incidence of hospital-acquired conditions. Use of observation stays was not associated with increased rates of re-admission.

Acknowledgement/Funding: Janssen Scientific Affairs, LLC, Raritan, NJ, USA

P3711 | BEDSIDE
Outcomes associated with observation versus inpatient stays for pulmonary embolism
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¹University of Connecticut, Storrs, United States of America; ²Baylor College of Medicine, Houston, United States of America; ³University of Cincinnati, Cincinnati, United States of America; ⁴The Ottawa Hospital, Ottawa, Canada; ⁵Janssen Scientific Affairs, LLC, Raritan, United States of America

Background: Recent changes in reimbursement policies have led to an increased use of observation stays in the United States (US).

Objective: To compare length of stay (LOS), hospital costs, hospital-acquired conditions and readmission among pulmonary embolism (PE) patients managed through observation or inpatient stays.

Methods: We used the US Premier Hospital Database to identify patients with a primary diagnosis of PE (415.1x) from 11/2012–3/2015. Patients were also required to have claims for ≥1 diagnostic tests for PE on day 0–2 and evidence of PE treatment (i.e., anticoagulation, thrombolysis/pulmonary embolectomy or inferior vena cava placement). Patients managed through observation stays (intended to observe patients for short periods to determine appropriateness for inpatient admission with the determination of admission or discharge taking place within 48-hours) were ≥1.1 propensity score matched to those undergoing an inpatient stay. We compared LOS, total hospital costs (in 2015 US$) and rates of hospital-acquired conditions and re-admission between the cohorts.

Results: A total of 1,105 PE observation stays were matched to 1,105 inpatient stays. The baseline characteristics of the cohorts were well-balanced with standardized differences <10% for all characteristics. The overall study population had a mean: standard deviation LOS of 3.6±2.6 days and total hospital costs of $5,423±$5,770. Mean LOS was shorter for observation stays (2.6 days, p<0.001) vs. inpatient stays (Table). This corresponded to a mean $4,380 lower treatment costs for observation stay patients (p<0.001). Hospital-acquired conditions were less common among observation stay patients vs. inpatients (p<0.001); driven predominantly by reductions in the incidence of pneumonia and clostridium difficile infection. Re-admission for venous thromboembolism or major bleeding in the same or subsequent 2 months did not differ between the cohorts (p>0.16).

Conclusion: Compared to inpatient stays, observation stays were associated with reduced LOS, costs and incidence of hospital-acquired conditions. Use of observation stays was not associated with increased rates of re-admission.

Acknowledgement/Funding: Janssen Scientific Affairs, LLC, Raritan, NJ, USA

P3712 | BEDSIDE
Does anticoagulation for isolated below-knee deep vein thrombosis prevent pulmonary embolism? oOr increase possibility of bleeding?
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Background: Deep vein thrombosis (DVT) is the risk factor of pulmonary embolism (PE) but the efficacy of anticoagulation for isolated below-knee DVT (iBK-DVT) is uncertain and controversial. If iBK-DVT is diagnosed, depending on the severity of patient symptoms and the risk for thrombus extension, either anticoagulation or withholding of anticoagulation is suggested in American College of Chest Physicians (ACCP) guideline. However, the risk of bleeding and benefit of anticoagulation remain unclear.

Purpose: If iBK-DVT especially in the high risk patients does not increase development of PE, we can reduce unnecessary anticoagulants administration.

Methods: We identified patients with iBK-DVT diagnosed by lower extremity ultrasonography from January 2013 to December 2013 in our institute. Exclusion criteria were simultaneous detection of PE, and prior PE and/or DVT history. We retrospectively investigated patient characteristics, occurrence of PE and bleeding events.

Results: Of 179 patients who detected iBK-DVT,12 patients (6.7%) had PE at the same time. Therefore, 167 patients met the criteria. The mean age was 74±11 year-old, and the number of male was 67/167 (40.1%). The mean body mass index was 22.6±3.7 kg/m², D-dimer was 12.7±13.4 mg/dL, observation period was 479±291days, and all the patients were inpatient status. Of 167 patients, 41 (24.6%) patients had cancer, 64 (38.3%) patients underwent surgical operation, and 73 (43.7%) patients had symptom due to DVT. The patients with bilateral iBK-DVT were 44/167 (26.4%), only right side were 64/167 (38.3%), only left side were 59/167 (35.3%). The patients who were started or taking anticoagulants were 54/167 (32.3%) and patients without anticoagulants were 113/167 (67.7%). There was no significant difference between two groups in patient characteristics. During observation period, only one patient developed PE (non-massive type) in the no anticoagulation group. However, there was no significant difference in occurrence of PE between two groups (p=0.448). Bleeding episodes were observed in 17/167 (10.1%) patients. All the patients with bleeding events were taking anticoagulants, but no bleeding events were observed in patients without anticoagulants (p<0.05). According to the International Society on Thrombosis and Haemostasis (ISTH) criteria, 4 patients were defined as major bleeding and 13 patients were defined as minor bleeding.

Conclusions: The present study suggests that anticoagulation for iBK-DVT including high risk patients does not prevent occurrence of PE but can increase bleeding events. One patient developed PE, who had traumatic cerebral hemorrhage and tended to lie in bed for a long time, suggesting that patients with immobility should undergo lower extremity ultrasonography repeatedly to detect extension of DVT.

P3713 | BEDSIDE
Systemic review of management of trapped thrombus in patent foramen ovale
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Background: Patent foramen ovale (PFO) is found in 27% of adults, and is associated with high mortality in patients with pulmonary embolism. Trapped thrombus in PFO is rare clinical condition. It is believed that elevated right heart pressure caused by pulmonary embolism facilitates trapped thrombus in the PFO. Treatment options include anticoagulation, thrombolysis, and surgical removal, but optimal treatment strategy is unclear.

Purpose: The aim of this report is to systemic review of case reports to identify clinical manifestations and to compare clinical outcome of each treatment options.

Methods: We searched the PubMed database from 1991 through December, 2015, using the combined search terms “thrombus in PFO” or “paradoxical embolism”. Studies were limited to English language reports that included treatment outcomes for trapped thrombus in PFO and identified a total of 194 cases (186 studies).

Results: The patients consisted of 100 men and 94 women with a mean age of 59.3±16.4 years. The most frequently clinical presentations were dyspnea (79.4%), chest pain (33.0%), syncope or presyncope (17.5%), sign of stroke (16.5%), lower extremity edema (14.4%), and acute extremity ischemia (8.8%).
P3714 | BEDSIDE
Single-center experience on ultrasound-facilitated thrombolysis in patients with pulmonary embolism at high risk or intermediate-high risk
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Background: EkoSonic Endovascular System is a novel ultrasound-facilitated thrombolysis (UFT) technology providing a high efficacy with a reduced bleeding risk in patients with pulmonary embolism (PE). In this study, we aimed to present our single-center results on this UFT technology in pts with PE at intermediate-high and high risk (IHR, HR).
Methods: Our study was based on the retrospective analysis of the 83 pts with diagnosis of PE (F 42, M 41, 60±16.6 yrs) who underwent UFT treatment in a tertiary cardiovascular hospital. The diagnostic and prognostic work-up including multidetector computed tomography (MDCT), Echo, biomarkers, and PE severity index and its simplified version (PESI, sPESI) were performed in all pts. Qanadi score (QS) was used as the measure of the thrombotic burden in the pulmonary arteries (PA) as assessed by MDCT.
Results: Heart rate, BP and SatO₂% were 106±19 bpm, 116±25 mm Hg and 98±10%, respectively. Seventy-four pts were at IHR and 9 pts were at HR subgroups. The time delay from symptoms to UFT catheters into the target PA were successful in all pts. The dosage and treatment duration of tissue-plasminogen activator was 51,3±28.1 mg and 25,6±9.7 hours, respectively. For unilateral and bilateral placement, both the drug dosage and infusion duration were comparable (p=0.06). UFT resulted in dramatic improvements in triqsudic annular planar systolic excursion (TAPSE), cm 1.44±0.42 vs 2.02±0.29, p=0.001), right/left ventricle (RV/LV) diameter (1.35±0.2 vs 1.12±0.7, p=0.011), MPI 0.61±0.04 vs 0.58±0.05, p=0.011, s (9.7±2.9 vs 15.1±2.7) were significantly increased after UFT. No major bleeding was observed. None of the patients had stroke or transient ischemic attack. In hospital mortality was one and total mortality was four. Pulmonary hypertension was not developed during follow up. Of the 52 pts patients underwent control tomography angiography 24 hours after the completion of TT. Complete lysis of thrombus was observed in 28 of the 30 patients. The echocardiographic outcomes of the patients were presented in Table 1.

Conclusion: Low dose prolonged infusion of tPA is an effective and safe therapy in patients with massive PE. This protocol is also effective in decreasing PASP and restoration of RV functions.

Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>On admission</th>
<th>Post TT</th>
<th>Pre-discharge</th>
<th>6 month</th>
</tr>
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<tbody>
<tr>
<td>Right/minHg</td>
<td>55.40±8.30</td>
<td>33.20±3.27</td>
<td>29.43±1.35</td>
<td>27.80±0.31</td>
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<td>TAPSE, cm</td>
<td>1.44±0.42</td>
<td>2.02±0.29</td>
<td>2.16±0.24</td>
<td>2.21±0.30</td>
</tr>
<tr>
<td>MPI</td>
<td>0.61±0.04</td>
<td>0.58±0.05</td>
<td>0.53±0.08</td>
<td>0.45±0.09</td>
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<tr>
<td>RV/LV, %</td>
<td>98±10.1</td>
<td>98±10.1</td>
<td>98±10.1</td>
<td>98±10.1</td>
</tr>
<tr>
<td>RV/LV</td>
<td>1.44±0.42</td>
<td>2.02±0.29</td>
<td>2.16±0.24</td>
<td>2.21±0.30</td>
</tr>
<tr>
<td>PESI</td>
<td>99±33</td>
<td>1.39±1.04</td>
<td>1.39±1.04</td>
<td>1.39±1.04</td>
</tr>
<tr>
<td>sPESI</td>
<td>1.39±1.04</td>
<td>1.39±1.04</td>
<td>1.39±1.04</td>
<td>1.39±1.04</td>
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</tbody>
</table>

P3715 | BEDSIDE
Modified HASS BLED score for the assessment of bleeding risk in patients with pulmonary embolism
B. Dzudovic, S. Obrađović, N. Ratković, V. Milic, D. Vranes, L. Torbica, M. Sipić, Military Medical Academy, Clinic of Emergency Internal Medicine, Belgrade, Serbia
Background: So far there is no score for the assessment of bleeding risk that is validated in patients with acute pulmonary embolism (PE). However, for optimal bleeding prevention and management of PE, the development of a high quality risk score is urgently needed.

Methods: In a group of 168 consecutive PE patients, in a single center, three scores were assessed at baseline: new composed HASS3B2E2D score and two known scores: HAS BLED and CRUSADE as commonly used for the assessment of bleeding risk in patients with atrial fibrillation and with NSTEMI, respectively. Patients were followed for the occurrence of major bleeding during the first 3 days from admission in those who received systemic thrombolysis, and after 3 days as well as overall major bleeding regardless of the used treatment. C-statistic was calculated to estimate prediction power of the scores.

Results: Major bleeding in the first 3 days in PE patients who received systemic thrombolysis was significantly increased regarding the increment of the risk only when HASS3B2E2D score was used (p=0.013) (Figure 1). In all PE patients, regardless the treatment used, no significance was achieved in major bleeding occurrence after the third day of admission regarding the risk estimated by any of the used scores, although borderline significance existed between low bleeding risk and high bleeding risk using HASS3B2E2D score (p=0.053). Overall major bleeding was significantly increasing following the risk increment using only HASS3B2E2D score (p=0.002). C-statistic for the predictive power of HASS3B2E2D score for bleeding occurring in the first 3 days in PE patients who received thrombolysis was 0.74, 95% CI 0.57 - 0.9, and for bleeding after the third day and overall major bleeding c-statistics were 0.69, 95% CI 0.53 - 0.85 and 0.72, 95% CI 0.61 - 0.83, respectively.

Conclusion: Our newly composed HASS3B2E2D score is able to accurately stratify PE patients into the three bleeding risk groups: low, intermediate and high with very good prediction power for major bleeding especially in patients who
received systemic thrombolysis. Other risk scores, CRUSADE and HAS BLED, have not shown to be useful in PE patients.

P3717 | BEDSIDE
External validation of a multivariable claims-based prediction rule for in-hospital pulmonary embolism mortality

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Background: Guidelines suggest that a low-risk cohort of patients with pulmonary embolism (PE) may be managed with an abbreviated hospital stay. There is need for a claims-based prediction rule that pays and hospitals can use to efficiently risk stratify PE patients.

Objective: To validate the multivariable In-Hospital Mortality for Pulmonary Embolism (IMPACT) prediction rule using admission claims data.

Methods: This analysis was performed using Premier hospital claims data from 11/2012-3/2015 and included adults with a primary diagnosis of PE (415.1x). ≥1 diagnostic test claim for PE on day 0–2 and evidence of PE treatment (i.e., anti-coagulation, thrombolysis/pulmonary embolectomy or inferior vena cava placement). The previously derived and validated multivariable IMPACT rule (1/(1 + exp(-x)), where x = -(5.833 + (0.0208*age) + (0.402*myocardial infarction) + (0.368*chronic lung disease) + (0.464*stroke) + (0.638*prior major bleeding) + (0.298*atrial fibrillation) + (1.061*cognitive impairment) + (0.554*heart failure) + (0.364*renal failure) + (0.484*diabetes) + (0.523*coagulopathy) + (1.068*cancer)) was used to estimate patients' risk of in-hospital mortality. Low-risk was defined as in-hospital mortality ≤1.5%. IMPACT results are presented as prognostic test characteristic values and 95% confidence intervals (CIs).

Results: A total of 47,607 patients (mean ± standard deviation age: 61±17.0, 47% male) hospitalized for PE were included and 2.2% died in-hospital. The IMPACT prediction rule classified 17,093 (35.9%) as low-risk (0.6% died); with a sensitivity and specificity of ~90% and ~37%, respectively, a negative predictive value >99% and c-statistic of 0.75 (Table).

Conclusion: The IMPACT prediction rule was valid when implemented in the nationally representative Premier hospital database. The rule has high sensitivity for predicting in-hospital mortality, and may be valuable for identifying PE patients that are candidates for abbreviated hospital stays.

Acknowledgment/Funding: Janssen Scientific Affairs, LLC, Raritan, NJ, USA

Table 1: External validity of IMPACT for predicting in-hospital mortality

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Estimate (95% CI)</th>
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<tr>
<td>Low-risk, %</td>
<td>35.5</td>
</tr>
<tr>
<td>Sensitivity, %</td>
<td>89.6 (87.5–91.3)</td>
</tr>
<tr>
<td>Specificity, %</td>
<td>36.5 (36.0–36.9)</td>
</tr>
<tr>
<td>Negative predictive value, %</td>
<td>99.4 (99.2–99.5)</td>
</tr>
<tr>
<td>C-statistic</td>
<td>0.75 (0.74–0.77)</td>
</tr>
</tbody>
</table>

P3718 | BEDSIDE
Hypoxia as an independent predictor of right ventricular dysfunction and short term mortality in acute pulmonary embolism

M. Subramanian, S. Ramadurai, S. Gopalan, P. Arthur. Sri Ramachandra University, Chennai, India

Background: Although arterial blood gas analysis has been extensively evaluated in the diagnostic algorithm of patients with acute pulmonary embolism, the existing literature is controversial.

Objectives: The purpose of this study is to investigate the possible correlation between CT pulmonary artery obstruction indices (PAOI) and parameters of functional lung impairment, the correlation was stronger for PaO2 (r=-0.754, p=0.049). Multivariate regression analysis revealed that hypoxia is both an independent predictor of right ventricular dysfunction (OR 2.018, 95% CI 0.464–0.680, p=0.031) and 30 day mortality (OR 0.680, 95% CI 0.542–0.854, p=0.001). Receiver operating characteristic analysis revealed the optimal cutoff value of PaO2 for RV dysfunction and 30 day mortality was 72.5mmHg (AUC = 0.94, 95% CI 0.90–0.98) and 64.5mmHg (AUC= 0.934, 95% CI 0.89–0.97), respectively. At this cutoff value, the sensitivity (sens) and specificity (spec) values were 89.9% sens, 83.3% spec and 89.9% sens, 78% spec and, for RV dysfunction and 30 day mortality, respectively.

P3719 | BEDSIDE
Derivation and validation of a clinical prediction rule to identify low-risk acute pulmonary embolism

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Background: Accurate identification of low risk patients with acute pulmonary embolism who may be eligible for outpatient treatment or early discharge can have substantial cost saving benefit.

Purpose: The purpose of this study was to derive and validate a clinical prediction rule based on clinical information that is routinely collected in emergency departments to effectively identify PE patients at low risk of short term mortality. RV dysfunction, and other adverse complications. In addition, this study wanted to compare the prognostic ability of the clinical prediction rule with the previously validated Pulmonary Embolism Severity Index (PESI).

Methods: From our analysis of data on 452 adult patients with acute pulmonary embolism, we randomly allocated patients to derivation (75%) and internal validation (25%) samples. We derived and subsequently internally validated our prediction rule based on clinically significant variables that are routinely available at initial examination, that were categorized and weighted using coefficients in the multivariate logistic regression.

Results: Our final prediction rule consisted of 5 categorized patient variables (1, 2, or 3 points, respectively): systolic blood pressure (<120, 100–119, <99 mmHg), diastolic blood pressure (<80, 65–79, <64 mmHg), heart rate (<80, 81–100, >101; beats/min), PaO2 (<80, 60–79, <59 mmHg), and modified ECG score (<2, 2–4, >4). The 30 day mortality rates were 0% in low risk (0–6 points), 7.5%–8.8% in intermediate risk (7–10 points), and 18.2–18.8% in high risk (>11 points) patients across the derivation and validation cohorts. The incidence of RV dysfunction also showed a similar trend (21.5–21.9% in low risk, 74.3–74.5% in intermediate risk, and 96.9–98.0% in high risk). The rule had a high sensitivity (range, 95–96%), and a high negative predictive value (range, 95–98%) for predicting 30 day mortality and RV dysfunction, respectively. The area under receiver-operating characteristic curve was 0.79 (95% CI, 0.76–0.82) for our prediction rule and 0.70 (95% CI, 0.67–0.74, p=0.003) for the PESI score. In comparison to the PESI, our prediction rule significantly improved both the discrimination (integrated discrimination improvement, p=0.002) and reclassification (net reclassification improvement, p=0.003) of the model for short term mortality.
Conclusions: This simple prediction rule accurately identifies patients at low risk of short term mortality, RV dysfunction, and other non fatal outcomes. Further validation of our prediction rule is necessary before useful in the selection of patients eligible for outpatient treatment.

P3720 | BEDSIDE
Admission glucose level predicts in-hospital mortality in patients with acute pulmonary embolism who were treated with thrombolytic therapy.

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Background: Elevated admission serum glucose level is associated with unfavourable clinical outcomes in various clinical conditions. The aim of this study was to investigate the relationship between admission glucose levels and in-hospital and long-term adverse clinical outcomes in patients with pulmonary embolism (PE) treated with thrombolytic therapy.

Methods: A total of 183 consecutive confirmed acute PE patients (98 female and 85 male; mean age 61.9±15.7 years) who were treated with thrombolytic therapy enrolled in the study. The study population was categorised into four quartiles according to admission serum glucose levels (group I: glucose <115 mg/dL; group II: glucose 115–141 mg/dL; group III: glucose 141–195 mg/dL; and group IV: glucose >196 mg/dL).

Results: In-hospital mortality was significantly higher in group IV (28.8%) compared to group III (15.2%), group II (6.6%), and group I (2.1%) (p<0.001) (Table 1 and Figure 1). In multivariate analysis, admission glucose level (OR 1.013, 95% CI 1.004–1.021, p=0.004) and admission anaemia (OR 0.602, 95% CI 0.380–0.955, p=0.03) were independent predictors of in-hospital mortality. The mean follow-up period was 34 months. During long-term follow-up, all-cause mortality, recurrent PE, major and minor bleeding were similar among the four groups.

Table 1. In-hospital outcomes

<table>
<thead>
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<td>(n=45)</td>
<td>(n=46)</td>
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<tr>
<td>All-cause mortality</td>
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<td>3 (6.6%)</td>
<td>7 (15.2%)</td>
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<tr>
<td>Major bleeding</td>
<td>5 (10.6%)</td>
<td>6 (13.3%)</td>
<td>7 (15.2%)</td>
<td>8 (17.7%)</td>
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<tr>
<td>Intracranial hemorrhage</td>
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<td>0 (2.2%)</td>
<td>0 (2.1%)</td>
<td>0 (2.1%)</td>
</tr>
<tr>
<td>Red cell transfusion</td>
<td>3 (6.3%)</td>
<td>4 (8.8%)</td>
<td>4 (8.8%)</td>
<td>5 (11.1%)</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>0 (2.1%)</td>
<td>1 (2.2%)</td>
<td>1 (2.1%)</td>
<td>4 (8.8%)</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>1 (2.1%)</td>
<td>2 (4.4%)</td>
<td>4 (8.6%)</td>
<td>15 (33.3%)</td>
</tr>
<tr>
<td>Use of inotropic drug</td>
<td>1 (2.1%)</td>
<td>1 (2.2%)</td>
<td>5 (10.8%)</td>
<td>15 (33.3%)</td>
</tr>
<tr>
<td>Mechanic ventilation</td>
<td>1 (2.1%)</td>
<td>2 (4.4%)</td>
<td>6 (13%)</td>
<td>14 (31.1%)</td>
</tr>
</tbody>
</table>

Values in parentheses are percentages.

Conclusions: Admission glucose level is a simple, inexpensive, easily available, and effective laboratory parameter for predicting in-hospital mortality in patients with PE.

CARDIOMYOPATHIES

P3721 | BEDSIDE
Paradoxical prolongation of QT interval during exercise in patients with hypertrophic cardiomyopathy.

R. Coppi1, C. Ferrantini2, B. Scelini2, C. Poggesi2, A. Mugelli1, I. Olivetto3, 1University of Florence, Department of NeuroFarBa, Florence, Italy; 2University of Florence, Department of Clinical and Experimental Medicine, Florence, Italy; 3Careggi University Hospital (AOU), Florence, Italy

Background: In LQT1 patients, prolongation of action potential duration (APD) due to reduced Iks is associated with QTc prolongation in response to both epinephrine and exercise. We recently showed that ventricular myocytes from patients with Hypertrophic Cardiomyopathy (HCM) have markedly prolonged APD, associated with down regulation of K+ currents, as well as delayed relaxation due to alterations of intracellular Ca2+ handling (Coppi et al., Circulation 2013). Thus, we determined the effects of isoproterenol (ISO) on APD and Ca2+ transients in ventricular myocytes of patients with HCM and the changes of QTc interval and diastolic function during exercise.

Methods: Ventricular myocytes were isolated from myocardial samples of 11 HCM patients who underwent septal myectomy and 4 non-hypertrophic surgical patients (Controls). A total of 150 HCM patients and 62 control subjects underwent standard exercise ECG test (Bruce treadmill protocol). Eighty-five HCM patients and 40 control subjects underwent exercise echocardiography. All clinical procedures were performed at the Referral Center for Cardiomyopathies of Careggi University Hospital in Florence, Italy.

Results: In myocytes (paced at 0.2 Hz) from HCM patients, ISO (10–7 mol/L) prolonged APD at 90% repolarization (APD90) by +26±8%, whereas ISO shortened APD90 in control myocytes (-20±4%, P<0.01, Fig.1). Moreover, intracellular Ca2+ transients were also prolonged during exposure to ISO. In patients with HCM (117 of 150), QTc prolongation by an average of 41±24 ms from a baseline value of 439±36 ms. This paradoxical prolongation of QTc during exercise results in shortening of the QT interval (Fig. 2). In agreement with the reduced diastolic period, E/A ratio was significantly reduced in HCM patients at peak exercise (Fig.3), while it was unaffected in controls.

Conclusions: Abnormal balance of inward and outward ion currents in HCM ventricular cardiomyocytes may determine a reduced lusitropic response to beta-adrenergic stimulation, due to insufficient APD shortening. In HCM patients, exercise led to a QTc prolongation, accompanied by shortening in QT interval, which in turn reduced the diastolic filling time. This may contribute to impaired ventricular relaxation and reduce myocardial perfusion during stress or exercise. This abnormal response is likely to underlie the reduced exercise tolerance and stress-induced angina in patients with HCM.

Acknowledgement/Funding: Italian Ministry of Health (RF-2013-02356787 and GR-2011-02350583), Gilead Sciences Inc.

P3722 | BEDSIDE
Associations of modifying gene polymorphisms with clinical phenotype in patients with hypertrophic cardiomyopathy.

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Introduction: Variation of phenotypic manifestations in patients with hypertrophic cardiomyopathy (HCM) is explained by both sarcomere gene mutations but also polymorphisms of modifying genes encoding beta-adrenergic receptor proteins (b-AP) and renin-angiotensin-aldosterone system (RAAS).

Aim: To assess associations of polymorphism between genes encoding b-AP (ADRB1, ADRB2) and RAAS (ACE, AGTR1, CYP11B2 and CMA1) proteins and clinical manifestations observed in patients with HCM based on gender.

Methods: A total of 285 Belarusian patients with HCM have been examined, who entered in a single-centre study (187 males and 98 females, mean-age 46.2±12.9) and 276 healthy individuals (103 females and 173 males), The PCR and RFLP methods studied polymorphism of the renin-angiotensin-aldosterone system genes: AGT (T174M), AGTR1 (1166A>C), CMA1 (-1903A>G), ACE (I/D polymorphism) CYP11B2 (-344C>T). As well as genes of b-adenrenergic receptors: ADRB1 (Ser49Gly, Arg389Gly), ADRB2 (Arg16Gly, Gln27Glu).

Results: Multifactorial analysis showed associations between the episodes of unsustained ventricular tachycardia in ADRB2 gene GC genotype carriers (Gln27Glu polymorphism) (OR 4.31; 1.08–29,03; 95% CI). Progression of heart failure was associated with ADRB2 gene GC genotype (Gln27Glu polymorphism) (OR 4.31; 1.08–29,03; 95% CI). Progression of angina was frequently defined in ACE gene ID genotype carriers (OR 2.44; 1.23–4.86; 95% CI) and ID gene ACE carriers (OR 2.17; 1.18–4.10; 95% CI) and CMA1 gene AA genotype carriers (OR 2.09; 1.05–4.29; 95% CI). Atrial fibrillation was seen in ACE gene ID genotype carriers...
Prevalence of familial forms of dilated cardiomyopathy in Czech patients with recent-onset disease and initial outcomes of whole exome sequencing

M. Kubanek1, A. Krebsova1, L. Pihera2, V. Stranecky3, M. Macke4, J. Paderova3, T. Paiecek4, V. Melenovsky1, S. Kmoch2, J. Kautzner1, A. Nomura1, N. Serizawa1, Y. Inagaki1, A. Suzuki1, K. Fukushima2.

Single photon emission computed tomography is the marker of P3724 | BEDSIDE AZV-MZ 15-27682A; IKEM 00023001 to M.K.; causes of familial DCM.

Conclusion: Associations between polymorphisms of modifying genes and phenotypic HCM manifestations may be of use as additional assessment criteria to define the severity of the disease.

Prevalence of familial forms of dilated cardiomyopathy in Czech patients with recent-onset disease and initial outcomes of whole exome sequencing

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Psychiatric illness is commonly used to diagnose cardiac sarcoidosis (CS). The relationship between SPECT findings and clinical outcomes has not been reported. We examined the usefulness of perfusion defect of thallium-201 (TL) scintigraphy for the prediction of cardiac event from corticosteroid therapy started.

Event-free survival rates in patients with cardiac sarcoidosis

P3724 | BEDSIDE Single photon emission computed tomography is the marker of cardiac event risk in cardiac sarcoidosis patients

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Prognostic value of left atrial diameter

<table>
<thead>
<tr>
<th></th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
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<tbody>
<tr>
<td></td>
<td>MILDH</td>
<td>MODH</td>
</tr>
<tr>
<td>Left atrial diameter (mm)</td>
<td>RR</td>
<td>95% CI</td>
</tr>
<tr>
<td>NYHA class</td>
<td></td>
<td></td>
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<tr>
<td>(I-II/III-IIV)</td>
<td>5.7</td>
<td>2.8-11.5</td>
</tr>
<tr>
<td>MILDH</td>
<td>4.6</td>
<td>2.9-9.3</td>
</tr>
<tr>
<td>MODH</td>
<td>3.1</td>
<td>1.6-3.2</td>
</tr>
<tr>
<td>SEVH</td>
<td>1.4</td>
<td>1.0-2.1</td>
</tr>
</tbody>
</table>

CI: confidence interval, MILDH: ≤30mm, MODH: >30 to ≤30mm, SEVH: >30mm, NYHA: New York Heart Association.

LaDiam was a strong prognostic factor in mildH patients, independent of atrial fibrillation or NYHA class, less significant in patients with modH and not important in patients with sevH. LaDiam prognostic value decreased according to the severity of hypertrophy.

P3727 | BEDSIDE

Systolic function reserve using two-dimensional strain imaging in hypertrophic cardiomyopathy: comparison with essential hypertension

W. Hamed, H.M.B. Badran, M.F.N. Noamany, N.F.A. Ahmed. Menoufiya University, Cardiology, Shebin El-kom, Egypt

Background: Although patients with hypertrophic cardiomyopathy (HCM) have normal ejection fractions at rest, the investigators hypothesized that these patients have differentially abnormal systolic function reserves, limiting their exercise capacity compared with patients with hypertension (HTN).

Methods: Forty patients with HCM (mean age, 39±12 years), 20 patients with HTN with LVH, and 33 healthy individuals underwent resting and peak exercise echocardiography using two-dimensional strain imaging. Peak longitudinal systolic strain (e(sys)) and strain rate were measured in apical views. Circumferential e(phys) and left ventricular (LV) twist were analyzed from short-axis views. LV systolic dysynchrony was measured from regional longitudinal strain curves as the standard deviation of time to peak strain (time from the beginning of the Q wave on electrocardiography to peak e(sys)) between 12 segments. The difference between resting and peak exercise values were analyzed, and functional reserve was calculated as the difference divided by the resting value.

Results: In patients with HCM, resting values for longitudinal e(sys), systolic strain rate, early diastolic strain rate, and atrial diastolic strain rate were significantly lower, while circumferential e(phys) and twist were higher, compared with patients with HTN and controls (P<0.0001). Functional systolic reserve increased during exercise in controls (17±6%), increased to a lesser extent in patients with HCM (10±16%), and was markedly attenuated in patients with HCM (-23±28%) (P<0.001). At peak exercise, even with augmented circumferential e(phys) and twist in patients with HCM (P<0.01) compared with those with HTN, both remained lower than in controls (P<0.001). LV dysynchrony was amplified during exercise in patients with HCM compared with those with HTN (P<0.001). Within the entire population, exercise capacity was clearly correlated with systolic functional reserve. However when separately, it was mainly related to resting LV dysynchrony and diastolic function in patients with HCM, whereas it was linked to age and LV wall thickness in those with HTN.

Conclusions: Peak exercise with echocardiography and strain indices have been proposed to aid in the classification (>50%); thus familial screening should be performed in all first-degree relatives. Also, when LVNC is associated with a cardiomyopathy the role of the genetic test seems to be important to categorize these patients.

P3729 | BEDSIDE

Diagnostic yield from endomyocardial biopsy in cardiomyopathies

T. Gkiosos, C. O'Mahony, S. Mohiddin, N. Sekhri, O. Watkins, E. Wicks, P.M. Elliott. St Bartholomew’s Hospital, Inherited Cardiovascular Disease Unit, London, United Kingdom

Background and aims: The value of endomyocardial biopsy (EMB) in the management of cardiomyopathies is unresolved. We sought to investigate the impact of EMB in the management of an unselected cohort of cardiomyopathy patients.

Methods: We retrospectively analysed patient records of patients admitted to our institution for EMB between 2004 and 2015. Patients were grouped in 7 distinct phenotypes according to presentation: Arrhythmia (ventricular tachycardia/ventricular fibrillation arrest with no obvious structural disease), hypertrophic cardiomyopathy (unexplained or atypical left ventricular hypertrophy – LVH), diastolic dysfunction (dilated cardiomyopathy), restrictive cardiomyopathy (restrictive or constrictive pericardial disease), amyloidosis, arrhythmogenic right ventricular cardiomyopathy – ARVC, inflammation (any of the above, but with signs of myocardial injury or inflammation), and a mixed phenotype defined as features from 2 of the above mentioned groups.

Histology was considered diagnostic if a definite diagnosis was reported and non-specific histologic findings were revealed in 24 (68.5%). In six patients (25%), GT showed more than one mutation. Most of genetic disorders were located in sarcomeric proteins (44.4%), but also in desmosomal proteins (11.1%), proteins related to myopathies (18.5%), congenital heart malformations (11.1%) and channeleopathies (14.8%).

Results: From 2009 to 2015, 89 patients (56.2% male with a median age at diagnosis 44.5 [IQR 28.5; 57.5] years) were enrolled and followed up 3.2±1.9 years. Isolated LVNC occurred in 85.4%, whereas it was associated to morphological syndromes in 9%, and congenital heart disease in 5.6%. Medium left ventricular ejection fraction was 46.3±13.9% at diagnosis. Twenty-eight patients (31%) described previous familial history of cardiomyopathy or sudden death. FS was carried out to 77.5% of patients and the result was positive in 37 (53.6%); 31.9% with one member affected, and 21.7% with ≥2 members affected. GT was performed in thirty-five patients (39.3%), of those, potentially pathogenic mutations were revealed in 24 (68.5%). In six patients (25%), GT showed more than one mutation. Most of genetic disorders were located in sarcomeric proteins (44.4%), but also in desmosomal proteins (11.1%), proteins related to myopathies (18.5%), congenital heart malformations (11.1%) and channeleopathies (14.8%).

P3728 | BEDSIDE

Role of family screening and genetic testing in patients with left ventricular non-compaction of the myocardium


Background/Introduction: Left ventricular non-compaction of the myocardium (LVNC) is a morphological trait with a wide spectrum: from normal variants to a pathological phenotype. Both sporadic and familial forms have been described. In this group of patients, a wide variety of genetic mutations have been described. Phenotypic variability, genetic heterogeneity and the absence of large follow-up registries may justify the lack of genotype-phenotype association.

Purpose: The aim of this study is to evaluate the value of family screening (FS) and genetic testing (GT) in a cohort of patients with LVNC.

Methods: Patients who fulfilled echocardiographic criteria (based on Chin criteria) and cardiac magnetic resonance (CMR) criteria for LVNC (based on Petersen criteria) were prospectively included and followed-up in our familial cardiomyopathy unit. FS with electrocardiogram and echocardiogram was proposed to all first-degree relatives. GT with Next Generation Sequencing was performed in case of family history of cardiomyopathy, positive family screening or sporadic case with reduced ejection fraction (<45%).

Survival by histologic findings

<table>
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<th>HR</th>
<th>95% CI</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>Non specific findings</td>
<td>1.0</td>
<td>0.9-1.1</td>
<td>0.90</td>
</tr>
<tr>
<td>Disease specific findings</td>
<td>9.0</td>
<td>3.0-26.5</td>
<td>&lt;0.005</td>
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</tbody>
</table>

HR: hazard ratio, CI: confidence interval.
diagnostic if non-specific features were found. Survival analysis was performed for each phenotype, according to findings on histology.

**Results:** 177 procedures were analysed. Most patients were male (67.8%) with a mean age of 50.3±14.7 years. The most frequent histologic findings were interstitial fibrosis (67.8%), hypertrophy (43.7%) and myocyte disarray (13.9%). Inflammation was described in 4.4% of biopsies and amyloid deposits in 6.9%. In the whole population, histology verified the clinical diagnosis in 26.8% of patients. The yield was significantly higher in patients presenting with a restrictive phenotype (55.2%). Diagnostic histologic findings were found in only 8.3% of patients with a DCM phenotype. Inflammations occurred in 6.5% of patients, with no previously related deaths, irrespective of phenotype, site of biopsy, vascular access and number of samples acquired. Disease specific findings on histology were associated with significantly worse prognosis (HR 9.013, CI 3.064–26.517; p<0.05) during follow up.

**Conclusions:** EMB can be performed safely in cardiomyopathy patients. The diagnostic yield varies with cardiomyopathy subtype, being highest in RCM. The presence of diagnostic features is associated with poorer prognosis.

**P3730 | BEDSIDE**

**Algorithm of device-therapy in patients with dilated cardiomyopathy**

T. Vakhnanskaia, T.V. Kurushka, T.M. Kaptiukh, L. Sivitskaya, A.V. Frolov

1. Institute of Genetics and Cytology, National Academy of Science, Minsk, Belarus; 2. Institute of Medicine and Cytology, National Academy of Science, Minsk, Belarus

The purpose of this study was to determine the algorithm of optimal device-therapy in patients (pts) with dilated cardiomyopathy (DCM) by means of multivariate regression analysis of risk factors sudden cardiac death (SCD) and predictors of cardiac resynchronization therapy (CRT) response.

**Material and methods:** The study enrolled 213 DCM pts (male 70.9%; aged 48.9±11.4 years; NYHA 3.1±0.2; LVEF 28.6±12.9). A comprehensive study on electrocardiography, HM ECG, 7-min ECG by software “Intecard-7” with an estimate of HER, AC, DC, QTd and mTWA was fulfilled. Virological screening by PCR method was performed in 135 pts who had noted a link of first symptoms HF with viral infection. Genetic analysis of LMNA gene was performed by SSCP and sequencing was performed in 135 pts who had noted a link of first symptoms HF with viral infection. Diagnostic histologic findings were confirmed in 26.8% of patients. The yield was significantly higher in patients presenting with a restrictive phenotype (55.2%). The results of survival analysis were associated with significantly worse prognosis (HR 9.013, CI 3.064–26.517; p<0.05) during follow up.

**Conclusions:** EMB can be performed safely in cardiomyopathy patients. The diagnostic yield varies with cardiomyopathy subtype, being highest in RCM. The presence of diagnostic features is associated with poorer prognosis.

**P3731 | BEDSIDE**

**The value of primary and secondary right ventricle involvement in people carrying mutations in LMNA gene: results from a 8 year study**

G. Perotto, S. Sala, S. Benedetti, C. Di Resta, M. Ferrari, P. Della Bella

1. San Rafaele Hospital of Milan (IRCCS), Milan, Italy; 2. San Rafaele Hospital of Milan (IRCCS), Department of Arrhythmology and Electrophysiology, Milan, Italy; 3. San Rafaele Hospital of Milan (IRCCS), Laboratory of Clinical Molecular Biology and Cytogenetics, Milan, Italy

**Background:** In cardiomyopathy associated with LMNA gene mutations, right ventricle (RV) impairment is usually secondary to left ventricular dilation or dysfunction. However, a primary RV involvement has been described in people carrying particular mutations in LMNA gene, sometimes overlapping with arrhythmogenic right ventricular cardiomyopathy.

**Purpose:** We aimed to define, in patients bearing LMNA gene mutations, prevalence and prognostic implications of secondary vs. primary RV impairment.

**Methods:** To date, 26 patients (mean age 42±18 y; 58% males) with LMNA gene mutations have been enrolled in our center with a FU of 8±5 y. All the patients had baseline echocardiogram and cardiac magnetic resonance (CMR); regular FU including 2-year ECG, echocardiogram and 24-h Holter monitoring was obtained. RV impairment was defined as the presence of any degree RV dilation or dysfunction. It was classified as secondary in the presence of dilated cardiomyopathy or significant left ventricle (LV) systolic or diastolic dysfunction. In the other cases it was defined as primary, also including the presence of RV late gadolinium enhancement (LGE) at CMR in the absence of any other RV abnormality.

**Results:** Of the 26 patients enrolled, 12 (46%) had normal RV, while 4 (15%) and 10 (39%) had primary vs. secondary RV involvement, respectively. The prevalence of 1st degree AV block—a known prognostic index in patients with LMNA gene mutations—was significantly higher in patients with any form of RV involvement compared to those without (12/14 vs. 4/12 respectively, p=0.02). In all the patients (4/4) with primary RV involvement baseline ECG showed 1st degree AV block. A total of 13 patients (2/12, 3/4, and 8/10 respectively) underwent ICD implant. By 8 FU, the incidence of malignant ventricular arrhythmias (VT, VF, appropriate ICD shocks) was significantly higher in patients with secondary RV involvement (6/10) vs. normal or primary involved RV (1/12 and 0/4; p<0.01). The incidence of heart failure in patients with secondary involved vs. normal vs. primary involved RV was 8/10 vs. 1/12 vs. 1/4 (p<0.01). Similarly, the incidence of de novo dilated cardiomyopathy was very low in the latter groups (1/12 and 0/4).

During FU, 2 patients died and 3 underwent heart transplantation, all of them in secondary RV impairment group. No significant differences were found among groups in age, gender, mutation type, and incidence of advanced bradyarrhythmias (2nd/3rd degree AV blocks) or atrial tachyarrhythmias (atrial fibrillation or flutter).

**Conclusion:** In carriers of LMNA mutations, 1st degree AV block is significantly associated with both primary and secondary RV structural or functional involvement. However, secondary forms of RV disease are associated with the occurrence of malignant ventricular arrhythmias and heart failure. Primary involvement of the RV, LGE on CMR included, is not associated with significant arrhythmic or mechanical events at 8 FU.

**P3732 | BEDSIDE**

**Post-myocarditic dilated cardiomyopathy: characterization and long-term prognosis**


1. University Hospital Rinnati, Cardiovascular Department, Trieste, Italy; 2. University Hospital Rinnati, Trieste, Italy

**Background:** Dilated cardiomyopathy (DCM) is the final common pathway of
different pathogenetic processes and presents a significant prognostic heterogeneity, possibly related to its etiological variety. The characterization and long-term prognosis of post-myocarditic dilated cardiomyopathy (P-MDCM) remain unknown. This study assesses the clinical- instrumental evolution and long-term prognosis of a large cohort of patients with P-MDCM.

Methods: We analyzed 175 DCM patients consecutively enrolled from 1993 to 2008 with endomyocardial biopsy (EMB) data available. P-MDCM was defined in presence of borderline myocarditis at EMB or persistent left ventricular dysfunction 1 year after diagnosis of active myocarditis at EMB. Other patients were defined as idiopathic dilated cardiomyopathy (IDCM). Analysis of follow-up evaluations was performed at 24, 60 and 120 months.

Results: We found 72 PM-DCM out of 175 enrolled patients (41%). Compared to IDCM, PM-DCM patients were more frequently females and less frequently presented a familial history of DCM. No other baseline significant differences were found. During the long-term follow-up (median 154, 1st-3rd interquartile range 78-220 months) PM-DCM patients showed a trend towards slower disease progression. Globally, 18 (25%) PM-DCM patients vs 49 (48%) IDCM patients experienced death/Heart Transplantation (HTx) (p: 0.045). The prognostic advantage for PM-DCM patients became significant beyond 40 months of follow-up. At multivariable time-dependent Cox analysis, PM-DCM was confirmed to have a global independent protective role (HR=0.53, 95% CI 0.28-0.97, p=0.04).

Conclusions: PM-DCM is characterized by better long-term prognosis compared to IDCM. An exhaustive etiological characterization appears relevant in the prognostic assessment of DCM.

P3734 | BEDSIDE
Val122Ile familial transthyretin (TTR) amyloid cardiomyopathy in African-American patients: a worse prognosis than wild-type TTR amyloid cardiomyopathy
Brigham and Women’s Hospital, Boston, United States of America

Background: The gene for a familial amyloid transthyretin (TTR) cardiomyopathy, Val122Ile, is found in 3.8% of the African-American population. The degree of penetrance is unknown, but the gene is associated with an increased risk of heart failure, regardless of presence of typical amyloid phenotype. There are conflicting data regarding survival in Val122Ile versus wild type TTR cardiac amyloidosis (ATRwT), a disease of elderly men. With 1 recent international multicenter database study (THAOS) suggesting similar outcomes. It is important to know the natural history, since new drugs may slow all forms of TTR amyloidosis, and trials of new agents are enrolling both ATRwT and ATRrT, including Val122Ile. We therefore evaluated all patients seen with typical Val122Ile amyloid cardiomyopathy in a single center, and compared outcome to a group of ATRwT.

Methods: 35 Val122Ile patients (10 female) with amyloid cardiomyopathy were seen by a single physician (RHF) over an 8 year period and compared to records of 35 randomly selected patients with ATRwT (2 female). Onset of cardiac symptoms likely due to amyloidosis was estimated. Date of diagnosis was based on cardiac biopsy or (for Val122Ile) either biopsy or typical echo with positive genetic testing. Death was determined by national database of deaths.

Results: Mean age at diagnosis did not differ between groups: Val122Ile =71.4 yr, SSA =73.9 yr. There was a significant difference in sex distribution in sex distribution between Val122Ile (28% female) versus ATRwT (6% female, p: <0.01), consistent with the known male prevalence of ATRwT. Median actuarial survival from diagnosis differed statistically between groups, being 49 months in Val122Ile and 70 months in SSA (p: <0.05) (GRAPH). To determine whether delayed diagnosis in Val122Ile was responsible for the worse prognosis, we evaluated time to first symptoms in each group. Among those in whom initial symptoms could be determined (31 Val122Ile and 32 ATRwT) there was a trend toward earlier diagnosis in Val122Ile: mean time to diagnosis was 21.6 months in Val122Ile and 32.4 months in ATRwT and (P=NS).

Conclusions: 1.Contrary to previous suggestions, patients with Val122Ile amyloid cardiomyopathy have a significantly worse prognosis from diagnosis than do patients with ATRwT. 2. This difference cannot be explained by a delayed diagnosis in the Val122Ile patients, as they had a trend toward earlier diagnosis.

3. These findings underscore the poorer prognosis in Val122Ile compared to ATRwT amyloid cardiomyopathy, despite the fact that both diseases are due to cardiac infiltration with TTR-derived amyloid and possibly suggest a faster deposition in Val122Ile.

4. The poor prognosis in Val122Ile, a disease to which 3.8% of the African-American/Afro-Caribbean population is predisposed, underscores the pressing need for high clinical suspicion when heart failure occurs in this population.

Acknowledgement/Funding: Harold Grinspoon Charitable Foundation, David Lloyd, Jr. Foundation and Friends of Burt Cardiac Amyloidosis Fund.
TR had more severe left ventricular systolic (wall motion score index: 2.2±0.20 vs 1.84±0.32, p<0.05) and diastolic dysfunction (E/A: 1.34±0.84 vs 0.82±0.28, p=0.002) and higher pulmonary artery systolic pressure (45±11.9 vs 37.9±12.5 mmHg, p=0.002). In addition, patients with reversible TR showed higher values of right ventricular 2D strain (27.5±1.6 vs 19.3±0.6, p=0.001) and higher right atrial volume (48.0±18.6 vs 36.5±11.4 ml). Overall, major complications (acute heart failure and cardiogenic shock) occurred in 43 patients (40.2%). Acute heart failure was significantly more common in patients with reversible TR (55.6 vs 27.5%, p=0.008).

Conclusions: Reversible TR is detected in about one quarter of patients with TTS. Early evaluation of TR grade by echocardiography should be performed systematically in all TTS patients to identify those at higher risk of acute heart failure.

ADULT CONGENITAL HEART DISEASE

P3737 | BEDSIDE
Conduit puncture for electrophysiological procedures in patients with Fontan circulation

Background: Electrophysiological procedures are challenging in patients who underwent lateral tunnel and extracardiac conduit Fontan operation, because the caval veins are not connected to the atria and veins. Methods: We consecutively included 8 patients (median age (interquartile range), 21.5 (16.5–25.8) years; 5 men) who underwent catheter ablation or pacemaker implantation via Fontan conduit puncture. In 4 and 4 patients, lateral tunnel and extracardiac conduit Fontan operation have been performed, respectively.

Results: In 7 of 8 patients, Fontan conduit puncture via the right femoral vein and the inferior vena cava was successfully performed without complications under intracardiac echocardiographic guidance. In 3 patients with the Fontan conduit made of the pericardium, a Bronckenbroukh transseptal needle or a radiofrequency transseptal needle with a snare was used. In 4 patients with the Fontan conduit made of Gore-tex, a radiofrequency transseptal needle with a snare, and percutaneous transluminal angioplasty balloon were used. In 1 patient with extracardiac conduit made of the pericardium, conduit puncture was failed due to interruption of the both femoral veins. Fontan conduit puncture time was significantly longer in patients with the conduit made of Gore-tex than in patients with the conduit made of the pericardium [91.0 (59.8–130.5) and 11.5 (10.0–18.3) minutes, respectively; p=0.020].

Conclusions: Conduit puncture is feasible and safe in patients with lateral tunnel and extracardiac Fontan circulation. Puncture of the Gore-tex conduit is more difficult than the pericardium conduit.

P3738 | BEDSIDE
Biventricular interactions and their impact on systemic ventricular function and exercise capacity in adults with a subaortic right ventricle
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Introduction: In Switzerland there are an estimated 300–500 adults living with a systemic (subaortic) right ventricle (RV). This includes adults with prior atrial switch operations for complete transposition of the great arteries (D-TGA) and adults with congenitally corrected TGA (ccTGA). Although midterm survival is favorable, late outcome is compromised by RV dysfunction. The loading conditions of the subpulmonary left ventricle (LV) altered by interatrial shunting through baffle leaks or by obstruction of the LV outflow tract impact on the position of interventricular septum and hence, the geometry of the RV. We retrospectively investigated exercise capacity and RV function in patients with a systemic RV in relation to LV loading conditions.

Methods: We identified 161 adults with cc-TGA or d-TGA with prior atrial switch operations from a nation-wide registry. In 79 stable patients (pts), a cardiopulmonary exercise study and cardiac MRI or transthoracic echocardiography (in patients with a pacemaker) was performed within 12 months. Volume load (VOL) of the subpulmonic LV was defined as baffle leak with Qp:Qs >1.5, and pressure load (PRESS) as LV outflow tract peak gradient >20 mmHg. Exercise capacity (peak-VO2 and RV function (RV-EF)) were compared between pts with LV pressure or volume load and those without (CONTR). For RV-EF measurement we used only MRI data (available in 66 pts.).

Results: Mean age was 33±10 y, 70% were male. N=9 (11%) had cc-TGA, n=70 (89%) D-TGA and an atrial switch procedure. N=60 (76%) were in the CONTR group, n=12 (15%) in the PRESS group and n=7 (9%) in the VOL group. Cardiac MRI was done in 58 pts (73%), 21 pts (27%) had a pacemaker. Mean VO2max in all 79 pts was 25±7 ml/min/kg (70% of predicted) and did not differ between CONTR and PRESS (Fig). However, pts with a baffle leak (VOL) had a lower exercise capacity (VO2max 21±3 ml/min/kg [p=0.038] or 62±9% of predicted). Mean RV-EF was 48±9% and mean LV-EF was 62±9%. RV-EF did not differ between CONTR and VOL but was higher in pts with a LV outflow tract obstruction (46±5% in CONTR and VOL [n=44] vs. 52±8% in PRESS [n=12], p=0.048). The VOL had an isolated secundum ASD with pulmonary to systemic blood flow Qp:Qs ratio<1.5, mean 1.2±0.6 (1.1–1.5).

A symptom-limited treadmill exercise test with respiratory gas exchange analysis, transthoracic color Doppler echocardiographic study and Quality of life (QoL) (using the SF36 questionnaire (SF36q)) were repeated in all pts before and 24 months after the procedure.

Results: The device was successfully implanted in all pts (procedure time 20±2.5 (8–37) minutes, fluoroscopy time 8.2±4.4 (6–12) minutes). There were no major complications. The defect echo diameter was 7.2±3.9 (5–15) mm. The diameter of the implanted devices ranged from 6 to 18 mm. After 24 months of ASD closure, all the pts showed a significant improvement of exercise capacity. 7 QoL parameters (except mental health) improved at 24 months of follow-up compared with baseline. The mean SF36q scale increased in 141 (76.2%) pts of mean 42.2±20.1 (9–71). The right ventricular dimension decreased in 153 pts (82.7%) (Table 1).

Table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before ASD closure</th>
<th>24 months after ASD closure</th>
<th>p value</th>
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<tr>
<td>Time of exercise (min)</td>
<td>13.1±5.2</td>
<td>18.1±4.1</td>
<td>&lt;0.001</td>
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<tr>
<td>VO2 peak (ml/kg/min)</td>
<td>11.2±5.1</td>
<td>15.8±5.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SF36q scale 0–100</td>
<td>38.3±22.9</td>
<td>81±27.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Right atrial area cm²</td>
<td>20.9±1.7</td>
<td>16.7±1.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Right ventricular area cm²</td>
<td>18.9±1.5</td>
<td>11.7±1.4</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Conclusions: ASD closure in patients with borderline shunt resulted in a significant and long-term clinical and hemodynamic improvement after percutaneous treatment.
Conclusions: Hybrid therapy with CA’s and TCPccs showed good clinical outcomes of SVT treatment in adult congenital heart disease patients after APC-Fontan procedure. Multiple sessions of CA without TCPccs was associated with increased risk of recurrence of SVT.

P3740 | BEDSIDE

Does the ECG still carry prognostic power in contemporary patients with repaired tetralogy of Fallot?

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Background and purpose: Surgically repaired Tetralogy of Fallot (TOF) patients (pts) carry an increased risk of sudden cardiac death (SCD) due to sustained ventricular tachycardia (VT) or fibrillation (VF). The ECG is considered a useful tool for the risk stratification of these pts, based on studies from previous decades. Recent advances in surgical and lifelong medical management have changed the outlook of these pts, and may have altered the relative contribution of the ECG as a risk stratification tool.

Methods: In this retrospective study, we analyzed ECG parameters of consecutive surgically repaired TOF pts seen in a single tertiary outpatient clinic between 1989 and 2007, followed up until 2015, with the combined end-point of death or appropriate ICD shock. The relation between this endpoint and QRS duration, QTc and QT dispersion was analyzed using Cox regression.

Results: A total of 389 pts were included (mean age: 29.4±12.9 years, 57.3% male). Thirty-three patients died and 11 had an appropriate ICD shock (mean age: 48.16 [36.53–57.45]), giving a cumulative event rate at 5, 10 and 15 years was 3.7 and 10% respectively. On univariate Cox regression, QRS duration (HR: 1.26 per 10ms increase, 95% CI: 1.11–1.44, P<0.001) and QTc (HR: 1.13 per 10ms increase, 95% CI: 1.07–1.20, P<0.001) were strong predictors of outcome. ROC analysis demonstrated a low accuracy for QRS duration (AUC 0.69, best cut-off of 140 msec by ROC analysis, 180msec by termplot, see Figure). QTc was somewhat more accurate (AUC 0.71), with a cut-off of 460 msec.

Conclusions: Death and appropriate ICD shocks remain relatively common in contemporary young patients with repaired TOF. ECG indices maintain their prognostic power, albeit with a low accuracy and, thus, need to be integrated with other prognostic markers in clinical practice.
antibiotic prophylaxis should take place with every ACHD patient during regular clinical contacts to close this knowledge gap.

P3742 | BEDSIDE
22 years of FU of coarctation of aorta in adults - High further intervention rate (40%) but good prognosis
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Background: Coarctation of the aorta (CoA) is associated with premature mortality with a mean survival age of 35 years despite early repair. Treatment paradigms are continually changing and contemporary data on CoA are needed.

Methods: The Norwich and Papworth (NORRAP) dataset was set up in 1993 to record demographics, treatment and outcomes of adult congenital heart disease (ACHD) patients in the east of England. We report on the CoA subset.

Results: In total 2322 patients were included in the dataset and of these 223 patients had CoA (9%): 146 males and 77 females, mean age 40 years (range 16–94). Hypertension was documented in 34% and coronary heart disease 6%. 91% received a corrective procedure (80% surgical and 11% percutaneous) and of these 38% required more than one procedure.

Methods: End to end Subclavian flap Patch Interposition grafts Unknown

Table 1. Type of Surgical intervention at corrective surgery

<table>
<thead>
<tr>
<th>Type of repair</th>
<th>Total</th>
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<th>2nd</th>
<th>3rd</th>
<th>4th</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>End to end anastomosis</td>
<td>102</td>
<td>19</td>
<td>30</td>
<td>10</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>Subclavian flap repair</td>
<td>19</td>
<td>77</td>
<td>7</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
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<td>30</td>
<td>4</td>
<td>10</td>
<td></td>
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<tr>
<td>Interposition grafts</td>
<td>10</td>
<td>9</td>
<td>0</td>
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<td>6</td>
<td></td>
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</tbody>
</table>

Figure 1. Number & type of interventions.

Conclusion: There is a high initial intervention rate in CoA with about 40% requiring additional intervention. The serious complication rate was low in our cohort suggesting that prognosis may be improving over time.

P3743 | BENCH
G263X MYBPC3: clinical Update of an autochthonous and penetrant mutation. An example of allelic heterogeneity
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Background: Hypertrophic cardiomyopathy (HCM) is a relatively frequent disease (1:500 individuals) and potentially devastating. It is considered one of the most frequent forms of cardiomyopathy with a mean survival age of 35 years despite early repair. Genetic studies by direct sequencing were performed in index patients and identified additional intervention. The serious complication rate was low in our cohort suggesting that prognosis may be improving over time.

Methods: G263X MYBPC3 mutations carriers in order to help establishing genotype/phenotype correlations due to the fact that, to the best of our knowledge, this mutation was not reported in any other regions worldwide.

Purpose: The aim of this study was to update the clinical phenotype of all identified G263X MYBPC3 carriers in order to help establishing genotype/phenotype correlations due to the fact that, to the best of our knowledge, this mutation was not reported in any other regions worldwide.

Results: 34 mutations carriers were identified; 29 patients satisfied HCM criteria, 85% penetrance, 97% if we only consider affected 40 years old. Around 15% of index cases had family history of SCD. 62% of patients were diagnosed asymptomatic. Although 3 patients presented angina pectoris and other 3 syncope, dyspnea was the most common symptom (14/16 patients at 8 years). 8 had Non-sustained ventricular tachycardia in monitoring (24%). The average LVWT was about 20 mm and only 4 patients did not present significant Left ventricular outflow tract obstruction. 3 patients suffered a cerebrovascular accident (CVA) and only one presented systolic dysfunction, affecting interestingly in both cases the NCCM phenotypes. Cardioverter defibrillator was implanted in 4 patients. According to ESC Guidelines from 2014, only 3 patients presented high risk (with 3 classical risk factors); and 3 moderate risk of sudden cardiac death, being the average SCD Risk low.

Conclusion: There is a high initial intervention rate in CoA with about 40% requiring additional intervention. The serious complication rate was low in our cohort suggesting that prognosis may be improving over time.

P3744 | BEDSIDE
Acute complications of pulmonary artery aneurysms: new challenges in acute and critical cardiac care
J. Nuche Berenguer, J.M. Montero Cabezas, G. Martinez-Ales Garcia, M.J. Ruiz Cano, C. Jimenez Lopez-Guarch, S. Alonso Charterina, 1 University Hospital 12 de Octubre, Madrid, Spain; 2 Leiden University Medical Center, Cardiology, Leiden, Netherlands; 3 University Hospital La Paz, Madrid, Spain; 4 Heart and Diabetes Center NRW, Bad Oeynhausen, Germany

Background: Pulmonary arterial hypertension (PAH) is a well-known risk factor for pulmonary artery aneurysms (PAA) in patients with PAH. PAH is a potential cause of death in patients with PAA. The aim of this study was to describe the clinical characteristics and outcomes of patients with PAA, with the goal of reducing the risk of complications in this setting.

Methods: This is a retrospective, observational study (2000 to 2015). In 475 PAH patients, computed tomography or magnetic resonance were performed to identify PAA. Among 199 patients, 87 PAA (43.71%) were detected. Mean PA diameter was 47.35±7.46 mm. PAH time course was longer patients with PAA than in those without PAA (71.9±1.4 months (p: 0.024)) respectively). However, there were no significant differences in mean PA pressure (55.3±1.3 months (p: 0.12)) or pulmonary vascular resistances (17.4±13.4 (p: 0.20)). In patients with PAA, significant linear relationship between PA diameter and PH time course was detected (r: 0.199 (p: 0.008)).

Results: Among 87 PAA, complications were identified in 11 patients (12.6%): 7 LMIMAC, 1 bronchial compression (right middle lobe); 1 PA dissection; 1 both LMIMAC and bronchial compression; 1 both PA dissection and LMIMAC.

Conclusions: PAA that finally had to be resected. The only significant difference in basal character-istics (age, sex, etiology, PVR, mPAP, PAH time course and PA diameters) was identified without complications was PAA diameter (complicated: 53.36±8.69; non-complicated: 46.7±6.87; p<0.03).

CRM: NCCM phenotype

Conclusions: G263X MYBPC3 autochthonous mutation has a huge penetrance reaching 97% in over 40 years old. In general it has a low SCD risk but severe LVWT. CRM represents a crucial diagnostic tool in this entity. Moreover, this common mutation represents a great example of allelic heterogeneity, with variable phenotypic expression in carriers with distinct cardiomyopathies (HCM and NCCM), raising again the question of whether they are actually different manifestations of the same cardiomyopathy spectrum.

ACUTE INTENSIVE CARDIOVASCULAR CARE

P3745 | BEDSIDE
Acute complications of pulmonary artery aneurysms: new challenges in acute and critical cardiac care
J. Nuche Berenguer, J.M. Montero Cabezas, G. Martinez-Ales Garcia, M.J. Ruiz Cano, C. Jimenez Lopez-Guarch, S. Alonso Charterina, 1 University Hospital 12 de Octubre, Madrid, Spain; 2 Leiden University Medical Center, Cardiology, Leiden, Netherlands; 3 University Hospital La Paz, Madrid, Spain; 4 Heart and Diabetes Center NRW, Bad Oeynhausen, Germany

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P3745 | BEDSIDE
Prognosis and predictive factors of in-hospital mortality of cardiogenic shock complicating ST-elevation myocardial infarction, in the modern era of wide reperfusion strategies

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Background: Cardiogenic shock (CS) has previously been described as a dreadful complication of ST-segment elevation myocardial infarction (STEMI). However, management of CS and STEmI improved, with a wide utilization of reperfusion therapy.

Purpose: The objectives of our study were to determine the characteristics, prognosis and predictive factors of in-hospital mortality of CS complicating STEMI, in the modern era of wide reperfusion strategies.

Methods: We analysed data collected in The Regional Acute Myocardial Infarction Registry of Brittany (ORBf), an 8 years prospective and systematic registry of 8500 patients admitted to an interventional cardiology center of Brittany (France) for management of STEMI. Multivariate Cox model was carried out to identify risk factors of intra-hospital mortality.

Results: 689 patients (8%) developed a CS during their hospitalization for STEMI, including 597 patients who had a coronary angioplasty in the acute phase and constituted the studied group. Mean age was 66±13, 401 patients were male (67%). Sudden death was the 1st symptom in 91 patients (15%), 266 patients (44%) were in CS at admission. 45 patients (8%) were first treated by fibrinolysis, whereas 552 (92%) had primary angioplasty. Median delay between occurrence of symptom and reperfusion therapy was 204 minutes. Culpit lesion was left main trunk in 68 patient (10%), whereas 345 (57%) had multivessel disease. 225 patients (37%) were treated with mechanical circulatory assistance, 207 (41%) with mechanical ventilation. 64 patients (10%) presented mechanical complications. 268 patients (45%) died during the in-hospital follow-up. Multivariate analysis using a Cox model identified 5 independent factors significantly associated with mortality: age (Hazard ratio: 1.034; 95% CI: 1.02–1.04), Killip class 3 or 4 at admission [HR: 1.49; 95% CI: 1.13–1.95], fibrinolysis [HR: 1.51; 95% CI: 1.14–2.00], post percutaneous coronary intervention TIMI flow <3 [HR: 2.54; 95% CI: 1.50–4.30], and mechanical ventilation [HR: 1.51; 95% CI: 1.14–2.00].

Conclusions: Despite modern strategies, including wide reperfusion therapies, CS in the acute phase of STEMI still represents a therapeutic challenge, with a high mortality rate. We identified 5 risk factors of intra-hospital mortality: age, Killip class 3 or 4 at admission, post percutaneous coronary intervention TIMI flow <3 and mechanical ventilation.

P3746 | BEDSIDE
Decreased length of stay in the intensive cardiac care unit with preserved clinical outcome over the last decade

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Background: Significant advances in the medical and invasive treatment of acute myocardial infarction (MI) and new interventional procedures have occurred in the last decade.

Objective: To evaluate whether these changes influenced the hospitalization length of stay in the intensive cardiac care unit (ICCU).

Methods: We retrospectively evaluated the clinical and demographic characteristics of all the patients hospitalized at our tertiary center ICU during the last 10 years. The data was obtained from the hospital medical information system and validated manually in 5% of the patients. In order to evaluate temporal changes during this time period, patients were divided into two periods; an earlier period (2005–2009) and a recent period (2010–2015).

Results: We enrolled 5110 patients between 2005–2009, and 2509 between 2010–2015. ICCU length of stay decreased by almost one day between the two periods (5.2 vs. 5.1 days, P<0.02). This decrease in the ICCU length of stay didn’t change the diagnosis of these patients, as the total hospitalization length of stay was prolonged. The recurrence hospitalization rate were similar in these two groups (P>0.72). This decrease occurred despite an increase in the age of the patients (median age 63 vs. 65 years, P=0.004) and patients had more comorbidities - hyperlipidemia (52% Vs 58%, P<0.001) and hypertension (55% Vs 61%, P<0.001). The decrease in ICCU length of stay was evident in all types of admissions; post elective procedures: 4.6 to 3.1 days (P<0.001), arrhythmia’s (not related to ACS): 4.2 to 2.9 days (P<0.001), ST elevation MI: 3.7 to 2.3 days (P<0.001) and non-ST elevation MI: 3.6 to 2.1 days (P<0.001).

Conclusion: Length of stay in the ICU dropped significantly over the last decade, even though the patients were older and had more comorbidities. The decrease didn’t change the total mortality and re-hospitalization rate. Prospective studies are needed to evaluate whether this will reduce overall hospitalization costs.

P3747 | BEDSIDE
Semi-critical care unit for initial post-operative in adult cardiac surgery

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Background: Cardiac surgery involves a significant consumption of healthcare resources. The creation of semi-critical care units aims to optimize hospital resources ensuring a close post-operative clinical control.

Objectives: Analyze the semi-critical care unit impact on clinical evolution of post-operative cardiac surgery patients.

Methods: 1234 consecutive patients who were admitted for cardiac surgery at our hospital between November 2012 and April 2015 were retrospectively analyzed. We compared those admitted before and after the semi-critical care cardiac unit (SCCU) setting-up, which was in May 2014 (pre-SCCU: 674 patients, post-SCCU: 650 patients). Hospital stay (days in intensive care or conventional unit) and in-hospital mortality rates were analyzed.

Results: Global baseline characteristics: age 67±12 years, hypertension 65%, dyslipidemia 59%, diabetes 33%, lung disease 13%, kidney failure 14%, vascular disease 15%, stroke 6.5%. Type of surgery: valvular 54.5%, coronary 27%, aortic 8.4%, plus coronary 11.8%, aorta 1.5%, others 5.2%. No significant differences were found in baseline characteristics or logistic Euroscore1: 9.3 (pre-SCCU) vs 8.4 (post-SCCU), p=0.074. Average intensive care unit stay: 4.9±11 days (pre-SCCU) vs 2.9±6 (post-SCCU), p=0.001. Average total hospital stay: 13.5±15 days (pre-SCCU) vs 12.7±11 (post-SCCU), p=0.012. Admission to intensive care unit from SCCU: 8 patients (1.2%). Mortality in SCCCU: 2 patients (0.3%). In-hospital mortality of post-operative cardiac surgery patients were similar (4.9% pre-SCCU and 3.5% post-SCCU, p=0.275).

Conclusions: The creation of a semi-critical care unit for post-operative cardiac surgery patients reduces global hospital stay and intensive care unit stay, without worsening in-hospital prognosis.

P3748 | BEDSIDE
Can echocardiography improve the risk prediction for peri-operative mortality in patients undergoing coronary bypass surgery? A prospective study

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Objective: To assess the ability of transthoracic echocardiographic (TTE) parameters to predict operative mortality and morbidity in patients undergoing coronary artery bypass grafting (CABG) and to compare their prognostic value to that obtained by the Society of Thoracic Surgeon (STS) score.

Materials and Methods: We prospectively collected the clinical and biological data necessary to calculate the STS score in patients hospitalized for CABG. A preoperative TTE was performed for each patient. Primary outcome was 30-days mortality or major morbidity (i.e. stroke, renal failure, prolonged ventilation, deep sternal wound infection, reoperation) as defined by the STS. Secondary outcome was prolonged hospitalization (> 14 days).

Results: 172 patients were included (mean age 66.1±10.2 years, 12.2% were women). The primary outcome occurred in 33 patients (19.2%) and 28 patients (16.3%) had a prolonged hospital stay. Independent predictive factors for the primary outcome were an increased left atrial volume (>-31 ml/m²) [OR=3.166, IC 95% [1.266; 8.015], p=0.014] and a decreased tricuspid annular plane systolic excursion (TAPSE <20 mm) [OR=2.709, IC 95% [1.144; 6.410], p=0.023]. The addition of these two parameters to the STS score improved significantly the model prediction capacity: Hazard ratio (HR) for the addition of TAPSE was 1.673 (IC 95% [1.045; 2.680], p=0.030) for the addition of TAPSE and STS score and 1.770 (IC 95% [1.121; 2.777], p=0.013) for the addition of both TAPSE and STS score.

Acute intensive cardiovascular care 765
P3749 | BEDSIDE
A new experience in music therapy in patients with heart failure and early post-infarction angina; A substudy of the MUSIC-HF study

K. Minami, M. Kurobe, S. Muto, S. Furudono, H. Suenaga, T. Nunohiro, S. Takeshita, H. Nakashima, Nagasaki Harbor Medical Center City Hospital, Department of Cardiology, Nagasaki, Japan

Background: Obstructive sleep apnoea (OSA) is associated with acute myocardial infarction (AMI). OSA represents a risk factor for cardiovascular morbidity after AMI.

Purpose: To examine the effects of continuous positive airway pressure (CPAP) on all-cause mortality in patients with acute myocardial infarction complicated by moderate to severe OSA.

Methods: In total, 260 consecutive patients with AMI who underwent primary percutaneous coronary intervention were included in this study. After overnight polysomnography, CPAP was recommended if the apnoea-hypopnea index (AHI) was >15 events/h. CPAP mean daily use of >4.0 h/day was considered necessary for the treatment to be effective. Patients were divided into three groups: (1) the non-OSA group (AHI <5 events/h, n=124); (2) the CPAP group (moderate to severe OSA treated with CPAP, n=44) and (3) the no-CPAP group (moderate to severe OSA, patient refused CPAP, n=92).

Main outcome measure was all-cause mortality.

Results: The median follow-up duration was 1495 days. The no-CPAP group exhibited significantly higher rates of all-cause mortality compared with the non-OSA group and the CPAP group (12.0% vs. 4.8% vs. 2.3%, log-rank p=0.039). There was no difference in all-cause mortality between the non-OSA group and the CPAP group (p=0.44).

Conclusion: Long-term CPAP application in patients with AMI experiencing moderate to severe OSA significantly reduced the incidence of all-cause mortality to the same level as that in patients with non-OSA.

P3750 | BEDSIDE
Nitroglycerin better than nitroglycerin maintains renal blood flow in patients with hypertensive urgencies


The treatment of hypertensive emergencies and urgencies should take into account the state of the vital organs blood flow. But only few medical studies investigated renal blood flow in this category of patients. The aim of our study was to compare the anti-hypertensive efficacy of Nitroglycerin and Urapidil and their impact on renal blood flow. But only few medical studies investigated renal blood flow (kidney level) (picture).

P3751 | BEDSIDE
Long-term effects of continuous positive airway pressure on all-cause mortality in patients with moderate to severe obstructive sleep apnoea and acute myocardial infarction

K. Minami, M. Kurobe, S. Muto, S. Furudono, H. Suenaga, T. Nunohiro, S. Takeshita, H. Nakashima, Nagasaki Harbor Medical Center City Hospital, Department of Cardiology, Nagasaki, Japan

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Conclusion: Long-term CPAP application in patients with AMI experiencing moderate to severe OSA significantly reduced the incidence of all-cause mortality to the same level as that in patients with non-OSA.

P3752 | BEDSIDE
Development and validation of a simple prediction model for predicting post-discharge acutely decompensate heart failure in acute coronary syndrome

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Background: Acutely decompensate heart failure (ADHF) in patients with acute coronary syndrome (ACS) is associated with worse prognosis. Accuracy and early identification of patients at high risk for this complication could be of clinical significance.

Purpose: The aims of this study were: a) to describe the incidence of ADHF hospitalization; b) to develop a clinical prediction model for predicting risk of ADHF readmission in patients discharge after an ACS and c) to evaluate the prognosis impact of ADHF hospitalization.

Methods: Between January 2011 and December 2014, 1487 consecutive ACS patients were included after hospital discharge. Post-discharge ADHF readmissions and death were collected at 1-year in 98.5% of cases. A derivation cohort (n=1000) and a validation cohort (n=487) were used to develop and validate respectively the clinical prediction model.

Results: A total of 79 patients (5.3%) presented ADHF readmission.
shows the adjusted hazard ratios of the variables included in the prediction model. Both, discrimination and calibration, were good in the derivation cohort (c-index = 0.874 and Hosmer-Lemeshow p value = 0.338); and in the validation cohort (c-index = 0.848 and Hosmer-Lemeshow p value = 0.691). Moreover, ADHF hospitalization was associated with a higher risk of 1-year mortality (adjusted HR: 2.35, 95% CI 1.41–3.93; p=0.001).

Multivariate regression analysis for ADHF

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (&gt; year)</td>
<td>1.06</td>
<td>1.03–1.08</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female</td>
<td>1.77</td>
<td>1.11–2.83</td>
<td>0.017</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1.64</td>
<td>1.03–2.63</td>
<td>0.039</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>3.09</td>
<td>1.92–4.95</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Admission heart rate (&lt;10 bpm)</td>
<td>1.13</td>
<td>1.03–1.23</td>
<td>0.01</td>
</tr>
<tr>
<td>Killip ≥2 during index hospitalization</td>
<td>1.65</td>
<td>1.01–2.69</td>
<td>0.047</td>
</tr>
<tr>
<td>CVD-SEP (&lt;10 mL/hydr/1.73m²)</td>
<td>0.88</td>
<td>0.78–0.98</td>
<td>0.023</td>
</tr>
<tr>
<td>Anterior STEMI or undetermined ACS</td>
<td>1.82</td>
<td>1.10–3.01</td>
<td>0.019</td>
</tr>
</tbody>
</table>

Conclusion: In ACS patients, post-discharge ADHF readmission at 1-year is relatively common and confers poor prognosis. A simple pre-discharge prediction model accurately identifies those patients at high risk for this complication. More intensive care of patients with high risk clinical profile may be warranted to improve prognosis.

### P3753 | BEDSIDE
Myocardial injury and long-term mortality in patients with carbon monoxide poisoning

H. Sunman¹, M. Erat¹, K.G. Yaya³, E. Aktog¹, H.F. Sahani¹, T. Cimen¹, A. Akyel¹, E.D. Arslan³, S. Oztan³, S. Aciek¹, M. Dogan¹, E. Yeter¹, Diskapi Yildirim Beyazit Education and Research Hospital, Department of Cardiology, Ankara, Turkey; Diskapi Yildirim Beyazit Education and Research Hospital, Department of Emergency, Ankara, Turkey.

**Background:** Carbon monoxide (CO) poisoning is a serious health problem, which is associated with a high incidence of severe morbidity and mortality. Deaths due to CO poisoning are mostly related to myocardial injury. Predictors associated with myocardial injury at discharge are less defined in this patient population.

**Purpose:** This study was conducted to identify the predictors of myocardial injury and to determine the association between myocardial injury and long-term mortality in CO-poisoned patients.

**Methods:** This retrospective study included 1099 adult patients with CO poisoning, who presented to the Department of Emergency, between January 2008 and January 2013. Patient age, gender, comorbidities, smoking, troponin levels and survival status were retrieved from patients’ hospital records. Myocardial injury was defined by a cardiac troponin I level ≥0.6 ng/mL. Follow-up information for all-cause mortality was evaluated at the beginning of 2016.

**Results:** Myocardial injury occurred in 125 (11.4%) of 1099 patients. The mean age of the patients with myocardial injury was 46±19.5 years. At a mean follow-up of 5.2±1.7 years, there were 48 deaths (4.4%). Long-term mortality was more frequently observed in patients with myocardial injury than without (16 [12.8%] of 125 vs 32 [3.3%] of 974, respectively) (p=0.001). Age, gender, diabetes mellitus, coronary artery disease were the independent predictors of myocardial injury in multivariate logistic regression analysis.

**Conclusion:** The presence of myocardial injury is correlated with long-term mortality in CO-poisoned patients and age, gender, diabetes mellitus and coronary artery disease are the independent predictors of myocardial injury.

### P3754 | BEDSIDE
Gut permeability, low-grade endotoxemia and platelet activation in community-acquired pneumonia


**Background and objective:** Patients hospitalized for community-acquired pneumonia (CAP) are at increased risk of cardiovascular complications, which have been related to enhanced platelet activation, but the underlying mechanism is still unclear. Aim of the study was to assess the pathway involved in platelet activation, in the early phase of CAP.

**Methods:** Two-hundred-seventy-eight consecutive patients hospitalized for CAP were recruited and followed-up until discharge. Hospitalized patients matched for sex, age and comorbidities but without acute infectious diseases were used as controls. At admission and at discharge, plasma levels of sP-selectin, a maker of in-vivo platelet activation, serum soluble NOX2 (sNOX2-dp), a marker of Nox2 activation, serum levels of lipo-polysaccharide (LPS) and zonulin, a marker of gut permeability, were analysed.

**Results:** Compared to controls, at hospital admission patients disclosed enhanced blood levels of sP-selectin, sNOX2-dp and LPS. A multivariable regression analysis showed that baseline sP-selectin remained independently associated to serum LPS (β=0.415; p<0.001), sNOX2-sp (p=0.260; p<0.001) and the Pneumonia Severity Index score (β=0.197; p<0.001).

**Conclusions:** In conclusion, CAP patient can disclose enhanced platelet activation, which is related to LPS-mediated Nox2 activation. Enhanced gut permeability seems be implicated in inducing enhanced circulating levels of LPS in CAP patients.

**Acknowledgement/Funding:** Grant n. C26A13WSXJ Sapienza University of Rome.
Purpose: The purpose of this study was to evaluate the prognostic impact of hypothermia in emergency room in patients with AMI. Methods: We analyzed consecutive 1,101 patients (852 men, and mean age 68±13 years old) with AMI from the data of Mie ACS Registry in Japan, which is a prospective and multicenter registry. Patients were divided into two subgroups by the body temperature (BT) at presentation in emergency room. Patients with BT under 35°C were defined as hypothermia. Patients with BT over 35°C and under 37.4°C were defined as normothermia. Patients with BT over 37.5°C were excluded from this analysis. Primary end point was defined as cardiovascular death and non-fatal MI. Results: During average follow-up time of 406 days (range, 1 to 1052 days), 89 patients (8.1%) reached primary end point. Average age and prevalence of male gender were similar in two groups. Prevalence of hypertension was lower in hypothermia group. However, prevalence of diabetes mellitus was similar in two groups. Hypothermia group showed significantly higher glucose level compared to that in normothermia group. (219.3 ± 177.2 mg/dl, P < 0.01) Patients with hypothermia also showed lower systolic and diastolic blood pressure (118.7±30.9 vs. 135.2±29.1 mmHg, P < 0.01), lower heart rate (73.4±18.7 vs. 78.9±19.1 mmHg, P < 0.01), lower glucose level (48h: 2.25 [1.22–4.15] after adjustments for HR [CI]: 0.27 [0.12–0.61]), and attenuated the association of the time category with mortality (statistically nonsignificant) in the Cox model. Conclusions: These data suggest that AMI-to-cardiac rupture time contributes to a significant risk of in-hospital mortality; however, making a quick diagnosis and initiating prompt surgical interventions are crucial to improve outcome in patients with cardiac rupture after AMI.

P3758 | BEDSIDE
Impact of blood transfusion on in-hospital myocardial infarctions according to patterns of acute coronary syndrome: insights from the BleeMACS registry

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1. St. Marianna University School of Medicine, Kawasaki, Japan; 2. Medical University, Cambridge, Munster, USA; 3. Kitasato University, Cardiovascular Medicine, Sagamihara, Japan; 4. Tokai University (Tokyo), Cardiology, Isehara, Japan; 5. Dokkyo Medical University, Medical University, Cambridge, Munster, USA; 6. Dokkyo Medical University, Nippon Medical Center, Cardioiology, Tochigi, Japan; 7. Dokkyo University, Nippon Medical University, Tokyo, Japan; 8. Saitama International Medical Center, Cardiology, Hidaka, Japan

Background: Despite the known association of cardiac rupture after acute myocardial infarction (AMI), which substantially increases the risk of death, it is not clear whether cardiac characteristics are associated with increased risk of in-hospital deaths among patients with AMI complicated by cardiac rupture.

Methods: The multicenter mechanical complications registry is a retrospective registry, and is being conducted at eight medical universities in Eastern Japan. Among a total of 10,305 consecutive AMI patients, we included 183 patients with cardiac rupture after AMI and examined incident in-hospital deaths during a median duration follow-up of 26 days. Patients were stratified into three groups according to AMI-to-cardiac rupture time, and into a less-than-24-hour group (n=111), a 24–48-hour group (n=20), and a greater-than-48-hour group (n=52).

Cox proportional hazards regression was used to estimate hazard ratio (HR) and 95% confidence interval (CI) for hospital mortality.

Results: Eighty-seven (48%) patients experienced in-hospital death and 126 (67%) had cardiac surgery. In multivariable Cox regression, a nonlinear association was observed among these three groups for mortality (HR [CI]: <24h: 1.0; reference, 24–48h: 0.73 [0.27–1.86]; >48h: 2.25 [1.22–4.15] after adjustments for age, sex, Killip classification, percutaneous coronary intervention, blood pressure, creatinine, peak creatine kinase MB fraction, left ventricular ejection fraction, and type of rupture. Cardiac surgery was independently associated with a reduction in HR of mortality (HR [CI]: 0.27 [0.12–0.61]), and attenuated the association of the time category with mortality (statistically nonsignificant) in the Cox model.

Conclusions: These data suggest that AMI-to-cardiac rupture time contributes to a significant risk of in-hospital mortality; however, making a quick diagnosis and initiating prompt surgical interventions are crucial to improve outcome in patients with cardiac rupture after AMI.
Conclusion: AF during the acute phase of ACS was associated to negative higher rates of cardiogenic shock (A=14.1% vs B=12.7% vs C=6.4%, p=0.009), groups.

Background: Nagoya, Japan

EAT, SCAT and plasma samples were collected from CAD patients in order to determine any associations between omentin and CAD pathogenesis.

Purpose: We investigated the expression of omentin in EAT and subcutaneous adipose tissue (SCAT) in CAD patients and compared them to non-CAD subjects known about its role in epicardial adipose tissue (EAT) and coronary artery disease.

Methods: Coronary angiographies from 16384 patients were retrospectively analyzed, selecting those with coronary ectasia, defined as diameter >1.5 times the size of adjacent normal segments of the same or another coronary artery. Prevalence of cardiovascular risk factors, mortality after a mean follow-up period of 8.3 years, and therapeutic regimens were analyzed.

Results: A total of 144 patients (0.9% of the analyzed population), 83.3% male, aged 64±12 had at least one ectasic coronary artery, with 109 (75.7%) presenting the expression of omentin in EAT (r = -0.63, p=0.027). On the other hand, there was no correlation between omentin expression in EAT and EAT volume or visceral fat area.

Conclusion: AF during the acute phase of ACS was associated to negative outcomes, although there was no significant statistical difference between AF groups.

COMORBIDITIES AND RISK FOR CAD

P3760 | BEDSIDE
Clinical profile, mortality and implications of antithrombotic therapy in coronary ectasia


Introduction: Coronary ectasia, defined as the abnormal dilation of one or more coronary arteries, appears occasionally in patients with ischemic heart disease. Our aim is to describe the prevalence of coronary ectasia among patients following a coronary angiography in our centre and the features of this population, as well as to analyze the all cause mortality rate and the impact of antplatelet and anticoagulant therapy on it.

Methods: Coronary angiographies from 16384 patients were retrospectively analyzed, selecting those with coronary ectasia, defined as diameter >1.5 times the size of adjacent normal segments of the same or another coronary artery. Prevalence of cardiovascular risk factors, mortality after a mean follow-up period of 8.3 years, and therapeutic regimens were analyzed.

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Conclusion: AF during the acute phase of ACS was associated to negative outcomes, although there was no significant statistical difference between AF groups.

P3762 | BEDSIDE
Assessment of immune mediators in plasma: a new diagnostic tool for detection of coronary artery disease after heart transplantation

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Purpose: Coronary artery disease of transplanted heart, so-called cardiac allograft vasculopathy (CAV) remains a common cause of death after heart transplantation (HTx) and one of the most limiting aspects for long-term graft survival. Due to denervation of the transplanted heart, CAV is obviously clinically silent and tends to be diagnosed at an advanced stage. Annually performed invasive coronary angiography is still the recommended routine procedure to evaluate this disease, because a solid non-invasive biomarker has yet to be discovered.

Methods: In order to investigate the cytokine microenvironment in these patients, we performed profiling of plasma samples of patients after HTx (n=31) with an inflammatory condition moderate or severe CAV (ISHL II 2 or 3) and a control group of patients without CAV (ISHLT 0, n=23) at least 5 years after HTx. We focused on IL-4, IL-6, IL-10, IL-17, IL-21, IL-23, IL-31, IFN-g, TNF-α and sCD40L in order to uncover potential changes in the Th1/2/17 balance. Furthermore, we hypothesized that certain mediators, being present in blood in higher amounts than others, may serve as non-invasive biomarkers for CAV.

Results: There were no significant differences between the groups for IL-6, IL-23, IL-33, IFN-g and sCD40L concentrations. Although IL-4, IL-21 and IL-31 concentrations were higher in CAV sera, they did not show any statistical significance (p=0.058-0.067). However, IL-10 and TNF-α concentrations were significantly elevated in plasma of CAV patients (p<0.05). Eleven combinations of mediator levels correlated with each other in both - the CAV and non-CAV group. There were 15 combinations that correlated with each other in the non-CAV patients but only two of them (IL-21 vs. IL-33 and IL-6 vs. sCD40L) could be found solely in the CAV patients.

Conclusion: The detection of higher IL-10 and TNF-α concentrations in plasma of CAV patients indicates a systemic pro-inflammatory process associated with the development of CAV. The simultaneous increase of IL-21 and IL-33 or IL-6 and sCD40L may additionally suggest an acceleration of this process. Thus, cytokine quantification could be helpful to identify the patients with increased risk of developing CAV after HTx.

P3761 | BEDSIDE
Expression of the adipocytokine omentin increases in the epicardial adipose tissue of non-obese coronary artery disease patients

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Background: Omentin, an adipocytokine secreted by visceral adipose tissue, protects against obesity-linked cardiovascular complications. However, little is known about its role in epicardial adipose tissue (EAT) and coronary artery disease (CAD).

Purpose: We investigated the expression of omentin in EAT and subcutaneous adipose tissue (SCAT) in CAD patients and compared them to non-CAD subjects in order to determine any associations between omentin and CAD pathogenesis.

Methods: EAT, SCAT and plasma samples were collected from CAD patients (n=15, 23.3±3.1 kg/m²) who underwent coronary artery bypass graft surgery and non-CAD (control) patients (n=10, 20.8±3.9 kg/m²) who underwent elective surgery for aortic or mitral valve replacement surgery. Omentin messenger ribonucleic acid (mRNA) expression was measured using real-time polymerase chain reaction analysis, while plasma concentrations were measured using an enzyme-linked immunosorbent assay. EAT volume and visceral fat area was determined with 64-slice computed tomography.

Results: Omentin mRNA expression in EAT and EAT volume were higher in CAD patients (343±158 ng/ml compared with the controls (751±1579 ng/ml, p<0.015), and has a significant negative correlation with the expression of omentin in EAT (r = -0.63, p<0.027). On the other hand, there was no correlation between omentin expression in EAT and EAT volume or visceral fat area. Further, male patients showed a tendency for having increased omentin levels in EAT, but this trend was not found to be significant.

P3763 | BEDSIDE
Long-term prognosis and potential years-of-life lost by acute coronary syndromes

A. Cordero1, M. Rodriguez-Manero2, M. Garcia-Carrilero1, C. Gunturiz1, J.M. Garcia-Acuna2, M. Pedroira1, R. Lopez-Paloz1, V. Bertomeu-Martinez1, J.R. Gonzalez-Juanatey2. 1 University Hospital of San Juan, Alicante, Spain; 2 University Clinical Hospital of Santiago de Compostela, Santiago de Compostela, Spain

Background: Coronary heart disease incidence is the leading cause of mortality...
in developed countries and is linked to potential years-of-life lost (PYOLL). Since acute coronary syndromes (ACS) are the most frequent clinical form of presentation we evaluated PYL-loss in a cohort of ACS patients.

Methods: Observational study of all consecutive ACS patients admitted to two hospitals between 2009 and 2013. Patients were classified in ST-elevation ACS and non-ST-elevation ACS. PYOLL was assessed by the difference between the age of patients when they died and the life expectancy published by the Spanish National Statistics Institute (78.6 years for men and 84.7 for women). Premature ACS was codified when age was <55 in males or <60 in women.

Results: We included 331 patients, mean age 68.0±12.0 years, 69.05% males and 1512 (45.0%) ST-elevation ACS. Patients with non-ST elevation ACS had significantly higher mean age (69.7±12.4 vs. 66.0±13.2 years), prevalence of hypertension (67.6% vs. 56.6%) and diabetes (36.1% vs. 23.9%) but lower prevalence of current smoking (26.4% vs. 31.8%) and lower mean GRACE score (127.9±35.3 vs. 145.3±43.9). Revascularization was performed more frequently in ST-elevation ACS (77.2% vs. 70.2%; p<0.01). Hospital mortality was higher in ST-elevation ACS (5.3% vs. 3.6%; p<0.02). During follow-up, median time 38 months, 523 (16.0%) patients died and, as shown in the figure, all-cause mortality rate was higher in non-ST-elevation ACS (21.0% vs. 11.3%; long-rank p<0.01). The multivariate analysis, performed by Cox regression, identified non-ST-elevation as independently associated to higher mortality (HR: 1.30 95% CI 1.10–1.57; p<0.01). The overall PYOLL were 4.01±7.1 years and no difference no difference (p=0.11) was observed in mean PYOLL between ST-elevation ACS (4.8±7.9 and 95% non-ST-elevation ACS (3.7±6.7). Multivariate linear regression, adjusted by GRACE score and medical treatment at discharge, identified female gender (B: 2.18; 95% CI 1.75–2.62), current smoking (B: 2.94; 95% CI 2.47–3.42), ST-elevation ACS (B: 4.44 95% CI 3.68–5.19) and premature ACS (B: 7.69 IC 95% 7.40–7.98) as positively associated with PYOLL; revascularization was negatively associated with PYOLL (B: 0.46; 95% CI 0.02–0.92).

Conclusions: Patients admitted for non-ST-elevation ACS have 30% higher long-term mortality. ACS drive to 4 PYOLL and no difference is observed between both types of ACS and we identified female gender, current smoking, ST-elevation ACS and premature ACS as independent predictors of PYOLL whereas revascularization had an inverse association.

P3764 | BEDSIDE
the endothelin gene-1 (EDN-1) glu105Glu (rs5369) gene polymorphism in the EDN-1 is associated with risk of developing acute coronary syndrome in mexican patients
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Background: Atherosclerosis is a complex multifactorial and polygenic disorder resulting from endothelial dysfunction (ED) and enhanced inflammatory response to various forms of injurious stimuli to the arterial wall. Several molecules have been associated with the vascular physiology and severity of coronary diseases. In particular, endothelin 1 (ET-1) exerts proatherogenic activities, acts as modulator of vasoconstrictor tone and vascular remodelling, and it is able to induce platelet aggregation and expression of adhesion molecules.

Purpose: The aim of the present study was to evaluate the role of ET-1 (EDN1) gene polymorphisms as susceptibility markers for acute coronary syndrome (ACS)

Methods: We included 218 Mexican patients with ACS (148 males, mean age of 60.4±11.7) and, as control group, a cohort of 204 healthy unrelated individuals (83 males, mean age of 59.4±9.8) with neither symptoms nor previous diagnosis of cardiovascular problems. EDN-1–974CNA (rs3087459), EDN-1–1394TNG (rs185441), and EDN-1 Glu105Glu (rs5369) single nucleotide polymorphisms were genotyped using 5’ exonuclease TaqMan genotyping assays on an ABI Prism 7900 HT Fast Real time PCR System, according to manufacturer’s instructions.

Results: The results showed an increased frequency of EDN-1 Glu105Glu (rs5369) polymorphism in ACS patients compared to healthy subjects (p=0.004). At multivariate analysis, EDN-1 Glu105Glu (rs5369) polymorphism was the only independent predictor of ACS (OR 2.65, 95% CI 1.34–5.16, p=0.005).

Conclusions: Resulting data suggest that EDN-1 Glu105Glu (rs5369) polymorphism could be involved in the risk of developing ACS in Mexican patients.

P3765 | BEDSIDE
Association of the HDL with mRNA expression of pro- and anti-calcifying genes in the epicardial adipose tissue from patients with coronary artery disease
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Introduction: High-density lipoproteins (HDL) could retard the arterial calcification by inducing the secretion of OPG and reduce TNF-α expression. Adipokines secreted from epicardial adipocytes could diffuse into the coronary arteries, contributing to the pathogenesis of cardiovascular disorders. Genes encoding proteins such as osteopontin (OPN), osteoprotegerin (OPG) and TNF-α could be expressed in the EAT.

Aim: To determine if the composition and distribution of high-density lipoproteins are associated with the expression level of mRNA of OPG, OPG and TNF-α in the EAT.

Methods: We enrolled 14 patients with stenosis valvular aortic (controls) and 13 with coronary artery disease (CAD). Gene expression was evaluated in the EAT from both groups by qPCR. HDL were separated via sequential ultracentrifugation, followed by electrophoresis.

Results: HDL size distribution showed a shift to large HDL subclasses in the CAD compared with the controls. HDL-cholesterol was significantly lower in the CAD group. HDL 3a, 3b and 3c showed a concentration lower of total-cholesterol in the patients. Triglycerides and phospholipids of the HDL 2a were higher whereas that HDL 3b and 3c showed a concentration lower of both lipids in the CAD group compared to the controls. The EAT from CAD patients showed to increase of 77% in the expression of OPG mRNA. The expression of OPG mRNA was twice higher and TNF-α was expressed 33% less in the CAD patients compared with the controls. A linear regression model showed that OPN (β=0.429, P<0.029) and HDL 3c-triglycerides (β=-0.403, P=0.046) were associated with the gene expression level of OPG and TNF-α, respectively.

Lipd Group Subclasses Lipid Level Control CAD CAD CAD CAD

| Lipd Group Subclasses | Lipid Level Control CAD CAD CAD |
|-----------------------|-------------------|-------------------|-------------------|
| TC                    | 10.24±0.64        | 8.48±0.31         | 9.53±0.67         | 5.48±0.40         |
| HDL 2a                | 4.62±0.07         | 6.67±0.09         | 3.68±0.04         | 3.45±0.11         |
| HDL 3a                | 4.52±0.18         | 8.64±0.30         | 3.13±0.17         | 3.73±0.21         |
| HDL 3b                | 2.93±0.04         | 5.67±0.02         | 2.58±0.02         | 1.91±0.09         |
| HDL 3c                | 1.00±0.01         | 1.92±0.39         | 18.68±0.03        | 12.75±1.03        |

Data are shown as mean ± SE. Student’s t test (†p<0.001, *p<0.05). TC: total cholesterol; TG: triglycerides; PH: phospholipids.

Conclusion: HDL 3c-triglycerides were associated statistically with the expression of TNF-α mRNA in the EAT. The EAT of the CAD group showed a gene expression higher of OPG and OPG compared with the controls, these results suggest that EAT contribute with the expression of genes pro- and anti-calcifying.

P3766 | BEDSIDE
Noninvasive screening test for diagnosis of nonobstructive coronary artery disease
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Background: Traditionally the gold standard for diagnosis of coronary artery disease (CAD) is detection of significant stenosis by coronary angiography. However, most myocardial infarctions result from ruptures of plaques that did not significantly compromise coronary lumen before the event. It was proved that significant stenosis is associated with stable CAD but nonsignificant coronary atherosclerosis is associated with unstable angina and acute coronary syndrome.

Purpose: To reveal predictors of nonsignificant coronary atherosclerosis using morphological and functional parameters in suspected CAD patients without obstructive CAD.

Methods: From coronary angiography database (20.402 patients) we selected 3.829 patients without obstructive CAD. Selected patients were divided into two

Conclusions: Resulting data suggest that EDN-1 Glu105Glu (rs5369) polymorphism could be involved in the risk of developing ACS in Mexican patients.
groups in a random way (1.812 - studied group and 1.817 - test group). Clinical and functional parameters of studied group patients were compared: 316 with nonsignificant coronary atherosclerosis (narrowing less than 50% of lumen) and 1.366 with smooth coronary artery. Predicting equation was built using linear regression model.

Results: According to multivariate analysis, arterial hypertension (OR 2.79; 95% CI 1.53–5.09; p<0.001), ecocardiographic signs of aortic atherosclerosis (OR 1.50; 95% CI 1.03–2.19; p=0.036), age (OR 1.05; 95% CI 1.02–1.07; p<0.001) and gender (OR 0.51; 95% CI 0.37–0.70; p<0.001) appeared to be independent predictors of nonsignificant coronary atherosclerosis. Based on ROC analysis, a cutoff value of 0.204 for equation of linear regression in studied group patients had 65% sensitivity and 61% specificity for detection of nonsignificant coronary atherosclerosis. For patients of test group sensitivity was 62% and specificity 66%. The simplicity and availability of the method allow it to use as a screening tool on that very stage when preventive lipid-lowering therapy could be the most effective.

Conclusion: Nonsignificant coronary atherosclerosis can be predicted in patients with suspected CAD by testing based on gender, age, arterial hypertension and ecocardiographic signs of aortic atherosclerosis with relatively good sensitivity and specificity.

P3767 | BEDSIDE Subclinical hypothyroidism as a new risk factor for coronary atherosclerosis
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Background: Mild thyroid failure promote athrogenic dyslipidemia, hyperhomocysteinemia, insulinresistance and that's why subclinical hypothyroidism (SH) can potentiate coronary atherosclerosis. Clinical picture of SH is not specific, and some cohort trials are necessary to evaluate prevalence of SH in cardiovascular risk patients and role of SH in coronary atherosclerosis.

Purpose: To reveal SH role in coronary atherosclerosis in heart ischemic disease (HID) patients and determine indications for screening of thyroid gland activity in cardiovascular risk patients.

Methods and results: We examined 870 HID patients, who underwent standard coronaryangiography. Height, weight and body mass index (BMI) were assessed in all participants. Lipid profile and homocysteine level were assessed before coronarography. Thyroid-stimulating hormone (TSH) level was measured by reagents of 3 generation in order to evaluate thyroid function.

Middle age of our patients was 56.65±0.29 years. There was no difference between men and women in age. In 12.1% HID patients SH was revealed. In women TSH level was higher than in men (3.30±0.23 IU/l vs. 2.20±0.07 IU/l; p<0.01).

Elevation of TSH level correlated with BMI in all groups of patients (p<0.001).

SH was associated with risk of obesity (OR=3.43, CI: 1.80–6.53). SH was diagnosed in 8.8% of men and in 23.5% of women. Female sex was associated with SH which was associated with risk of obesity (OR=3.43, CI: 1.80–6.53). SH was diagnosed in 8.8% of men and in 23.5% of women. Female sex was associated with SH, which was associated with risk of obesity (OR=3.43, CI: 1.80–6.53).

Conclusion: SH was associated with atherosclerotic dyslipidemia and hyperhomocysteinemia in HID patients. SH is an independent risk factor for coronary atherosclerosis. Screening for TSH level is necessary for all cardiovascular risk patients.

P3768 | BEDSIDE Inference of non-obstructive coronary artery disease for cardiovascular events in dialysis patients
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Background: Little is known about the impact of non-obstructive coronary artery disease (CAD) on cardiac adverse events among dialysis patients.

Purpose: The purpose of this study was to evaluate clinical importance of non-obstructive CAD.

Methods: We retrospectively investigated 247 (69.1±11.2 years, 75.7% male) dialysis patients who underwent elective coronary angiography without subsequent revascularization during March 2005 to July 2015. Quantitative coronary angiography (QCA) derived % stenosis was used to divide the patients into 3 groups (no apparent CAD: <20%, non-obstructive CAD: 20–50%, obstructive CAD: >50%). The primary outcome was 5-year cardiovascular death and acute myocardial infarction (AMI).

Results: 109 patients (44.1%) had non-obstructive CAD and 99 patients (40.0%) had obstructive CAD. Within 5 year, 52 patients developed cardiovascular death and AMI. (2 patients in no apparent CAD group, 23 patients in non-obstructive CAD group and 27 patients in obstructive CAD group). Kaplan-Meier curve showed that the rates of cardiovascular death and AMI were significant difference among 3 groups (log-rank test, P<0.014).

In the Cox regression model, both non-obstructive CAD and obstructive CAD in 5-year cardiovascular death and AMI event rates were significantly associated with higher adjusted by other risk factors of no apparent groups (HR 4.46, 95% CI 1.047–19.036, P=0.043). HR 5.60 95% CI 1.315–23.849, P=0.020).

Conclusion: In this study, non-obstructive CAD had similar risk of 5-year cardiovascular death and AMI to obstructive CAD in dialysis patients.

P3769 | BEDSIDE Admission hyperglycemia and severity of the acute coronary syndrome
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Background: Acute hyperglycemia is common in acute coronary syndromes (ACS), regardless of a previous history of Diabetes Mellitus (DM). Several studies have showed that admission hyperglycemia (AHG) in ACS is associated with worse outcomes, and the most recent guidelines recommend the use of hypoglycemic agents in ACS when blood glucose is >180mg/dL.

Purpose: To determine the prognostic significance of AHG and its relation with the severity of the ACS.

Methods: Retrospective study of patients admitted to our service with the diagnosis of ACS between September 2011 and April 2015, with a blood glucose test at admission. Patients were divided in two groups according to the AG (1 – >180mg/dL, 2 – <180mg/dL). Data from the admission and in-hospital evolution were collected.

Results: We included 784 patients with ACS, predominantly men (66.1%), with a mean age of 69.3±13.2 years, 36.3% with known DM. The in-hospital mortality (IHM) was 5.7%. The average AG was 180 mg/dL (known DM - 248mg/dL, unknown DM - 141mg/dL), higher in women (206 vs 166, p<0.001). Group 1 comprised 33.6% of the patients. The mean age in group 1 was higher (71.3 vs 68.2 years; p=0.002). There was no significant difference in the number of STEMI cases nor in the Manchester triage color. Patients in group 1 presented with chest pain as the main symptom less frequently (62.1% vs 81.4%, p<0.001). Group 1 had a higher number of patients with Killip class III ou IV at admission (14.8% vs 3.6%; p<0.001), new onset atrial fibrillation (5.3% vs 2.1%; p=0.016) a higher number of mechanical complications (1.5% vs 0.2%; p=0.046), a higher need of inotropic support (9.8% vs 2.1%; p<0.001), temporary pacing (6.1% vs 1.7%; p<0.001), invasive mechanical ventilation (5.7% vs 1.3%; p=0.001) and non-invasive ventilation (5.7% vs 1.7%; p=0.002). IHM was significantly higher in group 1 (11.4% vs 2.9%, p<0.001).

In the multivariate analysis, with age, sex, comorbidities (including known DM), past history and medication as covariates, AHG was an independent predictor for the need of temporary pacing (p=0.004) and mechanical ventilation (p=0.007).

Conclusion: Every patient with ACS should have a blood glucose measurement at admission. AHG is associated with a more severe presentation and in-hospital evolution, therefore its control must be included in the management of these patients. In this study, AHG was an independent predictor for the need of temporary pacing and mechanical ventilation during hospitalization.

Kaplan-Meier curve
Acute coronary syndromes in patients with diabetes mellitus - do HbA1c levels predict severity of coronary artery disease and affect 1-year prognosis?

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Introduction: Acute coronary syndromes (ACS) are an important cause of morbidity and mortality in patients with diabetes mellitus (DM). These patients have more severe coronary artery disease (CAD) and worse prognosis. Elevated HbA1c levels correlate with microvascular complications, but its relationship with macrovascular complications is less well established.

Purpose: This study intends to evaluate the relationship between HbA1c levels and severity of the lesion, as well as identify which factors significantly affected 1-year prognosis in patients with DM and ACS.

Methods: We performed a retrospective, descriptive and correlational study with all patients admitted to a cardiology department with an ACS between the 1st of October 2003 and 31st of August 2014. All patients with DM were included and their baseline characteristics, admission data and therapy were analyzed. The 1-year follow-up was done by phone call by a Cardiologist. We performed a univariate and multivariate statistical analysis of mortality and hospitalization using SPSS.

Results: There was a total of 2818 patients with an ACS, 783 (27.8%) of whom had DM, with a mean HbA1c level of 7.8%. There were no differences in HbA1c levels between patients with normal coronary arteries (p=0.06), single vessel CAD (left anterior descending artery; p=0.4; circumflex artery; p=0.9), right coronary artery (p=0.1) and left main coronary artery disease (p=0.8); single versus 2-vessel CAD (p=1.0), single versus 3-vessel CAD (p=0.47) and 2 versus 3-vessel CAD (p=0.282). HbA1c levels had no impact on 1-year hospitalization rate (p=0.282) and mortality (p=1.0). The factors that were significantly associated with an increased mortality were: age older (p=0.01); reduced left ventricular ejection fraction (p=0.01); past history of angina (p=0.01); ACS (p=0.01), percutaneous coronary intervention (PCI) (p=0.01), pacemaker/CDI (p=0.01), valvular heart disease (p=0.01), heart failure (p=0.01), peripheral arterial disease (p=0.01), stroke/transient ischemic attack (p=0.01) and chronic kidney disease (p=0.01). The following post-discharge medical therapy was associated with an increased 1-year mortality: nitrates (p<0.01), ivabradine (p=0.01), diuretics (p=0.01), aldosterone receptor antagonists (p=0.01) and dabigatran (p=0.01). Patients who underwent coronary catheterization (p=0.01) and PCI (p=0.01) had a lower mortality rate. Post-discharge medical therapy with aspirin (p=0.01), clopidogrel (p=0.01), beta-blocker (p=0.01) and angiotensin converting enzyme inhibitors (p=0.01) were all associated with a lower mortality rate at 1-year.

Conclusions: Patients with an ACS and DM, HbA1c levels show no correlation with severity of coronary artery disease and affect 1-year mortality.

Acute coronary syndromes in patients with diabetes mellitus - do HbA1c levels predict severity of coronary artery disease and affect 1-year prognosis?

P3771 | BEDSIDE

Hierarchical analysis of cardiovascular disease risk factors in the secondary prevention: A classification analysis within the GREECS study

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Background: Cardiovascular risk factors have been clearly estimated as regards primary cardiovascular disease (CVD) prevention; nonetheless, evidence regarding secondary prevention demands further confirmation.

Purpose: To evaluate the most important CVD risk factors under the context of secondary cardiovascular disease prevention.

Methods: From October 2003 to September 2004 a sample of 6 Greek hospitals was selected and almost all consecutive 2,172 Acute Coronary Syndrome (ACS) patients were enrolled. In 2013-14, 10-year follow-up was performed in 1,918 participants. Age, sex, obesity, current smoking, MedDietScore, physical activity, family history of CVD, hypertension, hypercholesterolemia and diabetes mellitus were evaluated in relation to the development of 10-year ACS prognosis based on hierarchical classification analysis using Fisher linear discriminant function. Further risk assessment was performed through multiple logistic regression models.

Results: 10-year incidence was 40% in males and 32% in females (p<0.001). In CVD-risk factors classification only some of them led to a significant association concerning ACS prognosis. The predominant risk predictors were diabetes mellitus (OR=1.918; p<0.001) and family history of CVD (Wilk's L=0.998, p=0.04); whilst all others were in the second highest rank. Age- and gender- specific analysis confirmed that the aforementioned ranking was irrespective of participants' age and gender. Additionally, multiple logistic regression models, adjusted for the above mentioned factors, confirmed these findings; patients with diabetes or family CVD history at baseline had 26% (OR=1.26, 95% CI: 1.01, 1.57) and 29% (OR=1.28, 95% CI: 1.04, 1.58) higher 10-year risk for recurrent ACS events, respectively, compared with their free-of-these-factors counterparts.

Conclusions: Patients with family history of CVD or abnormal glycemic status seem to be more susceptible to a new cardiac episode; it is thus obvious that these findings may be of high importance in the rehabilitation process or risk estimation for more accurate and to-the-point clinical assessment.

Association of osteopontin level with coronary atherosclerosis and osteoporosis in male patients with stable coronary artery disease


Objective: To measure plasma levels of osteopontin in patients with stable coronary artery disease depending on the severity of atherosclerosis, coronary atherosclerosis and coronary artery calcification.

Material and methods: 111 male patients with verified stable coronary artery disease undergoing coronary artery bypass grafting were included in the study. The mean age of the patients was 59.8 (55.70) years. The inclusion criteria were as follows: age >75 years; stable angina I- III functional class. The exclusion criteria were as follows: severe comorbidities, angina IV functional class, severe heart failure, prior coronary revascularization. All patients underwent coronary angiography, multislice computed tomography (MSCT), densitometry, echocardiography, blood sampling to measure osteopontin levels.

Results: 14.4% of patients had single-vessel coronary artery disease (CAD), 24.3% - two-vessel CAD, 61.3% - three-vessel CAD. Mild coronary artery (CA) lesions were found by the Syntax Score in 44.2% of patients, moderate in 36.0% of patients, and severe - in 25.2% of patients. Minor coronary artery calcification (CAC) was detected in 9.9% of patients, mild CAC - in 7.2% of patients. Patients, moderate - in 25.2% of patients, severe - in 57.7% of patients. 52.2% of patients had osteopenia, 27.9% of patients - osteoporosis, and 19.8% of patients had normal bone mineral density. Plasma osteopontin levels were 50% higher in patients with the Syntax score above 22 compared to those patients who had the Syntax score below 22 [7.5 (5.14-8.97) vs 5.14 (4.30-7.96) ng/ml, p=0.01]. Osteopontin levels were 48% higher in patients with diabetes mellitus - do HbA1c levels predict severity of coronary artery disease and affect 1-year prognosis.

Conclusion: Osteopontin levels in patients with coronary artery disease correlate with the severity of coronary atherosclerosis, particularly in patients over 60 years, as well as with the parameters of left ventricular remodeling.

Body weight does not affect systemic PK exposure parameters of MDCO-216 in healthy volunteers and CAD patients

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Introduction: MDCO-216, a complex of dimeric recombinant apolipoprotein A-1 Milano (ApoA-1 M) and a phospholipid (POPC), is currently under development as a biologic agent to improve cardiovascular outcomes by reducing plaque burden in patients with atherosclerotic disease. Decision of fixed vs body size-adjusted dosing represents one of the challenges of biologics development. The purpose of this study was to assess the pharmacokinetics (PK) and explore the effect of body size/weight on systemic exposure parameters of MDCO-216.

Methods: 24 healthy volunteers (HVs) received a single dose of MDCO-216 (5, 10, 20, 30 or 40 mg/kg) or placebo (in 2:1 ratio) as a 2 hour IV infusion in a double blind, randomized design in the second phase of the study. 24 stable coronary artery disease (CAD) patients received MDCO-216 in the same manner except for the 5mg/kg dose. Serial blood samples were collected for drug levels and PK parameters were calculated using non-compartmental analysis.

Results: MDCO-216 was safely administered as single ascending doses and well tolerated.
tolerated without generating any antibiotic antibodies. Plasma mean (SD) half-life of MDCO-216 was almost identical, 56.6 (14.2) h in HVs and 52.5 (15.7) h in patients. tram in both groups ranged between 2 to 4 hours. Exposure parameters of AUC and Cmax increased with dose in a dose-proportional or nearly dose-proportional manner. Among the dosing cohorts, inter-subject variability in PK parameters was low with a SCV ranging from 7.1 to 43.2 and 1.5 to 20.8 for AUC and Cmax, respectively. Regression analysis between BW and BMI vs. AUC and Cmax did not indicate any significant correlation with almost flat lines.

Conclusions: This data demonstrate that body size, such as body weight, does not significantly impact on systemic exposure of MDCO-216 after single infusions. A fixed dose rather than BW-adjusted dose may be considered in future clinical trials with MDCO-216 in relevant patient populations.

P7774 | BEDSIDE
Paradoxal presence of spare A2A receptors in patients with coronary artery disease with positive exercise stress test

Background: During muscle exercise, cardiac oxygen-consumption increases and the resulting low oxygen level in myocardium triggers coronary vasodilation. This adaptive response to hypoxia that is mimicked during the exercise stress test (EST) is controlled notably by the vasodilator adenine via the A2A receptor (A2AR). According to the spare receptor pharmacological theory, activation of only a weak fraction of A2AR (evaluated using the KD variable) results in maximal cAMP production (evaluated using the EC50 variable), and hence in coronary vasodilation in the context of a large number of unoccupied A2AR. In coronary artery disease (CAD), myocardial ischaemia limits coronary response to exercise during EST.

Purpose: We looked for the presence of spare A2AR in CAD in order to adapt coronary vasodilatation in hypoxic/ischemic condition.

Methods: Seventeen patients with angiographically-confirmed CAD and 17 control subjects were studied. We addressed adenosine-plasma concentration and the mononuclear cell-expression of the pool of A2AR. The presence of spare A2AR at the mononuclear cell-surface was specifically addressed using an innovative pharmacological method.

Results: EST was positive in 82% of patients, and in none of the controls. Adenosine plasma-concentration increased by 60% at peak exercise in patients only (p < 0.01). Most patients (65%), and none of the controls, had spare A2AR (identified when EC50/KD=0.1) and low A2AR expression (mean -37% compared with controls, p < 0.01). All patients with spare A2AR had a positive EST whereas the subjects without spare A2AR had a negative EST (p < 0.05).

Conclusions: We conclude that spare A2AR are specifically found in CAD patients with positive EST. Paradoxically, spare A2AR in CAD fail to adapt coronary vasodilation in hypoxic/ischemic condition.

Acknowledgement/Funding: Aix-Marseille University and AP-HM

P7775 | BEDSIDE
Increased adenosine tissue bradykinin receptors gene expression profiles in obese patients with 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 and atherosclerotic vascular function. The aim of this study is to examine kinin receptors gene expression levels in the adipose tissue in obese patients with and without CAD.

Methods: Obese patients (BMI >30kg/m²) undergoing coronary angiography were part of the study. We included 15 patients with CAD (9 male, 64±8 years old) and 9 patients without CAD (6 male, 63±8 years old). Subcutaneous white adipose tissue biopsies were obtained from the site of parametasis before the procedure and analyzed for bradykinin receptor type 1 (BR1) and 2 (BR2) gene expression by RT-quantitative PCR.

Results: Adipose tissue analysis revealed increased BR1 and BR2 gene expression levels in obese patients with CAD compared to those without CAD. More specifically, BR1 gene expression levels were 654±345 in patients with CAD versus 107±99 in patients without CAD and BR2 gene expression levels were 458±165 in patients with CAD versus 133±107 in patients without CAD (p < 0.05 for both). No statistical significant correlation were found between BR1 and BR2 gene expression levels and patients BMI.

Conclusions: There is a divergence in BR1 and BR2 gene expression in adipose tissue between obese patients who exhibit or do not exhibit CAD. Our findings may have implications in the pathophysiology and treatment of atherosclerosis and should be further investigated.

P7777 | BEDSIDE
Clinical impact of a newly diagnosed cancer in patients with acute coronary syndrome undergoing emergent percutaneous coronary revascularization
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Background: Information, such as concomitant cancer, is uncertain in patients with acute coronary syndrome (ACS). We aimed to investigate clinical impact of a newly diagnosed cancer in ACS patients who underwent emergent percutaneous coronary intervention (PCI).

Methods: From April 2007 to September 2012, we investigated prevalence and clinical outcome of a newly diagnosed cancer in 1698 ACS patients undergoing emergent PCI, except for the patients who had previously diagnosed with cancer.

Results: During follow-up periods (15±3.5months), 44 new cancer cases (2.4%) were identified. The patients with cancer were significantly older than those without cancer (73±10 vs. 64±12 years, p<0.001), and hemoglobin concentration was significantly lower in cancer group than in without cancer group (12.9±2.1 vs. 13.9±2.0, p<0.003). They were identified as gastrointestinal cancer (n=11), lung cancer (n=11), urinary cancer (n=9), hematological neoplasia (n=9), and others (n=3). Multivariate logistic analysis showed that age, male, and anemia (Hb<12g/dL) were independent predictors of newly diagnosed cancer (odds ratio [95% CI]: 1.05 [1.02–1.09], 2.94 [1.24–6.97], and 2.30 [1.45–6.42], p<0.001, p=0.014, and p=0.019, respectively). Among 23 patients who received surgery (median period from PCI to surgery was 11-months, and pre-operative discontinuation of DAPT was 7-days), no cardiac death, 3 stent thrombosis and 2 major bleeding complications occurred after surgery.

Conclusion: We should consider concomitant cancer and the importance of screening cancer surveillance, especially when suffering from anemia in elderly patients.

P7778 | BEDSIDE
A new point-of-care device to measure erythrocyte aggregation: a proof of concept study. LAREHK-1/LAREHK-2
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Background: Erythrocyte aggregation (EA) is a reversible phenomenon which is increased in patients with acute coronary events. Current EA measurement techniques involve cell counting on a flow cytometer. We developed a new point-of-care device, LAREHK-1/LAREHK-2, to measure EA in blood and to determine whether it could be considered as a biomarker of cardiovascular function.

Methods: We used a new point-of-care (POC) device to optically measure EA kinetics in 30th through a standard blood collection tube (EDTA). EA kinetics was measured in 24 patients hospitalized in cardiology including 11 a few days after an acute coronary syndrome and 45 healthy blood donors. Eighteen patients received antplatelet drugs including 11 dual therapy. Five patients received anti-coagulant drugs.
Results: A mathematical model was fitted to each short term EA kinetics curve. Model square regression coefficients ranged from 0.96 to 0.99. The table shows computed half life. The measure is highly specific of EA.

P3779 | BEDSIDE
Insulin-like growth factor-binding protein 7 (IGFBP 7) as a new biomarker in coronary heart disease
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Objective: Insulin-like growth factor-binding protein 7 (IGFBP 7) is a new biomarker related to heart failure and cardiac hypertrophy, however, its role in atherosclerosis has not been defined. The aim of the study was to establish whether IGFBP 7 may act as an independent risk factor of coronary artery disease (CAD) occurrence and advancement, if IGFBP 7 has potential relations with classical as well as new biomarkers of cardiovascular risk (carotid intima-media thickness, cIMT), and whether IGFBP 7 may be a marker of mortality in the group of patients with myocardial infarction (MI) during mid-term follow-up (average period of 2.8 years).

Patients and methods: The study group was composed of 233 patients with MI and 100 patients with stable CAD. Traditional risk factors of atherosclerosis as well as new – IGFBP 7 concentrations and cIMT were assessed. The control group was composed of 100 healthy individuals.

Results: In the study group (MI and CAD patients) IGFBP 7 concentrations were significantly higher as compared to the controls – median 35.1ng/mL (p<0.00001) and 32.7ng/mL (p<0.0001) vs. 25.2ng/mL, respectively. The value of 38.7ng/mL has been assigned as a cut-off value (AUC=0.703, 95% CI: 0.648–0.753). IGFBP 7 concentration did not correlate with a degree of coronary vessels occlusion, but it was significantly correlated with age (p<0.0001), male gender (p<0.0001) and cIMT (p<0.05). IGFBP 7 concentrations were found to increase in patients with Killip class IV (p<0.05). In the group of MI patients who died during in-hospital stay, IGFBP 7 concentration was elevated (p<0.001).

Conclusion: IGFBP 7 is an independent risk factor of CAD occurrence, but not its advancement. cIMT is a good predictor of both the presence and the progress of disease.

P3780 | BEDSIDE
Contemporary long-term prognosis of acute coronary syndrome complicated with heart failure depending on the Killip class at admission

Introduction: The Killip class classification for heart failure is used to predict short-term mortality in patients with acute coronary syndrome (ACS). Purpose: To determine the contemporary long-term prognosis of ACS with acute heart failure graded according to the Killip classification.

Methods: Cohort study of consecutive patients with ACS diagnosis hospitalized in the coronary care unit from 2004 to 2009. Follow-up was done by clinical review or telephone contact and death or cardiovascular events were recorded, as well as the cause of death.

Results: 5070 patients were included with a complete follow up after a mean of 5.8±2.6 years. The clinical characteristics were analysed in relation with Killip class at admission (shown in Table). A stepwise gradient in the adjusted hazard ratio (HR) for mortality was observed with increasing Killip class: class > I HR 4.35 (95% CI 3.81 to 4.97) unexpectedly, in a landmark analysis excluding deaths <30 days after admission, patients in Killip class IV had a lower adjusted long-term mortality than those in class II or III (shown in Figure)

Conclusion: The heterogeneity in early versus late risk in patients with Killip class IV heart failure it is present in our contemporary cohort, highlighting the importance of an appropriate early treatment in cardiogenic shock patients.
modeling was used to assess the relationship of the admission hemoglobin level and Killip class.

**Results:** Nine hundred patients with ACS (mean age 64±13 years; 74% male), 37.2% with ST- elevation ACS and 62.8% non-ST-elevation, were included. Hemoglobin admission levels ranged between 9.7 and 17.7 (median 14.4) g/dl. Seventy-two and sixty-nine percent of the patients evolved in Killip I, II, 123 in Killip III and 17 in Killip IV and their median (interquartile range) admission hemoglobin levels were 14.4 g/dl (13.2–15.4), 13.5 (11.9–14.9), 13.3 (12.2–14.5) and 13.0 (11.9–15.2), respectively. In ST-elevation ACS patients, after adjustment for differences in baseline characteristics (sex, age, creatinine at admission, ACS type and history of failure), for each 1 g/dl higher hemoglobin at admission the probability of evolving in Killip class III and IV decreased by 30% (OR=0.70, 95% CI 0.55–0.97, p=0.03 and OR= 0.70, 95% CI 0.51–0.94, p=0.019, respectively) with compared to those with Killip I. Using bioluminescence assay methods at the first 24 hours after admission to the hospital and at the dynamics of the disease on the 10th day. Follow-up period was 1 year.

**Conclusions:** In ST-elevation ACS patients lower admission hemoglobin level was associated with an increased risk for Killip class worsening during in-hospital stay.

P3782 | BEDSIDE

**Prognosis of outcome in patients with acute myocardial infarction in combination with mixed anxiety-depressive disorder**

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**Introduction:** Presence of mixed anxiety-depressive disorder (MADD) in patients with acute myocardial infarction (AMI) has an impact on comorbid pathology that is at increased risk at both short- and long-term period. Their precise prognosis is a matter of concern.

**Purpose:** To create a method of prognosing of adverse cardiovascular events in patients with MADD during 1 year after AIM.

**Methods:** We studied 196 patients both sexes with AMI (mean age 64±20,8 years). Patients were divided into two groups: 1st group – 88 patients with AMI without MADD; 2nd group – 108 patients with AMI with MADD. We researched activity of NAD and NADP-dependent dehydrogenases in platelets of patients using bioluminescence assay methods at the first 24 hours after admission to the hospital and at the dynamics of the disease on the 10th day. Follow-up period was 1 year.

**Results:** In the prospective study in patients without MADD cardiovascular adverse events were found in 36% of patients in the group without MADD and in 55% of patients in the group with MADD, which was significantly higher (p<0.05). Using logistic multivariate regression most informative indicators of the studied platelet enzymes activity were analyzed. For patients without MADD method of prediction of adverse cardiovascular events was based on calculating of the glyco-lemon relations coefficient (GLRC), representing a ratio: GLRC = NADH-dependent lactic dehydrogenase / NADH-dependent malate dehydrogenase. The value of the coefficient was < 0.250, patients had significantly higher number of adverse cardiovascular events (p<0.05). For patients with MADD method of prediction is based on calculating of the glutamate glutathione ratio coefficient (GGRC), representing a ratio: GGRC = (NADPH-dependent isocitrate dehydrogenase / NADPH-dependent malate dehydrogenase) glutathione reduction. If the value of the coefficient was > 1.67 KGLO patients had significantly higher number of adverse cardiovascular events (p<0.05).

**Conclusion:** Proposed methods of prognosing with adjustment for MADD can reveal patients who are at risk of cardiovascular adverse events development during 1 year after AIM which can be useful in the management of their treatment.

P3783 | BEDSIDE

**Ticagrelor improves peripheral arterial function in acute coronary syndrome patients: relationship with adenosine plasma level**

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**Background:** Ticagrelor a P2 Y12 receptor antagonist reduced significantly the incidence of major cardiovascular events in acute coronary syndrome (ACS) patients with non-ST elevation, and the higher the plasma level of ticagrelor, the more reduction occurred accounted by pleiotropic properties via a purinergic mechanism. Indeed, ticagrelor increases endogenous adenosine plasma level (APL). However the link between this “pleiotropic” property and the improvement in microvascular dysfunctions (MiD) remains poorly investigated.

**Purpose:** This study aimed to determine whether the increase of APL achieved with ticagrelor might improve endothelial dysfunction in primary ACS patients.

**Methods:** We prospectively randomized 60 primary ACS patients to receive ticagrelor (900 mg orally followed by 90 mg daily) or clopidogrel (75 mg daily followed by 600 mg followed by 75 mg daily). In addition all patients received 250 mg followed by 75 mg daily of aspirin. Exclusion criteria were NYHA II–III, cardiac arrest, contra-indications to antipileretel therapy, treatment with a P2Y12-ADP receptor antagonist for <1 month, a platelet count <100 g/l, history of bleeding diathesis, history stroke, recent surgery (preceding month), use of medication having known interference with ticagrelor, and bradycardia. Blood samples were collected in basal conditions (just before the primary loading dose) and after 30 days of treatment. To assess the MiD, we performed digital peripheral artery tonometry (PAT), at the same time to evaluate the hyperemia index (RHI). Endothelial dysfunction was suspected if RHI <1.67.

**Results:** In basal conditions, all the patients presented RHI <1.67, mean 1.37±0.12. APL and RHI (see figure) were not different between the two groups of patients. At day 30, APL increased significantly only in the ticagrelor group. The APL was more than 2-fold higher in patients taking ticagrelor than in patients taking clopidogrel. After 30 days, mean RHI increased weakly (mean +15%) in the clopidogrel group and strongly (+100%) in the ticagrelor group. We found a corre- lation between the increase in RHI and the increase in ticagrelor APL. No ischemic or bleeding events were recorded within 1 month. Treatment with ticagrelor improves peripheral arterial function compared to clopidogrel. Endothelial function responds to ticagrelor therapy within 30 days, long before the effects on clinical outcomes are seen. The underlying mechanism seems to be the APL increase. It was shown that ticagrelor dose dependently increased adenosine-mediated coronary blood flow in healthy human subjects. These effects occur mostly via the activation of A2A adenosine receptors.

**Conclusions:** Here we found that ticagrelor induces an increase in APL which correlates with the increase in RHI. Because low RHI is associated with higher rate of cardiovascular events, we studied the effects of ticagrelor on the plasma levels of adenosine during follow-up our study led to the hypothesis that adenosine-mediated effects of ticagrelor may explain the efficacy of the PLATO mortality benefit.

**Acknowledgement/Funding:** Aix Marseille University and AP-HM

P3784 | BEDSIDE

**Fatorial effects of evolocumab and atorvastatin on lipoprotein metabolism: the FLOREY stable isotope study**


**Background:** Monoclonal antibodies (mAbs) against proprotein convertase subtilisin/kexin type 9 (PCSK9), such as evolocumab, lower plasma low-density lipoprotein (LDL)-cholesterol concentrations. Evolocumab is approved for hyper- low-density lipoprotein (LDL) cholesterol, mixed-dyslipidaemia and familial hypercholesterolaemia. The current analysis is being studied for its effects on cardiovascular (CV) outcomes in statin-treated high-risk patients. The mechanism of action of anti-PCSK9 mAbs on lipoprotein metabolism in humans has yet to be investigated.

**Methods:** We carried out an 8-week factorial trial of the effects of atorvastatin (80 mg daily) and subcutaneous evolocumab (420 mg every two weeks) on the plasma kinetics of very-low density lipoprotein (VLDL)-, intermediate-density lipoprotein (IDL-) and LDL-apolipoprotein B-100 (apoB) in 81 normolipidemic, healthy men. In an independently conducted analysis, ApoB kinetics were studied using a stable isotope infusion of D3-leucine, mass spectrometry, and compartmental modelling.

**Results:** Atorvastatin and evolocumab independently accelerated the fractional catabolism of VLDL-apoB (P<0.001 and P<0.05, main effects, respectively), IDL-apoB (P<0.05 and P<0.005, main effects, respectively) and LDL-apoB (P<0.001, main effects, both interventions; Figure). Evolocumab but not atorva- tatin decreased the production of IDL-apoB (P<0.05) and LDL-apoB (P<0.01), which also contributed to the significant reductions in the plasma pool sizes of the corresponding lipoprotein particles. This benefit of LDL-apoB and LDL- cholesterol concentrations were significantly greater with combination therapy than with either intervention alone (P<0.001) and were accounted for by in- creased catabolism and reduced production of LDL particles. While evolocumab and not atorvastatin lowered the concentration of free PCSK9, atorvastatin lowered the concentrations of apoC-III and the lathosterol:cholesterol ratio. Both in- terventions decreased apoE; neither significantly altered lipoprotein lipase and cholesterol ester transfer protein mass.

**Conclusions:** The study demonstrates that the plasma concentration of atherogenic lipoproteins, particularly LDL-apoB, by accelerating their rate of catabolism. Reductions in IDL-apoB and LDL-apoB production also contributed to the reduction in LDL particle concentration with evolocumab. The kinetic effects were additional...
to those of atorvastatin, even within the lower ranges of plasma lipid and lipoprotein concentrations.

P3785 | BEDSIDE
New scoring model to predict bleeding events within 2 year after DES implantation

Background: Bleeding events after drug-eluting stent (DES) implantation was closely associated with prognosis of patients. Various scoring models estimating risk of bleeding were proposed but a little were available about DES implantation for stable angina pectoris (SAP). HAS-BLED score was simple scoring model evaluating bleeding risk of patients who use warfarin and widely used in real-clinical practices.

Purpose: Our aim in this study was to make a new scoring model to predict bleeding events within 2 year after DES implantation for SAP. Clinical predictive value was compare with HAS-BLED score applying to this study cohort.

Methods: We studied “all-comers” 1926 consecutive patients who underwent DES implantation for SAP (70±10 years, 72% male). Bleeding events was defined as a composite of type 5, 3, and 2 bleeding in Bleeding Academic Research Consortium (BARC) criteria. Bleeding related with procedure of DES implantation was excluded in this study. We assessed predictors using Cox proportional hazard regression analysis, the 30-day all-cause mortality risk was significant higher in patients with potassium level of 4.5–5.0 mmol/L (hazard ratio [HR] 1.52, 95% confidence interval [CI] 1.17–1.98), and the risk was even higher in patients with potassium level of 5.0 mmol/L, and a level of more than 5.0 mmol/L significantly increased mortality risk.

Results: Of these patients, 97 patients (5.0%) were suffering from bleeding events. The gastrointestinal (GI) bleeding was the most common site (n=57, 58%). The gastrointestinal (GI) bleeding was the most common site (n=57, 58%). The gastrointestinal (GI) bleeding was the most common site (n=57, 58%). The gastrointestinal (GI) bleeding was the most common site (n=57, 58%). The gastrointestinal (GI) bleeding was the most common site (n=57, 58%). The gastrointestinal (GI) bleeding was the most common site (n=57, 58%). The gastrointestinal (GI) bleeding was the most common site (n=57, 58%). The gastrointestinal (GI) bleeding was the most common site (n=57, 58%). The gastrointestinal (GI) bleeding was the most common site (n=57, 58%). The gastrointestinal (GI) bleeding was the most common site (n=57, 58%).

Conclusions: The definition of a healthy reference population and the number of subjects to include in 99th percentile estimations is still being debated within the scientific community as is the implementation of sex- or age-specific cut-off values. Our results suggest that troponin values might also be influenced by BMI and further research should address whether this correlation might be of clinical relevance.

P3787 | BEDSIDE
Relation of serum potassium levels to short-term outcomes in patients with ST-segment elevation myocardial infarction
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Background: Potassium homeostasis is an important determinant of cardiac function and current guidelines recommend maintaining serum potassium levels between 4.0 and 5.0 mmol/L in patients with acute myocardial infarction. However, these guidelines are based on studies conducted before beta-blocker and reperfusion era and recent trials have demonstrated an association between serum potassium and elevated mortality risk.

Purpose: To evaluate the impact of serum potassium on short-term outcomes in patients with ST-segment elevation myocardial infarction (STEMI).

Methods: We retrospectively analyzed 6613 patients diagnosed with STEMI who presented without renal insufficiency which was defined as creatinine >2.0 mg/dL or 175 umol/L in this study. After admission, serial serum potassium levels were measured at baseline, 6±2 hours and 24±4 hours for each patient. Then three measurements were averaged and recorded as mean serum potassium level. Patients were categorized into 5 groups to determine the relation between mean serum potassium level and short-term outcomes: <3.5, 3.5–<4.0, 4.0–<4.5, 4.5–<5.0 and ≥5.0 mmol/L.

Results: With regard to clinical outcomes, the lowest 7-day malignant arrhythmia, 7-day and 30-day all-cause mortality rates were observed in patients with mean serum potassium level of 4.0–4.5 mmol/L, whereas mortality was higher in patients with potassium levels ≥4.5 mmol/L. In multivariate Cox-proportional regression analysis, the 30-day all-cause mortality risk was significant higher in patients with potassium level of 4.5–5.0 mmol/L (hazard ratio [HR] 1.52, 95% confidence interval [CI] 1.17–1.98), and the risk was even higher in patients with potassium level of ≥5.0 mmol/L (HR 1.80, 95% CI 1.22–2.66), in comparison with the reference group of 4.0–4.5 mmol/L. In contrast to the association with 30-day all-cause mortality, no relationship was observed between serum potassium and the occurrence of 7-day malignant arrhythmia or 7-day all-cause mortality.

Conclusion: Among patients with STEMI, the lowest 30-day all-cause mortality was observed in those with mean serum potassium levels between 4.0 and 4.5 mmol/L, and a level of more than 4.5 mmol/L significantly increased mortality risk.

BLOOD MARKERS IN ACUTE CORONARY SYNDROME

P3786 | BEDSIDE
Reference values of high-sensitivity troponin T in a healthy reference population
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Background: High-sensitivity troponin assays are increasingly implemented into clinical routine in Europe and worldwide. The 99th percentile as a cut-off value for acute myocardial infarction differs between assays and populations.

Objective: To assess the 99th percentile of a high-sensitivity cardiac troponin T assay in a healthy reference population in Germany.

Methods: Healthy individuals (n=564) were included at two study centers (n=264 and n=300). Patients with cardiac, renal or metabolic diseases were excluded from the study. High-sensitivity cardiac troponin T was measured on the Cobas analytical system (Roché Diagnostics). The 99th percentile given by the manufacturer lay at 14ng/L.

Results: The proportion of men (50.2%) and women (49.8%) was similar in the study population, the median age was 44 years (IQR: 19–74), 35.6% off all persons had values below the limit of blank (3ng/L) and 70.2% had values below the limit of detection of this assay (5ng/L). The 99th percentile value in the overall population was 12.53ng/L. The 99th percentile values did not differ significantly between gender-, age- or BMI-based subgroups but lower values were estimated for women and persons with overweight (figure 1).

Conclusions: The definition of a healthy reference population and the number of subjects to include in 99th percentile estimations is still being debated within the scientific community as is the implementation of sex- or age-specific cut-off values. Our results suggest that troponin values might also be influenced by BMI and further research should address whether this correlation might be of clinical relevance.
Parathyroid hormone levels and high-residual platelet reactivity in patients receiving dual antiplatelet therapy with acetylsalicylic acid and clopidogrel or ticagrelor

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High on treatment platelet reactivity still represents a challenging issue, potentially vanishing the benefits of dual antiplatelet treatment in patients with coronary artery disease. However, very few is known on the determinants of suboptimal response to antiplatelet agents. Recent interests have emerged on the potential pro-thrombotic effect of parathyroid hormone (PTH). Therefore, the aim of the present study was to assess the impact of parathyroid hormone (PTH) on platelet reactivity in patients receiving DAPT after an acute coronary syndrome or PCI.

Methods: Patients treated with DAPT (ASA and clopidogrel or ticagrelor) were scheduled for platelet function assessment at 30–90 days post-discharge. By whole blood impedance aggregometry, HRPR was considered for ASPI test = > 82 AU/min (for ASA) and ADP test values > 417 AU/min (for ADP-antagonists).

Results: We included 362 patients on DAPT, 125 (34.5%) receiving clopidogrel and 237 (65.5%) on ticagrelor. Patients were divided according to PTH quartiles values (<45.8; 45.8–60.3; 60.4–88; ≥88.1 pg/ml). Higher PTH was associated with older age (p=0.001); renal failure (p=0.001), higher HDL cholesterol (p=0.006), and creatinine (p=0.001) and lower 25-OH cholecalciferol (p=0.001). Suboptimal response to ASA was infrequent (2.8%), and not influenced by the levels of PTH (p=0.57).

ADP-mediated platelet aggregation was significantly increased in patients with higher PTH (p=0.03), with an absolute increase in the prevalence of HRPP to ADP-antagonists for higher PTH (24.7% vs 40%, p=0.007 for 4th vs 1–3rd quartiles, adjusted OR [95% CI] = 2.04 [1.14–3.64], p=0.02). By the use of the ROC curve, we identified PTH levels above 96.7 pg/ml as the best predictor of HRPR in the univariable analysis (area under the curve: 0.69; p=0.04). By the use of the ROC curve, we identified PTH levels above 96.7 pg/ml as the best predictor of HRPR in the univariable analysis (area under the curve: 0.69; p=0.04). By the use of the ROC curve, we identified PTH levels above 96.7 pg/ml as the best predictor of HRPR in the univariable analysis (area under the curve: 0.69; p=0.04).

Conclusion: In patients receiving dual antiplatelet therapy for coronary artery disease, higher PTH levels are associated with an increased ADP-mediated platelet reactivity and suboptimal response to clopidogrel, especially for values above 96.7 pg/ml, while not influencing the effectiveness of ASA and ticagrelor.

Soluble galectin-3 is associated with premature myocardial infarction

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Background: Inflammatory responses are pivotal in the initiation and development of premature atherosclerotic lesions. Galectin-3 represents a valuable biomarker for both, progression and destabilization of atherosclerotic lesions. The present study aims to assess the involvement of galectin-3 in premature myocardial infarction.

Design: In this multicenter case-control study, we assessed circulating galectin-3 levels in 144 patients comprising 72 consecutive survivors of premature acute myocardial infarction (≤40 years) and 72 hospital controls frequency-matched for age, gender, and center.

Results: Patients with acute myocardial infarction showed significantly higher galectin-3 levels as compared to controls in the acute phase of acute myocardial infarction (2552±1992 vs. 1666±829 pg/ml; p<0.001) as well as in the stable phase 1 year after the index event (3692±1774 vs. 1666±829 pg/ml; p<0.001) (Fig.1). Circulating galectin-3 was significantly and independently associated with premature myocardial infarction in the logistic regression analysis (acute phase: adj. OR per 1-SD change 2.03, 95% CI 1.30–3.19; P=0.002). There was a significant correlation between circulating galectin-3 and leucocyte count (r=0.35, P<0.001); non-HDL cholesterol (r=0.23, P=0.014), and HDL cholesterol (r=−0.29, P=0.02). We observed an even more pronounced association between circulating galectin-3 levels and premature MI one year after index event with an unadjusted OR of 6.89 (95% CI 3.23–14.73; P<0.001) and significant higher galectin-3 levels in patients experiencing MACE (composite end point of all-cause death, re-myocardial infarction and stroke) in the stable phase of the disease [4675 pg/ml (3179–5203) vs. 3299 pg/ml (1916–4729); P=0.026].

Conclusion: We demonstrated that elevated levels of circulating galectin-3 are strongly associated with premature myocardial infarction. Galectin-3 might serve as link between dyslipidaemia as driving force of plaque formation with inflammation as initiator of plaque rupture in patients with premature acute myocardial infarction. Moreover in the stable phase of the disease galectin-3 levels were significantly higher in patients experiencing MACE, suggesting that the biomarker may reflect a global cardiovascular burden and might identify those patients at high risk to develop future cardiovascular events.

Blood markers in acute coronary syndrome

P3789 | BEDSIDE
Predictive and prognostic value of biomarkers of CI-AKI (contrast induced - acute kidney injury) in patients presenting with STEMI (ST-segment elevation myocardial infarction) treated by primary PCI


Background: Contrast induced acute kidney injury (CI-AKI) is associated with a high morbidity and mortality in coronary patients. We assess the predictive value of novel biomarkers of renal dysfunction, cystatin C and neutrophil gelatinase-associated lipocalin (NGAL) of the incidence of CI-AKI and their prognostic value on mortality in ST-segment elevated myocardial infarction (STEMI) patients treated by primary percutaneous coronary intervention (PPCI).

Methods: NGAL and cystatin C level were measured on admission, prior to pPCI, in 701 STEMI patients and were correlated to the occurrence of CI-AKI according to the various existing definitions. Association between biomarkers level and the incidence of CI-AKI, MACE and all-cause mortality at 1-year-follow-up was evaluated.

Results: Incidence of CI-AKI varied from 12.0% to 21.5% depending on the definition used. Increased levels of plasmatic NGAL and cystatin C were associated with a stepwise increase in the incidence of CI-AKI and the stage of renal failure. Both biomarkers predicted CI-AKI with receiver operating characteristic (ROC) analysis showing an area under curve of 0.60 for cystatin-C and 0.62 for NGAL, both p<0.05. MACE and all-cause mortality at 1-year-follow-up were also higher in the higher tertile for both biomarkers (p<0.01).

Conclusions: In STEMI, NGAL and cystatin C are correlated with the incidence and severity of CI-AKI, MACCE and all-cause mortality at one year. The definition used for CI-AKI has a major impact on the results.
P3791 | BEDSIDE
Circulating microparticles and clinical outcomes in persistent ST-segment elevation myocardial infarction complicated with cardiogenic shock
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Background: Cardiogenic shock (CS) is the leading cause of death in patients admitted for acute myocardial infarction (MI). Despite the recent advances in reperfusion and medical treatment mortality remains unacceptably high in CS patients. Whether cells of the blood compartment in CS patients are activated and release microparticles (MPs) that may be both messengers and biomarkers of cell damage is not known. cMP characterization on CS patients may be instrumental in early CS recognition and even patient risk stratification to improve management and reduce clinical outcomes.

Purpose: We aimed to investigate the cMP signature of ST-elevation MI (STEMI)-patients complicated by CS (CS) and of non-CS STEMI-patients (non-CS) in order to identify cMP subtypes and parental activated cells.

Methods: Clinically characterized STEMI patients with and without CS (36/group) were included in the present case-control study. Treatment was delivered according to guidelines and included primary percutaneous coronary intervention (pPCI). cMPs were characterized by triple-labelling flow cytometry.

Results: CS patients presented a mean age of 68.1 years and 24% were women. Baseline clinical characteristics were similar in both groups. Increased levels of leukocyte-derived (of neutrophil and granocyte origin) and platelet-derived cMPs were detected in CS compared to non-CS patients. A signature of cMPs derived from platelets, leukocytes, and endothelium discriminated CS in STEMI patients (ROC AUC 0.743) and predicted mortality in CS (ROC analysis AUC 0.869). In CS patients, higher number of platelet- and monocyte-cMPs and higher number of tissue factor-rich cMPs associated to worse MBG and TIMI flow.

Conclusion: MPs derived from proinflammatory and prothrombotic cells are found elevated in CS-STEMI patients. In treated as per guidelines CS patients, granulocytes and neutrophils remain activated and actively shed MPs. cMPs seem to be survival prognostic biomarkers for CS.

P3792 | BEDSIDE
Circulating erythrocyte microparticles and biochemical extent of myocardial injury in ST-elevation myocardial infarction
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Background: Red blood cell microparticles (RBCm) have drawn attention as to their potential prothrombotic and vasoconstrictive effects and have been shown to be elevated in patients with ST-elevation myocardial infarction complicated with cardiogenic shock. MPs derived from proinflammatory and prothrombotic cells are found elevated in CS-STEMI patients. In treated as per guidelines CS patients, granulocytes and neutrophils remain activated and actively shed MPs. cMPs seem to be survival prognostic biomarkers for CS.

Purpose: To identify the cMP signature of ST-elevation MI (STEMI)-patients complicated by CS (CS) and of non-CS STEMI-patients (non-CS) in order to identify cMP subtypes and parental activated cells.

Methods: Circulating RBCm were quantified with a flow cytometric method in blood drawn from STEMI patients after primary PCI. Creatine kinase-myocardial brain fraction was measured at predefined time points and the area under the concentration curve (CKMB-AUC) was calculated.

Results: The separations in metabolic profiles and changes of metabolites were instrumental in early CS recognition and even patient risk stratification to improve management and reduce clinical outcomes. The separations in metabolic profiles and changes of metabolites were instrumental in early CS recognition and even patient risk stratification to improve management and reduce clinical outcomes.

Conclusion: MPs derived from proinflammatory and prothrombotic cells are found elevated in CS-STEMI patients. In treated as per guidelines CS patients, granulocytes and neutrophils remain activated and actively shed MPs. cMPs seem to be survival prognostic biomarkers for CS.

P3793 | BEDSIDE
Metabolic profiling of plasma in unstable angina pectoris patients using ultra performance liquid chromatography and Q-TOF mass spectrometry (UPLC-Q-TOF MS)
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Background: Unstable angina pectoris, one of the most dangerous clinical syndromes due to myocardial ischemia and hypoxia, results in high morbidity and mortality rates worldwide. Despite recent advantages in understanding the pathophysiology of unstable angina pectoris, the identification of biomarkers for diagnosis, prognosis and treatment in unstable angina pectoris remains challenging. Metabolomics has proved a systemic global quantitative measurement for comprehensive analysis of the dynamic multi-parametric metabolic response of living systems to pathophysiological stimuli, drug treatment or intervention.

Purpose: In this study, we performed ultra performance liquid chromatography and quadrupole-time-of-flight mass spectrometry (UPLC-Q-TOF MS) based metabolic profiling in plasma of unstable angina pectoris patients, to detect potential diagnostic biomarkers and metabolic pathways associated with unstable angina pectoris.

Methods: Plasma samples from 120 patients with unstable angina pectoris and 39 healthy controls were collected for this work. After processing the TOF-MS data, pattern recognition methods were performed to figure out contributing metabolic markers. The construction, interaction and pathway analysis of potential biomarkers were analyzed by MetPA (Metabolomics Pathway Analysis) and database sources, including the KEGG, the Human Metabolome database, and METLIN, were used to identify the related metabolic pathways.

Results: The separations in metabolic profiles and changes of metabolites were instrumental in early CS recognition and even patient risk stratification to improve management and reduce clinical outcomes.

Conclusion: Erythrocyte microparticles appear to be related to total myocardial damage biomarker output. The exact pathophysiological routes for this inter- action need to be identified by future studies; the altered rheologic properties of RBCm which allows closer contact with the endothelium, the powerful oxida- tive effect of RBCm-contained hemoglobin (as opposed to normal RBC-contained hemoglobin), and other deleterious sequelae are some of the potential mecha- nisms. In any case, these results suggest that erythrocytes may be a – thus far virtually unexplored – player in the pathogenesis of ischemic injury in the acute phase of reperfusion STEMI.

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P3794 | BEDSIDE
A plasma extracellular vesicle protein signature as a biomarker for the diagnosis of unstable angina

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Background/Introduction: Annually, millions of patients enter the emergency department (ED) with chest pain suggestive of myocardial infarction (MI) or unstable angina (UA). MI can quickly be diagnosed based on elevated high-sensitive troponin. In contrast, no blood-based biomarkers are available for the diagnosis of UA (by definition troponin-negative) resulting in delayed recognition and treatment. The biomarker potential of extracellular vesicles (EV) in cardiovascular diseases is being increasingly recognized, owing to their active role in cell-cell communication, inflammation and coagulation.

Purpose: To evaluate whether a plasma extracellular vesicle (EV) protein signature can be used as a diagnostic biomarker for unstable angina.

Methods: From the MINERVA acute chest pain cohort, n=27 patients with UA and n=31 matched controls (i.e. matched for sex, age, history, risk factors and medication) were selected. The plasma EVs were precipitated in a total EV fraction (TEX) and in separate LDL, HDL and remaining (REX) EV subfractions using sequential precipitation. EV proteins were measured in these plasma fractions. SerpinF2, SerpinG1, SerpinC1, CD14, and Cystatin C were identified as potentially associated with UA by a mass spectrometry based proteomics and were measured in all plasma fractions of the individual patients with an immune-bead assay. Univariable and multivariable logistic regression, as well as the area under the receiver-operating-characteristic curve (AUC), were used to evaluate the diagnostic potential of the individual and combined biomarkers.

Results: The best individual markers to discriminate between UA and matched controls were SerpinC1 with the ratio HDL/REX and an AUC of 0.847 (95% CI 0.746–0.948) and SerpinC1 in the HDL fraction with an AUC of 0.844 (95% CI 0.741–0.947). The best combination of markers was SerpinC1-HDL + CD14-TEX and in separate LDL, HDL and remaining (REX) EV subfractions using

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Conclusion(s): This study shows that EV proteins can be used as diagnostic biomarkers for unstable angina in the emergency department.

Acknowledgement/Funding: Strategic grant KNAW to DdK, Netherlands Heart Foundation (2011T039), the UMC Utrecht and Netherlands Heart Institute to LT Feiring, Norway; 3 Oslo University Hospital, Ulleval, Center for Clinical Heart Research, Department of Cardiology, Oslo, Norway; 4 Oslo University Hospital, Rikshospitalet, Research Institute for Internal Medicine, Oslo, Norway; 5 Oslo University Hospital, Rikshospitalet, Department of Clinical Immunology and Infectious Diseases, Oslo, Norway.

P3795 | BEDSIDE
High osteoprotegerin levels are associated with adverse left ventricular remodelling in patients with ST-elevation myocardial infarction

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Background: Elevated levels of osteoprotegerin (OPG) have been reported in patients with ST-elevation myocardial infarction (STEMI) compared to patients with non-STEMI, unstable angina, and stable coronary artery disease (CAD). Recent studies have shown that OPG levels are associated with infarct size in STEMI patients, although the results have been somewhat inconsistent.

Purpose: The main aims of the present study were to elucidate the potential role of OPG in ischemia-reperfusion (IR) injury in STEMI patients. Associations between OPG and left ventricular (LV) remodelling, myocardial salvage index, final infarct size and microvascular obstruction (MVO), were assessed by cardiac magnetic resonance imaging (CMR).

Methods: The Postconditioning in ST-Elevation Myocardial Infarction (POSTEMI) trial was a prospective, randomised clinical trial investigating ischemic postconditioning (iPost) as cardioprotective strategy in STEMI patients. The effect of iPost on the primary endpoint of the study, final infarct size measured by CMR after 4 months, was neutral. The study population consisted of 272 patients with first-time STEMI, treated with primary percutaneous coronary intervention (PCI). Blood samples for serum OPG were drawn before and immediately after the PCI procedure, during in-hospital follow-up 8–20 hours (median 14.7) and 20–32 hours (median 23.8) after admission, and at 4-month follow-up. LV remodelling was defined as change in LV end-diastolic volume (delta EDV). CMR was performed both in the acute phase (median 2 days after the index event) and after 4 months, allowing assessment of final infarct size, LV ejection fraction (LVEF), myocardial salvage index, MVO and change in EDV. OPG levels were quantified by commercially available enzyme immunosassay.

Results: Patients with high OPG levels (above median, 4.46 ng/ml) measured in the time frame 20–32 hours after primary PCI had significantly larger increase in EDV (median 13.0 vs 1.0 ml, p<0.009, Figure). In addition to lower myocardial salvage (41.8 vs 68.0%, p<0.001), larger final infarct size (17.0 vs 8.2% of LV, p<0.001), lower LVEF (52.0 vs 60.5%, p<0.002) and higher frequency of MVO (60.9 vs 32.6%, p=0.012), compared to patients with low OPG levels. OPG remained significantly associated with delta EDV and final infarct size after adjustments in multivariate linear regression analyses including peak troponin values.

Conclusion: High levels of OPG are associated with impaired recovery of LV function and adverse left ventricular remodelling in STEMI patients.

Acknowledgement/Funding: Oslo University Hospital

https://academic.oup.com/eurheartj/article-abstract/37/suppl_1/599/2197552/18
hospital mortality, major adverse cardiovascular events, cardiopulmonary resuscitation, dialysis, use of inotropic agents, shock, late mortality, target vessel revascularization, stroke, and reinfarct were higher in the Q4 group compared with the other MHR quartile groups.

**Conclusion:** The results of this study have indicated that admission MHR is associated independently and significantly with short-term and long-term mortality in STEMI patients who undergo successful primary PCI.

P3759 | BEDSIDE

**Genetic determinants of simvastatin intolerance in ethnic Uzbek patients with coronary artery disease**

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**Background:** It is well-known that in majority of cases treatment with statins can be safe and well tolerated, but in some patients observed statin-induced adverse liver or muscle symptoms – the main reasons for statin discontinuation. Asian ethnicity – is one of the predisposing factors for statin-associated adverse effects.

**Objective:** To study possible effects of CYP3A5, CYP2C9, SLC01B1 and BCRP genetic polymorphism on simvastatin tolerance and safety in ethnic Uzbek patients with Coronary Artery Disease (CAD).

**Material and methods:** The prospective case-control research included 41 patient with CAD, who demonstrated statin-induced adverse liver effects (transaminase level increases 3 times and more – in 37 cases) or statin-induced elevation in muscle enzymes (of CK > 3×UNL – in 4 cases) at treatment with simvastatin with the dose of 20 mg/day for 3 months of treatment. Control group contained 41 patient treated with simvastatin with the dose of 20–40 mg/day for one year without side effects. The both groups of patients were similar in gender, age, original cholesterol and serum CK level. Patients were genotyped for polymorphisms in the genes coding for the cytochrome P450 (CYP) metabolically active enzymes: CYP3A5*1 (3986A_G), CYP2C9*2 (430C_T), CYP2C9*3 (1075A_C), and hepatic influx and efflux transporters: SLC01B1 (S21T_C) and breast cancer resistance proteins (BCRP; 421C_A). The research was performed by means of PCR-RFLP method.

**Results:** As a whole, all genotypes were in Hardy–Weinberg equilibrium. Among patients with simvastatin intolerance, compared to the control group, the following genotypes were observed more frequently with high level of confidence: CYP3A5 *3/*3, compared to genotype variants *1/*3 and *1/*1 (OR: 6.45, 95% CI: 2.38–17.44, P<0.001) and BCRP CA (patients with BCRP CC genotype were not observed among those examined) (OR: 3.73, 95% CI: 1.28–10.89, P<0.025) compared to the genotypic variant. For the combined genotypes CYP3A5*3/*3 and BCRP CA, in ethnic Uzbek patients with CAD, side liver effects from simvastatin treatment were also observed more frequently with high level of confidence (P=0.002). This may be due an increased content of the lactone of simvastatin in the liver (*CYP3A5_3*3/) and a low ratio of simvastatin lactone and acid in the blood of patients with liver damage.

**Conclusions:** Genotypes CYP3A5*3/*3 and BCRP CA are accompanied with the increase of statin-induced adverse liver effects in ethnic Uzbek patients with Coronary artery disease.

P3759 | BEDSIDE

**Unbiased gene expression signature in acute coronary syndromes identifies mediators of inflammasome signaling correlating with infarct size**

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**Introduction:** The inflammatory response during an acute coronary syndrome (ACS) initiates tissue repair. Maladaptive responses associated with a larger infarct size and higher peak CRP level lead to worse outcome. However, the up-regulation of pro-inflammatory mediators is desirable for both diagnostic and prognostic purposes. Because of their tissue specificity and stability in the plasma, microRNA (miRNA) hold promise as potential biomarkers.

**Purpose:** To evaluate the levels of circulating miRNA in STEMI patients.

**Methods:** Array analysis for 1146 miRNA was performed on plasma collected from patients with STEMI (N=18), stable angina (N=20) and sex/age-matched healthy controls (CTRL; N=18). For STEMI, the plasma was collected at the time of hospital admission (T0), 24 hours (T1) and 7 days (T2) after the reperfusion therapy. The array results were confirmed by qRT-PCR. The miRNA upregulated at any time-point after STEMI were further validated by qRT-PCR in a second population of 87 STEMI patients and 40 CTRL. ROC analysis was performed to establish specificity and sensitivity of each miRNA.

**Results:** Array data analysis showed that 10 miRNA were up-regulated at one or more time point after STEMI compared with stable angina and controls; the up-regulation of 6 of them was validated also by qPCR: miRNAS2 (T0, T1, T2 p<0.001 vs CTRL), 423–5p (T0 p<0.05 vs CTRL), 345 (T1 p=0.05 vs CTRL), 1233 (T2 p<0.05 vs CTRL, 362–3p (NS) and 483–3p (T2 p<0.05 vs CTRL). All the results were confirmed in the second population: miRNAS2 at T0 (p<0.05), T1 and T2 vs CTRL (p<0.001), moreover at T1 vs T0 (p<0.001) and T1 vs T2 (p<0.001); miRNA423–5p was higher at T0, T1 and T2 vs CTRL (p<0.001); miRNA345 was higher at T1 compared with CTRL (p<0.001); miRNA1233 was up-regulated at T1 vs CTRL (p<0.001); miRNA483–3p was higher at T0, T1 and T2 compared with CTRL (p<0.05, and p<0.001). Only for miRNA362–3p we could not confirm the data obtained in the first assay. In this second population, we also observed that the levels of all up-regulated miRNA returned to baseline levels after 30 days. ROC analyses, matched by sex and age, showed the good accuracy (AUC variation: 0.75–0.93) of miRNAs discriminating STEMI cases from CTRL. Finally, the creatine kinase MB values positively correlated with all the validated miRNAs (r varied between 0.27–0.41, p<0.05). The potential significance of each miRNA in STEMI patients. Our analysis identified 5 previously undescribed miRNA that are significantly up-regulated after STEMI. Investigation on their potential prognostic significance appears warranted.

P3800 | BEDSIDE

**Free circulating miRNAs (miR1, miR-133a, miR-208a, miR-499) differentiate clinical types of coronary disease: acute myocardial infarction, unstable angina and stable coronary artery disease**

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**Background:** The microRNAs (miRs) are small non-coding RNA molecules reg-
ultating expression of multiple genes, which can be quantified using reverse transcription-quantitative PCR methods. Some studies reported their utility in ST elevation myocardial infarction (STEMI) diagnostic process, whereas their diagnostic value in non-ST elevation acute coronary syndrome (NSTE-ACS) remains unclear.

**Purpose:** We sought to evaluate the expression of 5 free circulating miRs (miR-1, miR-21, miR-133a, miR-208a, miR-499) and UA from SCAD (miR-133a and miR-499) as a robust biomarker to distinguish not only NSTEMI patients from other individuals from other patients: miR-1 [area under the curve (AUC) 0.863, 95% CI 0.761–0.933, p = 0.035]. Three of analyzed miRs were able to differentiate any NSTEMI individual (p < 0.001), miR-133a 5.8-fold (p = 0.033) and miR-499 7.0-fold (p = 0.003) when comparing NSTEMI to UA patients, and additionally two of them were able to discriminate between UA and SCAD patients: miR-133a (p = 0.005) and miR-208a (p = 0.033). Three of analyzed miRs were able to differentiate any NSTEMI individuals from other patients: miR-1 [area under the curve (AUC) 0.863, 95% CI 0.761–0.933, p < 0.001], miR-133a (AUC 0.799, 95% CI 0.687–0.885, p < 0.001) and miR-499 (AUC 0.795, 95% CI 0.651–0.858, p < 0.001). MiR-1 elevation > 12.2 fold yielded a sensitivity of 74.4%, and specificity of 99.6%. MiR-21 elevation > 23.8 fold 74.4% and 84.9% MiR-499 elevation > -4.7 fold 64.1% and 93.8% for distinguishing NSTEMI vs others.

**Conclusions:** The present study describes a unique signature of three circulating miRNAs as a robust biomarker to distinguish not only NSTEMI patients from other individuals (miR-1, miR-208a, miR-133a, miR-499), but also NSTEMI from UA patients (miR-1, miR-133a, miR-499) and UA from SCAD (miR-133a and miR-208a).

**Acknowledgement/Funding:** This study was supported by the Polish Ministry of Science and Higher Education “Diamond Grant” project, research project: DIA12942.

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**P3801 | BESIDE**

**Early valuable risk stratification with hemoglobin level and neutrophil to lymphocyte ratio in patients with non-ST-elevation myocardial infarction having an early invasive strategy**

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**Objective:** The complete blood count (CBC) is the most widely available laboratory data in the early in-hospital period after acute myocardial infarction. We assessed the clinical utility of the combined use of hemoglobin (Hb) level and neutrophil to lymphocyte ratio (N/L) for early risk stratification in patients with non-ST-elevation myocardial infarction (non-STEMI).

**Materials and methods:** We analyzed 6157 consecutive patients with non-STEMI (65±12.4 years, male 69%) were included in the final analysis. Patients were categorized into three groups according to using the median value of N/L (4.42) and the presence of anemia (Hb <13 mg/dl in men and <12 mg/dl in women); group I, low N/L & no anemia (n=3170); group II, low N/L & anemia (n=162); group III, high N/L & no anemia (n=512). (n=512) (n=210) (n=162)

**Conclusion:** Although increase in serum creatinine level of 25% or 25% above baseline within 72 hours after contrast administration. Serum creatinine levels apart from this definition remains uncertain in patients with NSTEMI

**Acknowledgement/Funding:** Support from the Ministry of Science and Information Technology for Medical Diagnosis: This project was supported by the Polish Ministry of Science and Higher Education “Diamond Grant”, project: DIA12942.

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**P3802 | BESIDE**

**The relationship between the rate of increase in serum creatinine levels and long-term adverse clinical outcomes in patients with non-ST segment elevation myocardial infarction**

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**Background:** Contrast-induced acute kidney injury (CI-AKI) is associated with mortality, morbidity, and prolonged hospitalization in patients with non-ST-segment elevation myocardial infarction (NSTEMI). CI-AKI is defined as an increase in serum creatinine level of 0.5 mg/dl or 25% above baseline within 72 hours after contrast administration. Serum creatinine levels apart from this definition remains uncertain in patients with NSTEMI

**Methods:** 954 patients with NSTEMI who underwent CAG and/or PCI were analyzed. A total of 884 NSTEMI patients were enrolled. Patients were categorized into three groups according to the rate of increase in serum creatinine levels above baseline as group 1 (Δcre ≤ 10%), group 2 (10% < Δcre ≤ 25%) and group 3 (Δcre > 25%). Primary endpoints were defined as all-cause mortality, MI and cerebrovascular event at 1-year follow-up.

**Results:** Results are displayed in table 1.

**Demographic and clinical outcomes**

<table>
<thead>
<tr>
<th>Group</th>
<th>Δcre ≤ 10% (n=512)</th>
<th>10% &lt; Δcre ≤ 25% (n=210)</th>
<th>Δcre &gt; 25% (n=162)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>60±12±2</td>
<td>60±11±4</td>
<td>62±11±5</td>
</tr>
<tr>
<td>Male</td>
<td>374 (73.0)</td>
<td>163 (77.6)</td>
<td>106 (65.0)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>290 (56.6)</td>
<td>119 (56.7)</td>
<td>107 (66.0)</td>
</tr>
<tr>
<td>Depression</td>
<td>166 (66.4)</td>
<td>74 (35.2)</td>
<td>83 (50.2)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>221 (43.2)</td>
<td>88 (41.9)</td>
<td>70 (43.2)</td>
</tr>
<tr>
<td>Active smoking</td>
<td>253 (49.4)</td>
<td>114 (54.3)</td>
<td>60 (37.0)</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>52±19±9</td>
<td>52±19±9</td>
<td>49±6±10.7</td>
</tr>
<tr>
<td>GRACE score &gt; 140</td>
<td>138±6±35</td>
<td>133±7±36</td>
<td>141±6±35</td>
</tr>
<tr>
<td>Contrast volume (ml)</td>
<td>207±8±17±3</td>
<td>200±7±11±2</td>
<td>210±6±13±7</td>
</tr>
<tr>
<td>Baseline creatinine (mg/dl)</td>
<td>1.0±0.5</td>
<td>0.9±0.3</td>
<td>1.0±0.8</td>
</tr>
<tr>
<td>Primary end point (death/MI/CVE)</td>
<td>67 (13.1)</td>
<td>19 (9.0)</td>
<td>37 (22.8)</td>
</tr>
<tr>
<td>Death</td>
<td>22 (4.3)</td>
<td>6 (2.9)</td>
<td>21 (13.0)</td>
</tr>
<tr>
<td>MI</td>
<td>50 (9.8)</td>
<td>14 (6.7)</td>
<td>19 (11.7)</td>
</tr>
<tr>
<td>CVE</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

**Conclusion:** Although increase in serum creatinine levels of 25% or more above baseline is associated with long term adverse clinical outcomes; slight increases (<25%) do not affect the clinical outcomes in patients with NSTEMI

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**P3803 | BEDSIDE**

**Association of immature platelets with adverse cardiac and cerebrovascular outcomes**

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**Background:** Platelets play a pivotal role in the development of atherothrombotic events and platelet hyper-reactivity is associated with adverse prognosis in patients with acute coronary syndromes (ACS). Immature platelets (IPs) are newly-formed platelets with high dense granules content, a residual amount of mRNA and increased mean volume compared to older circulating platelets. Detection
of these platelets in the circulating blood reflects a high rate of platelet turnover. Recently an increased proportion of IPs has been proposed to be independent predictor of cardiovascular death in patients with CAD.

**Purpose:** To examine whether the level of IPs in patients with ACS predicts adverse cardiovascular events.

**Methods:** We recruited patients with ACS. We measured the immature platelet fraction (IPF) using an automated hematoanalyzer, after anti-platelet drug loading and performance of percutaneous coronary intervention. Patients were followed for a period of 6 months. Major adverse cardiovascular events (MACE) were defined as the composite of all-cause mortality, myocardial infarction, cerebrovascular event and hospitalizations due to cardiac causes.

**Results:** A total of 104 patients were recruited and had 6 months follow-up (mean age 67.2±13.26% females, 41.3% STEMI, 58.6% NSTEMI-UIP). They were divided to quartiles is caused by delayed on-th IPFs level. MACE according to quartile significantly differed between the quartiles (p=0.015). MACE according to quartile increased from the lower IPF half to the upper half (23% and 46%, respectively, p=0.013). The differences in MACE between the IPF quartiles and halves were driven by differences in the rates of hospitalizations due to cardiovascular causes. Mortality and re-infarction rates were low and did not differ between the different groups.

**Conclusion:** In this preliminary study of patients with ACS there appears to be an association between IPF level and cardiovascular outcomes at 6 months, driven by cardiac hospitalization rates. Further studies required to validate these findings.

**P3804 | BEDSIDE**

Impact of reticulated platelets on antiplatelet response to thienopyridines is independent of platelet turnover


**Background:** Reticulated platelets are associated with impaired antiplatelet response to thienopyridines. It is uncertain if this interaction is caused by decreased drug exposure due to high platelet turnover reflected by elevated levels of reticulated platelets or by intrinsic properties of reticulated platelets. This study sought to investigate if the effect of reticulated platelets on early antiplatelet response to thienopyridines is caused by platelet turnover or whether platelet turnover (comparison of correlations 120min/day 1: p=0.64 for entire cohort).

**Methods:** Elective patients undergoing coronary intervention were randomized to loading with clopidogrel 600mg or prasugrel 60mg (n=200). ADP-induced platelet reactivity was tested by impedance aggregometry 30–120min and day 1 after loading. Immature platelet count was assessed as marker of reticulated platelets by flow cytometry.

**Results:** Platelet reactivity increased with rising levels of immature platelet count. This effect was more pronounced in patients on clopidogrel as compared to patients on prasugrel. Overall, immature platelet count correlated well with on-treatment platelet reactivity at 120min (r=0.24, p<0.001). These correlations did not change over time in the entire cohort (Figure) and as the subgroups treated with clopidogrel or prasugrel indicating an effect independent of platelet turnover (comparison of correlations 120min/day 1: p=0.64 for entire cohort).

**Conclusion:** The association of immature platelet count with impaired antiplatelet response to thienopyridines is similar early and late after loading. This finding suggests as main underlying mechanism another effect of reticulated platelets on thienopyridines than platelet turnover.

**Acknowledgement/Funding:** This trial was supported by the German Heart Foundation/German Foundation of Heart Research and the University Heart Center Freiburg. Ba

**P3805 | BEDSIDE**

Incidence of capesentabin cardiac toxicity at rest and under effort: a prospective study

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**Background:** Capesentabin (CAPE) - widely used for chemotherapy (CT) of head/neck, stomach, gut, liver and breast cancer- may cause cardiac toxicity (TOX), mostly myocardial ischemia (MI), ventricular arrhythmias (VA), left ventricular dysfunction (LVD), bradarrhythmias. According to the literature, the most commonly reported TOX is rest cardiac ischemia with vaso spasmodic angina. Recently, cases of TOX of CAPE precipitated by effort have been reported. Since CAPE is given on ambulatory basis, for several weeks, the patients (pts) under CT might be at risk of toxicity during physical activity.

**Purpose:** To evaluate the incidence and clinical presentation of cardiotoxicity (at rest or under effort) in a group of pts undergoing CAPE chemotherapy for various tumors.

**Methods:** We prospectively studied 189 patients (pts), 114 males, 75 females, mean age 62, undergoing CT with CAPE alone or combined with other drugs. Cardiovascular risk factors (CVRF) were present in 133 pts (70 with >2 CVRF): 10 had ischemic heart disease (IHD). The pts had a clinical evaluation, ECG and echocardiogram (ECHO) before CT. A treadmill or bicycle stress test was planned before CT in those with IHD, after >10 days of CT for all, and again during the last week of CT in those with treatments lasting >4 weeks. We considered possible signs of TOX: typical angina with ECG changes; appearance of >2 mm segment elevation in >2 ECG leads (both at rest or after stress); >2 mm ST depression or Lown 3 VA at rest or during stress test; appearance of negative T waves at ECG; complete atrioventricular block (CAVB). All the pts with suspected TOX underwent a stress test >10 days after withdrawing CAPE and without additional cardiological therapy; those with LVD had also a new Echo; coronary angiography (CA) was performed in 3 pts. Only the pts with normal stress test and Echo after wash out, or with normal CA, were considered having had TOX.

**Results:** Amongst the 189 pts, 27 (14%) had TOX: 16 silent MI, 4 angina, 4 VA, 2 ECG signs of ischemia and LV dysfunction, 1 CAVB. Seven pts had rest TOX, 20 had TOX detected under stress test only. Among the 20 pts with TOX during stress test, 3 had angina, 4 atypical symptoms, 14 no symptoms; ECG showed ST segment elevation (up to 5 mm in up to 9 leads) in 6 pts, ST segment depression in 11, both ST elevation and depression in 3, frequent VA in 9. High sensitivity Troponin T was elevated in one pt only.

**Conclusions:** Cardiotoxicity was not infrequent during CT with CAPE. The clinical presentation ranged from myocardial ischemia to arrhythmias and/or LV dysfunction. It was triggered or worsened by physical effort in 20/27 pts, and in most cases was asymptomatic, even in presence of significant ECG changes and/or LVD. Patients treated with CAPE should be advised to avoid efforts, and should be routinely screened with ECG during CT.

**THROMBOSIS AND COAGULATION**

**P3806 | BEDSIDE**

Elevated lipoprotein a levels in patients with prosthetic valve thrombosis

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**Background:** Genetic studies and numerous epidemiologic studies have identified lipoprotein a (Lp(a)) as a risk factor for atherosclerotic diseases such as coronary heart disease and stroke. The structure of Lp (a) is similar to plasminogen and fibrin, inducing fibrin or Lp(a) as a risk factor for atherosclerotic diseases such as coronary heart disease and stroke. The structure of Lp (a) is similar to plasminogen and tissue plasminogen activator and it competes with plasminogen for its
binding site, leading to reduced fibrinolysis. Also, because Lp(a) stimulates secretion of PAI-1, it may lead to thrombogenesis.

**Purpose:** To investigate Lp (a) levels in patients with prosthetic valve thrombosis (PVT).

**Methods:** Blood samples for Lp (a) were obtained from 80 PVT patients (59 non-obstructive, 21 obstructive; 64 mitral, 16 aortic; 47 male; and 75 (61 mitral, 14 aortic; 44 male) controls with normally functioning prosthetic valves. All enrolled patients were under optimal anticoagulation and underwent transesophageal echocardiography. Patients who had dyslipidemia and using anti-hyperlipidemic therapy were excluded.

**Results:** The Lp (a) levels in PVT group were significantly higher than the controls (22 (16.2–39.4) mg/dL vs. 6.9 (2.9–23.8) mg/dL, p <0.001 (Figure 1). There was no significant difference between Lp (a) levels in patients with non-obstructive and obstructive PVT (22 (17.2–42) mg/dL vs. 19.8 (15–35.6) mg/dL, p = 0.353).

**Conclusion:** Elevated Lp (a) levels may be one of the esoteric causes of PVT in patients with sufficient anticoagulation.

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**P3807 | BENCH**

Concentration dependent effects of edoxaban on thrombin generation kinetics and physical characteristics of clot By CAT and TEG6 assay

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**Background:** Edoxaban is a recently approved factor Xa inhibitor. Concentration dependent effects of edoxaban on physical characteristics of clot and thrombin generation kinetics were studied in blood samples collected from healthy volunteers and patients with heart failure (HF) in this in vitro exploratory study (n=43).

**Methods:** Platelet-fibrin clot strength (P-FCS), and reaction time (R) in whole blood using the point-of-care TEG6s with the anticoagulant cartridge and endogeneous thrombin potential (ETP), lag time, peak thrombin concentration (PTG), and time to peak thrombin concentration (tPeak) in plasma using the calibrated automated thrombogram (CAT) assay were determined after 30 min of incubation with 0, 30 (therapeutic range), 300 (therapeutic range) and 900 nM (supratherapeutic range) edoxaban in citrated blood samples collected from healthy volunteers and patients with HF with and without hypercoagulability (defined as >65mm P-FCS). Results: Overall, a concentration dependent effect of edoxaban on R and lag time (indicators of anticoagulant effect), PTG, and tPeak (p for trend <0.001 for all) was observed. The anticoagulant effect was more pronounced in subjects with normal coagulability (Table).

**Conclusion:** The clinical suspicion of DVT is confirmed in 1 out of 4 patients referred for evaluation. The need of re-evaluation after 7 days is common and depends with respect to clinical and demographic characteristics, especially age and medical history.

**Acknowledgement/Funding:** Bristol Myers-Squibb and Pfizer

**P3808 | BENCH**

Demographic and clinical characteristics associated with initiation of individual oral anticoagulants among patients with newly diagnosed venous thromboembolism

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1 Bristol Myers-Squibb, Princeton, NJ, United States of America; 2 Bristol Myers-Squibb, Wallingford, CT, United States of America; 3 Pfizer, New York, United States of America; 4 Bristol Myers-Squibb, Hopewell, NJ, United States of America; 5 Bristol Myers-Squibb, Plainsboro, NJ, United States of America

**Background:** Vitamin K antagonists (especially warfarin) are the conventional oral anticoagulant (OAC) therapy for venous thromboembolism (VTE). Since November 2012, non-vitamin K antagonist oral anticoagulants, such as rivaroxaban, dabigatran, apixaban, and edoxaban, have been approved by FDA as alternatives to warfarin for VTE treatment.

**Purpose:** To identify demographic and clinical characteristics associated with initiation of individual OACs among patients with newly diagnosed VTE in current US clinical practice.

**Methods:** Using the MarketScan commercial and Medicare supplemental database, patients with newly diagnosed VTE between 9/1/2014 and 6/30/2015 and prescriptions of any OAC within 30 days of the index VTE event were identified. Patients with diagnosis of atrial fibrillation or use of inferior vena cava filter were excluded. Multinomial logistic regression was conducted to examine factors associated with initiation of specific OAC.

**Results:** Altogether 18,786 patients met eligibility criteria, including 8,595 on warfarin, 8,762 on rivaroxaban, 1,318 on apixaban, 104 on dabigatran, and 7 on edoxaban. Average age among warfarin, rivaroxaban, apixaban users was 59.2, 56.7, 61.5 years, respectively; corresponding mean score of Charlson Comorbidity Index was 2.26, 1.71, 2.12. Associations between key patient characteristics and initiation of different OACs were described in Table. Age≥65 years was associated with apixaban use compared to warfarin. Initiation of rivaroxaban (compared to warfarin and apixaban) was less likely in patients aged 65+ and those with renal disease, congestive heart failure, or history of stroke.

**Conclusion:** Profiles of newly diagnosed VTE patients initiating different OACs differ with respect to clinical and demographic characteristics, especially age and medical history.

**Acknowledgement/Funding:** Bristol Myers-Squibb and Pfizer

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**P3809 | BEDSIDE**

Management of deep vein thrombosis in a multidisciplinary team

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**Background:** Lower extremity deep vein thrombosis (DVT) is a common vascular condition. The clinical appearance of DVT ranges from mild local symptoms to fatal pulmonary embolism. A clinical risk score (Well's score) combined with D-dimer measurement selects patients appropriate for ultrasonographic evaluation.

**Purpose:** This study describes the flow of patients suspected for DVT with focus on the effort of a repeated ultrasonographic evaluation after 7 days in patients with a high clinical probability (Well’s score >1) and positive D-dimer but with a negative initial ultrasonographic evaluation. This setup is based on the pathophysiological rationale that repeated scanning detects propagating distal DVT.

**Methods:** Well’s score combined with D-dimer measurement were assessed prospectively to all patients suspected for DVT referred to the Emergency Department at a Hospital, during a 17 months period (Sep. 2014-Jan. 2016). Patients with DVT were managed in a multidisciplinary team that consists of a sonographer, an emergency physician, a cardiologist and a nurse with specialist knowledge in thrombosis and anticoagulation.

**Results:** During this 17 months period 452 patients were referred with suspected lower limb DVT, of which 91 patients (20%) had the diagnosis of DVT confirmed after the initial ultrasonographic evaluation. 174 patients (39%) had the ultrasonographic evaluation repeated after 7 days and in 17 patients (10%) of these patients was detected.

Overall 108 patients (24%) were diagnosed with DVT. They were all treated with anticoagulation: 6 (6%) with Low Molecular Weight Heparin because of cancer, 24 (22%) with Warfarin, 9 (8%) with Apixaban and 69 (64%) with Rivaroxaban.

**Conclusion:** The clinical suspicion of DVT is confirmed in 1 out of 4 patients referred for evaluation. The need of re-evaluation after 7 days is common and in 1 out of therapy the diagnosis is confirmed with the ultrasonographic re-evaluation. DVT patients are best managed in a multidisciplinary team with a structured setup where both the diagnosis and an appropriate follow-up can be done.

**Adjusted odds ratio (95% confidence interval)**

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Warfarin vs. Rivaroxaban</th>
<th>Warfarin vs. Apixaban</th>
<th>Rivaroxaban vs. Apixaban</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age≥65 years</td>
<td>1.185 (1.038, 1.353)</td>
<td>0.894 (0.832, 0.961)</td>
<td>0.754 (0.660, 0.862)</td>
</tr>
<tr>
<td>Female</td>
<td>0.945 (0.835, 1.068)</td>
<td>0.901 (0.845, 0.962)</td>
<td>0.954 (0.843, 1.080)</td>
</tr>
<tr>
<td>Renal disease</td>
<td>0.953 (0.807, 1.124)</td>
<td>0.591 (0.535, 0.651)</td>
<td>0.620 (0.522, 0.737)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>1.076 (0.897, 1.290)</td>
<td>0.698 (0.625, 0.780)</td>
<td>0.649 (0.536, 0.785)</td>
</tr>
<tr>
<td>History of ischemic stroke or transient ischemic attack</td>
<td>0.989 (0.773, 1.267)</td>
<td>0.734 (0.633, 0.851)</td>
<td>0.742 (0.573, 0.960)</td>
</tr>
<tr>
<td>History of bleeding</td>
<td>0.951 (0.750, 1.205)</td>
<td>0.787 (0.691, 0.895)</td>
<td>0.827 (0.649, 1.055)</td>
</tr>
</tbody>
</table>

Dabigatran and edoxaban users were excluded due to small sample size. *Statistically significant at 0.05 level. Baseline clinical characteristics measured during 12-month pre-index period.
Introduction and aims: C-KIN (Cancer & the Kidney International Network) was created in 2014 and aims at improving the management of cancer patients by developing clinical and scientific knowledge on the treatment of cancer in chronic kidney disease (CKD) patients. A specific working group: Thrombosis, Kidney disease, and Cancer (TKC) has been created. We present here the summary created in 2014 and aims at improving the management of cancer patients by the scientific rationale on the links between cancer, CKD and VTE (venous thromboembolism).

Methods: C-KIN TKC working group reviewed the literature (PubMed) and investigated about the potential links between 1) cancer-VTE, 2) CKD-VTE and 3) CKD patients are at higher risk to develop cancer. This risk begins for a glomerular filtration rate (<55 ml/min/1.73 m²) and increases linearly as GFR declines. On the other hand, CKD is frequent (12–25%) in cancer patients and CKD is a risk factor of mortality in cancer patients. Finally, every 10 ml/min/1.73 m² decrease in GFR is associated with an 18%-increase in cancer related mortality.

Conclusions: These 3 diseases are closely linked. It is important to screen and manage both cancer and CKD diseases in VTE patients and to reduce the dose of all medications in these patients if necessary. However, the trends and risks in VTE patients presenting both comorbidities (cancer and CKD) and their potential cumulative effects have not yet been clearly evaluated and there is a need of guidelines in this specific situation.

P3811 | BEDSIDE
Experience with tecarfarin, a novel vitamin K antagonist: use with reversing agents and in mechanical heart valve recipients

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Background: Tecarfarin is a non-CYP interacting, novel vitamin K antagonist currently under Phase 3 development for the purpose of anticoagulation for several indications, including the prevention of thromboembolism in atrial fibrillation and mechanical heart valves (MHVs).

Methods: We describe the clinical experience of the use of tecarfarin compared to warfarin (four clinical trials; n~784 participants) in patients requiring protocol anticoagulation reversal, as well as patients receiving anticoagulation for MHVs.

Results: Indications for a reversal agent included incidental INR elevation (46.2%), intercurrent medical illness requiring reversal prior to surgery (38.5%), and bleeding (15.4%). A total of 26 subjects on tecarfarin received a reversal agent in the 4 trials. Of these, all received vitamin K and two also received fresh frozen plasma concentrates (FFP). All subjects receiving a reversal agent experienced a return to the pre-specified target range within 24 h. Prevention of thromboembolism in MHVs was the indication for anticoagulation in 93 subjects (51 on tecarfarin in 2 clinical trials up to one year of treatment). Tecarfarin was not associated with an excess of adverse events compared to warfarin, and there were no instances of valve thrombosis.

Table 1

<table>
<thead>
<tr>
<th>Clinical study</th>
<th>Indication for reversing agent</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Incidental INR elevation</td>
<td>Need for surgery</td>
</tr>
<tr>
<td>CNL-502</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>CNL-504</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>CNL-505</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>CNL-509</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>12</td>
<td>4</td>
</tr>
</tbody>
</table>

Table 2

<table>
<thead>
<tr>
<th>MHV use</th>
<th>AE</th>
<th>Valve thrombosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Tecaarfarin</td>
</tr>
<tr>
<td>CLN-509</td>
<td>9/50</td>
<td>n/a</td>
</tr>
<tr>
<td>CLN-505</td>
<td>42/307</td>
<td>42/305</td>
</tr>
<tr>
<td>Total</td>
<td>51/357</td>
<td>42/305</td>
</tr>
</tbody>
</table>

Conclusions: Based on clinical trial experience to date, reversal of tecarfarin anticoagulation with vitamin K and FFP is feasible. The chronic use of tecarfarin in MHV recipients has not been associated with significant complications. Further confirmatory studies are required to evaluate the routine use of tecarfarin in clinical practice.

P3812
Table 1

<table>
<thead>
<tr>
<th>Resource utilization</th>
<th>% of patients with ≤1 event</th>
<th>Mean number of events per patient</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Riva (n=512)</td>
<td>Warf (n=512)</td>
<td>Riva (n=512)</td>
</tr>
<tr>
<td>Within 1 week</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospitalization</td>
<td>1.2%</td>
<td>3.1%</td>
<td>0.012</td>
</tr>
<tr>
<td>ER visit1</td>
<td>33.2%</td>
<td>33.2%</td>
<td>0.390</td>
</tr>
<tr>
<td>Outpatient visit1</td>
<td>91.2%</td>
<td>96.9%</td>
<td>1.543</td>
</tr>
<tr>
<td>Within 2 weeks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospitalization</td>
<td>2.1%</td>
<td>4.7%</td>
<td>0.022</td>
</tr>
<tr>
<td>ER visit1</td>
<td>34.5%</td>
<td>35.2%</td>
<td>0.407</td>
</tr>
<tr>
<td>Outpatient visit1</td>
<td>95.7%</td>
<td>98.4%</td>
<td>2.281</td>
</tr>
<tr>
<td>Within 3 weeks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospitalization</td>
<td>3.5%</td>
<td>5.7%</td>
<td>0.038</td>
</tr>
<tr>
<td>ER visit1</td>
<td>35.4%</td>
<td>36.3%</td>
<td>0.435</td>
</tr>
<tr>
<td>Outpatient visit1</td>
<td>97.9%</td>
<td>98.6%</td>
<td>3.076</td>
</tr>
<tr>
<td>Within 4 weeks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospitalization</td>
<td>4.1%</td>
<td>7.0%</td>
<td>0.045</td>
</tr>
<tr>
<td>ER visit1</td>
<td>36.7%</td>
<td>36.9%</td>
<td>0.458</td>
</tr>
<tr>
<td>Outpatient visit1</td>
<td>97.9%</td>
<td>98.6%</td>
<td>3.761</td>
</tr>
</tbody>
</table>

Riva: rivaroxaban; Warf: warfarin; ER: emergency room. Notes: 1Including the index outpatient/ER visit. 2Statistical differences for the mean number of events per patients between cohorts were obtained using non-parametric bootstrap procedure methods.

Conclusion: DVT patients treated with rivaroxaban following an OP/ER visits had significantly fewer hospitalizations and OP visits during the first two weeks compared to matched LMWH/warfarin users.

Acknowledgement/Funding: This research was funded by Janssen Scientific Affairs LLC, Raritan, NJ, United States.

P3814 | BEDSIDE
Impact of new oral anti-coagulant agents on in-vivo platelet aggregation in patients with non-valvular atrial fibrillation: Xa inhibitor vs. direct thrombin inhibitor
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Background: Little has been known about the effect of new oral anti-coagulant agents (NOAC) including selective Xa-inhibitor or direct thrombin antagonist on in-vivo platelet function in patients with non-valvular atrial fibrillation (NVAF).

Purpose: To investigate in-vivo platelet aggregation in patients with NVAF who received NOAC.

Methods: Eighty-four patients with NVAF (age 78±8 year-old) who received dabigatran, n=29, rivaroxaban: n=29, apixaban: n=26, but not received other anti-thrombotic drugs, were enrolled in this study. Platelet aggregation (PA) was measured by low (1.0 μM) and high (3.0 μM) concentration of adenosine diphosphate (ADP) which represent primary and secondary platelet aggregation respectively.

Results: Maximum PA ratio in low-concentration of ADP in rivaroxaban was significantly lower than that in dabigatran (p=0.03). Figure. Maximum PA ratios in high-concentration of ADP were not different in those agents.

Conclusions: This in-vivo study demonstrated that rivaroxaban had more anti-platelet effect in primary PA than dabigatran, but no differences were observed in the NOACs in secondary PA in patients with NVAF.

P3815 | BEDSIDE
The effect of dabigatran on thrombin generation in vitro
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Background: Dabigatran etexilate, a direct thrombin inhibitor (DTI), is at least as effective as warfarin in the prevention of thromboembolic complications of non-valvular atrial fibrillation and in the treatment of venous thrombo-embolism. Since dabigatran has a lower risk of major and intracranial bleeding than warfarin and since there is no need for routine monitoring with coagulation assays, dabigatran
Evidence for involvement of inflammatory changes of perivascular adipose tissue in the pathogenesis of DES-induced hyperconstricting responses in pigs in vivo - impact of 18F-FDG PET imaging

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Background: Recent studies implicated that the perivascular components, such as perivascular adipose tissue (PVAT) and adventitia, play important roles in cardiovascular disease as a source of various inflammatory mediators. However, it remains to be elucidated, whether coronary PVAT is involved in the pathogenesis of impaired coronary vasomotion in vivo, and whether 18F-FDG PET can detect coronary PVAT inflammation.

Purpose: We thus examined whether inflammatory changes in the coronary PVAT are associated with coronary hyperconstricting responses after drug-eluting stent (DES) implantation in pigs by using 18F-FDG PET imaging.

Methods: Everolimus-eluting stents (EES) were randomly implanted in pigs into either the left anterior descending or circumflex coronary artery while non-stented artery was used as a control. At 1 month after the implantation, coronary vasoconstricting responses to intracoronary serotonin (10 and 100 μg/kg) were examined by coronary angiography in vivo, followed by 18F-FDG PET/CT ex vivo imaging for measurement of 18F-FDG uptake normalized to blood pool as target to background ratio (TBR) in the coronary PVAT at the stent edges and the control sites. In addition, coronary vessels were harvested for measurement of radioactivity by autoradiography (ARG), immunohistochemistry, and gene expression by RT-PCR to examine inflammatory changes in the coronary PVAT at the stent edges and the control sites.

Results: Coronary vasoconstricting responses to serotonin (100 μg/kg) were significantly enhanced at the edges of the EES site compared with the control site (P<0.01, n=40) (Figures A–C). Notably, 18F-FDG PET/CT imaging demonstrated enhanced 18F-FDG uptake at the EES-implanted coronary vessel (Figures D, E) and significant association between the TBR and the extent of coronary vasoconstricting responses (P<0.01) (Figure F). In addition, ARG also showed that histological accumulation of 18F-FDG appeared to be remarkably enhanced at the edge of the EES site compared with the control site (Figures G, H) and was significantly associated with the extent of coronary vasoconstricting responses (P<0.01) (Figure I). Furthermore, analysis of histology and RT-PCR showed that the extent of inflammatory changes in the coronary PVAT evaluated by CD68 (macrophage maker) and interleukin-1β (IL-1β) were significantly enhanced at the edges of the EES site compared with the control site (Figures K, L), whereas adiponectin expression was significantly suppressed (all P<0.01) (Figures M, N).

Conclusions: These results suggest for the first time that inflammatory changes in the coronary PVAT are involved in the pathogenesis of DES-induced coronary hyperconstricting responses in pigs in vivo, and that 18F-FDG PET imaging might be useful for assessment of coronary PVAT inflammation.
surgical and percutaneous TVR were considered. Mean follow up was 24 months (6–60 months). 

**Results:** We analysed 190 lesions (from 169 patients) matching the inclusion criteria: stratum A [FFR 0.70–0.74] – 60 (31.6%) lesions; stratum B [FFR 0.75–0.80] – 50 (26.3%) lesions; and stratum C [FFR 0.81–0.85] – 80 (42.1%) lesions. For each stratum intention-to-reatravelizar was 85%, 72% and 54%, respectively. Overall and irrespective of actual revascularization, TLF was inversely proportional to baseline FFR value (20.8%, 16.7% and 11.1% for strata A to C, p<0.08). Considering only the deferred lesions, a progressive reduction in TLF was observed with increasing FFR levels A: 33.3% vs. B: 12.5% vs. C: 11.9% (p for trend <0.05; p = ns for A vs B). Events was mostly driven by TLR. Importantly, target lesion-related MI rate was equally low for both strata B (4%) and C (3.8%). There was no significant interaction between revascularization status and MI events in the follow up. Specifically for lesions with FFR 0.70–0.74, TLF was similar when revascularization were deferred or performed (12.5% vs 11.1%, p = ns).

**Conclusions:** Deferral of revascularization for coronary stenosis with FFR 0.75–0.80 is as safe as for those with FFR 0.81–0.85. At mid-term, revascularization in the 0.75–0.80 range is not associated with prognostic benefits.

**3820 | BEDSIDE**

**Validation of an open CT-FFR algorithm and the effect of computational fluid dynamics on flow boundary conditions on CT-FFR Accuracy**


**Background:** Computer tomography angiography (CT)-based fractional flow reserve (FFR) estimates offer non-invasive detection of lesion-specific ischemia. The diagnostic performance of CT-FFR to detect hemodynamically significant lesions with FFR ware (Fluent, ANSYS) to solve the Navier-Stokes equations. The diagnostic performance drop-off along the length of a coronary artery, termed the coronary transition diameter (the 3rd and 7/3rd powers, respectively). The third model used a direct (Murray’s law and Huo-Kassab’s rule) that relate coronary branch flow to vessel diameter (the 0.75–0.80 range is not associated with prognostic benefits).

**Methods:** Six patients with 320-row CT angiography and subsequent invasive FFR were retrospectively analyzed. The CT-FFR algorithm used the following components: a) a semi-automatic segmentation software to reconstruct the coronary lumen, b) an automated myocardial mass segmentation software to estimate the total myocardial blood flow demand, c) 3 models to estimate flow distribution in the coronary artery tree. The first two are allometric function-form relationships (Murray’s law and Huo-Kassab’s rule) that correlate coronary branch flow to vessel diameter (the 3rd and 7/3rd powers, respectively). The third model used a direct measurement of flow from the CT angiogram based on the rate of contrast opacification at individual coronary images in their own laboratory, and b) to determine how its accuracy changes with respect to three different models used for calculating the relative blood flow distribution amongst coronary artery tree branches.

**Results:** Out of 61 lesions interrogated by invasive FFR, 25 (41%) had FFR<0.8. AUC was highest using the TAG (AUC=0.83), followed by the HK (AUC=0.73) and Murray law CT-FFR models (AUC=0.68). BLank-McAulay limits of agreement were narrowest for the TAG (-0.18 to 0.14), followed by the HK (-0.24 to 0.12) and Murray law CT-FFR models (-0.26 to -0.19).

**Conclusion:** A CT-FFR algorithm using off-the-shelf components yields similar diagnostic accuracy as commercial CT-FFR. Three different models to determine the flow distribution in the coronary artery tree, required to perform a CT-FFR calculation, were tested using this algorithm. The contrast opacification gradient, which is measured directly on the patients’ CT angiogram (TAG) yielded the highest diagnostic accuracy to detect an invasive FFR<0.8, followed by the Huo-Kassab’s model which slightly outperformed Murray’s law model.

**3821 | BEDSIDE**

**Improved survival is associated with guideline-indicated treatments which persists and is greater for higher risk NSTEMI**

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**Purpose:** To investigate the association of NSTEMI guideline-indicated care on long-term survival according to GRACE risk. Methods: Multi-centre national cohort study (247 hospitals, England and Wales, 2003–2013) using data from the Myocardial Ischaemia National Audit Project (MiNAP). Patients were categorised into lowest (<70), low (71 to 87), and intermediate to high (≥88) GRACE risk of 6-month mortality. Optimal care was defined as the receipt of all guideline-indicated management for which each NSTEMI was eligible including aspirin, P2Y12 inhibitors, β-blockers, ACE/ARB, statins, aldosterone antagonists, echocardiogram, coronary angiography, cardiac rehabilitation, smoking cessation and dietary advice. Age, sex, deprivation, year and co-morbidity adjusted all-cause mortality rates per 100 person-years (AMR/100py) and survival was estimated using flexible parametric survival models with continuos time varying covariates.

**Results:** Among the 184,557 NSTEMI (mean age 71.1 (SD 13.5) years; 63.1% male), there were 39,542 (21.4%) deaths over 336,749 person years of follow-up. There were 9.0%, 11.6% and 79.4% NSTEMI in the lowest, low and intermediate to high GRACE risk groups. Overall, 22.8% (n=42,280) received optimal care. More patients in the lowest and low risk groups received optimal care (29.9 and 29.0%, respectively) compared with those in the intermediate to high risk group (21.2%). Compared to NSTEMI lowest risk, those at higher risk had lower rates of angiography (61.0 vs 92.2%), PCI (26.6 vs 54.4%), as well as lower rates of aspirin (97.2 vs 98.4%), P2Y12 inhibitors (92.3 vs 96.2%), β-blockers (92.4 vs 95.0%), ACE/ARBs (89.5 vs 92.4%) and statins (94.6 vs 97.9%) on discharge. Overall, suboptimal care was associated with significantly higher mortality rates (HR=0.82; 0.78–0.86; 95% CI 2.60–3.51) and 90% poorer survival (HR 1.90; 1.83–1.97). Although there was no significant difference in survival between suboptimal and optimal care for the lowest risk NSTEMI (HR 1.24; 0.87–1.77), low and intermediate to high risk NSTEMI receiving suboptimal care had a 45 and 95% increased risk of death respectively (HR 1.45; 1.15–1.82 and 1.95; 1.87–2.02). This effect remained significant over all time points of follow up only for the intermediate to high risk group (HR 1.70; 1.59–1.82 at 1 year, 1.75; 1.40–2.19 at 5 years and 1.69; 1.29–2.22 at 8 years) (Figure 1).

**Conclusion:** Higher risk NSTEMI are less likely to receive optimal care, but have significantly more to gain than their lower risk counterparts in terms of survival.

### Adjusted time-varying mortality rate and 95% confidence intervals by GRACE risk score according to receipt of optimal care

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**Figure 1**

**Conclusion:** Higher risk NSTEMI are less likely to receive optimal care, but have significantly more to gain than their lower risk counterparts in terms of survival.
Moreover, the impact of optimal guideline-indicated care for high risk persists at up to 8 years from index NSTEMI.

Acknowledgement/Funding: MH and TBD funded by BHF (PG/13/81/30474) and SGG funded by Heart and Stroke Foundation of Ontario.

3822 | BEDSIDE
Myocardial infarction and artificial time-constraint: a theoretical framework and national registry study of yearly, monthly, and weekly incidence variation


Introduction and purpose: Psychological stress may trigger a cardiovascular event, such as acute myocardial infarction (MI). Increased MI incidence coincides with recurrent time-periods during the year perceived as particularly stressful. We evaluated an Artificial Time-Constraint (ATC) model which postulates that the incidence of cardiovascular events varies in correspondence with the degree of time-constraint and stress during different time periods.

Methods and results: We tested the ATC model with Swedish population data on MI hospital admissions registered during eight years (1st January 2006 to 31st December 2013) in the national quality register SWEDHEART/RIKs-HIA (N=156,690). Poisson regression was used to analyse daily MI rates during days belonging to the Christmas and New Year holidays, turn of the month, Monday, weekend, and holiday in July compared to remaining control days while adjusting for environmental and age covariates. In support of the ATC model, MI rates were higher during Christmas and New Year holidays and on Mondays and lower in July and over weekends.

Conclusions: Daily MI incidence rates were significantly higher on Mondays and over the Holidays and lower in the weekends and during the vacation month of July, compared to control days. This may be systematically related to psychological stress induced by artificial time-constraint. Further research might clarify mechanisms useful in clinical practice.


3823 | BEDSIDE
Do centres that usually perform percutaneous coronary intervention trans-radially have inferior outcomes when operating trans-femorally?

W.J. Hulme1, M. Sperrin 1, E. Kontopantelis 1, M.A. Mamas 2 on behalf of NOMESCO classification for external causes of injuries.

Background: Over the last decade trans-radial artery access has become more common than trans-femoral access for Percutaneous Coronary Intervention (PCI) in the United Kingdom. Despite studies highlighting the benefits of this transition in practice, concerns remain that the resulting drop in trans-femoral activity has caused centre proficiency with this approach to diminish, compromising the safety and efficacy of procedures where femoral access is necessary.

Purpose: To evaluate the association of each centre’s recent experience of femoral access with procedural outcomes in femoral procedures.

Methods: This retrospective cohort study used procedures recorded in the British Cardiovascular Intervention Society (BCIS) PCI audit from 2007 to 2013 in England and Wales. Centres were split into one of three groups depending on the proportion of total procedures undertaken via the femoral artery in 2013, with patient and procedural characteristics for femoral procedures observed within these groups over time. ‘Recent femoral experience’ was defined as the number of femoral procedures performed by the centre in the 12 months prior to the procedure date. The proportion of femoral procedures was also considered. The association of these measures with 30-day mortality, after risk-adjustment, were then studied using multiple logistic regression.

Results: A total of 253,474 procedures were available for analysis. Unadjusted mortality in centres who were early-adopters of routine trans-radial access increased more rapidly than for centres who maintained high femoral activity, and this was driven by higher baseline risk. After case-mix adjustment recent femoral experience was found to have no effect on 30-day mortality (OR=0.99 per 0.1 increase in recent femoral proportion; CI: 0.96 to 1.01; p=0.220), with similar results when restricting to procedures with low clinical-complexity (OR=0.98 per 0.1 increase in recent femoral proportion; CI: 0.95 to 1.01; p=0.245).

Conclusions: Poorer outcomes in femoral procedures at high radial centres are driven by the propensity of these centres to utilise femoral access in the highest risk patients. Once differences in case-mix are adjusted for, femoral outcomes are similar between high and low radial proportion centres with no evidence to suggest that increasing unfamiliarity with the femoral technique is detrimental. The outcome gains achieved by the national adoption of radial access is not attenuated by decreased femoral experience, and centres should be encouraged to continue to adopt radial as the default access site for PCI wherever possible.

Acknowledgement/Funding: Work carried out as part of a Medical Research Council funded PhD project

3824 | BEDSIDE
Rate of motor vehicle accidents in patients with an implantable cardioverter defibrillator - A Danish nationwide study

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Background: Due to the risk of malignant arrhythmias, shocks and sudden incapacitation, patients with an implantable cardioverter defibrillator (ICD) are temporarily restricted from driving following ICD implantation and/or ICD shock. However, there is a paucity of data concerning the incidence of motor vehicle accidents (MVA) in ICD patients.

Purpose: We aimed to investigate the temporal risk of MVA in a nationwide cohort of ICD patients and matched controls.

Methods: Through nationwide registers, all Danish residents ≥18 years implanted with a first-time ICD between Jan. 1st 2008- June 30th 2012 were identified. These patients were matched 1:2 with controls on sex and age. During the study period, the Danish national recommendations for driving restriction after an ICD implantation were 1 week for primary and 6 months for secondary prevention ICD patients, provided that no ventricular arrhythmias were detected in the restricted period. The primary end-point was defined as non-fatal or fatal MVA in the period Jan. 1st 2008- Dec. 31st 2012. MVAs were identified through nationwide registers on accidents codes and death certificates according to the NOMESCO classification for external causes of injuries.

Results: We identified 4874 first-time ICD implantations and 9748 matched controls.

Conclusion: In a nationwide cohort of ICD patients, we found an overall increased risk of motor vehicle accidents, when compared with an age and gender matched control population. In subgroup analysis, secondary prevention ICD patients had a significantly increased risk of MVA when compared with controls,
while we were unable to demonstrate a significant risk difference between primary prevention patients and controls.

Acknowledgement/Funding: Arvid Nilssons Fond

INFLAMMATION AND LIPIDS – A DREADFUL DUET

3941 | BENCH
Neopterin Reacts Against Vascular Inflammation and Atherosclerosis
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Introduction: Neopterin, a GTP metabolite produced by activated macrophages after stimulation with interferon-γ released from T cells, is expressed at high levels in the carotid atherosclerotic lesions in patients with angina pectoris. However, the modulatory effect of neopterin on atherogenesis has not yet been reported.

Purpose: We aimed to clarify the effects of neopterin on vascular inflammation and atherosclerosis.

Methods: We assessed the atheroprotective effects of neopterin on human umbilical vein endothelial cells (HUVECs), human monocyte-derived macrophages, human aortic smooth muscle cells (HASMCs) in vitro, and aortic lesions in apolipoprotein E-deficient (ApoE−/−) mice in vivo. Further, we investigated the expression levels of neopterin in plasma and coronary lesions in patients with coronary artery disease (CAD).

Results: Neopterin significantly suppressed proliferation of HUVECs. Neopterin significantly suppressed tumor necrosis factor-α (TNF-α)-induced up-regulation of monocyte chemotactic protein-1 (MCP-1), intercellular adhesion molecule-1 (ICAM-1), and vascular adhesion molecule-1 (VCAM-1) in HUVECs. Neopterin attenuated TNF-α-mediated monocyte adhesion to HUVECs via down-regulations of VCAM-1, ICAM-1, and NF-κB. Neopterin shifted the phenotype overwhelmed to inflammatory M2 rather than pro-inflammatory M1 via NF-κB down-regulation during differentiation of human monocytes into macrophages. Neopterin significantly suppressed oxidized low-density lipoprotein-induced foam cell formation associated with reduced cluster of differentiation 36 (CD36) expression and increased both expressions and activities of ATP-binding cassette transporter A1 (ABCA1) and ATP-binding cassette transporter G1 (ABCG1) associated with LXR-α up-regulation in human monocyte-derived macrophages. Neopterin significantly suppressed angiotensin II-induced migration and proliferation without induction of apoptosis associated with down-regulation of c-Src, Raf-1, phosphorylated ERK1/2, and phosphorylated Akt, but not NF-κB, phospho-inositol 3-kinase, Bcl-2, Bax, and p38, in HASMCs. Four-week-infusion of neopterin into ApoE−/− mice significantly retarded the development of aortic atherosclerotic lesions with reduced monocyte/macrophage infiltration and lowered plasma levels of total cholesterol and pentraxin-3. In addition, neopterin expression in coronary arterial lesions and its plasma level were markedly increased in CAD patients compared with non-CAD patients, suggesting that neopterin increased to counteract the progression of atherosclerotic lesions.

Conclusions: Our results indicate that neopterin prevents atherogenesis by suppressing inflammatory responses, monocyte adhesion to endothelial cells, macrophage foam cell formation, VSMC migration and proliferation, and lowering plasma cholesterol levels. Thus, neopterin could serve as a candidate biomarker and novel therapeutic target for atherosclerotic cardiovascular diseases.

3942 | BENCH
Atherosclerotic conditions promote the packaging of microRNA-92 into endothelial microparticles
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Background: Microparticles (MP)-incorporated miRNAs (miRs) are biomarkers and effectors of cardiovascular diseases. Whether MP-miR expression is regulated in coronary artery disease (CAD) is unknown. We aimed to explore the expression of circulating MP-miRs in patients with CAD.

Methods and results: A total of 180 patients with angiographically excluded CAD (n=41), stable CAD (n=77) and acute coronary syndrome (ACS, n=62) were prospectively included in the study. Circulating MPs were isolated from patients’ plasma using ultracentrifugation. Flow cytometer and electron microscope were used to determine MP characterization. Nine miRs involved in the regulation of vascular performance - mir-126, mir-222, mir-let7d, mir-21, mir-26, mir-92a, mir-133, mir-30 and mir-199a - were quantified in circulating MPs by qPCR. Among those, mir-92a was significantly increased in patients with CAD compared to non-CAD patients. MP-sorting experiments showed that endothelial cells (ECs) were the major cell source of MPs containing miR-92. In vitro, oxLDL stimulation significantly altered endothelial miR sorting from ECs into MPs, with a predominant packaging of miR-92 into EMPs. Moreover, functional mir-92 is transferred from ECs to vascular smooth muscle cells (VSMCs) with implications on phenotype and function of recipient cells.

Conclusion: Atherosclerotic conditions promote the sorting of endothelial miR-92 from ECs into EMPs. Intercellular transfer of functional miR-92 via EMPs on VSMCs regulates recipient cell biology with potential implications on vascular disease progression.

3943 | BENCH
Peri-strut red blood cell release: the cause of in-stent neoatherothrombosis?

Background: In-stent neoahterothrombosis is characterized by the delayed appearance of the time markers of atheroma in the sub-intima, but the pathophysiology underlying this new disease entity remains unclear.

Methods and results: We collected 20 human coronary artery stents by removal from explanted hearts. The mean duration of stent implantation was 34 months. In all samples, neoatherothrombosis was detected, particularly in peri-strut areas. It consisted of foam cells and cholesterol clefts, with or without calcification, associated with neovascularization. Iron and glycophorin-A were present in peri-strut areas, as well as autofluorescent ceroids. Moreover, in response to neoatherothrombosis, immune granulomas could develop in the adventitia. Some of these observations could be reproduced in an experimental carotid stenting model in rabbits fed a high cholesterol diet. Foam cells were present in all samples, and peri-strut red blood cells (RBCs) were also observed, as shown by iron deposits and Bandeiraea simplicifolia isoflavon-B4 staining of RBCs membranes. Finally, in silico models were used to evaluate the compliance mismatch between the rigid struts and the distensible arterial wall, using finite element analysis. They showed that stenting approximately doubles the local von Mises stress in the intimal layer.

Conclusions: Our data show that stent implantation both in human and in rabbit arteries is characterized by local peri-strut RBCs accumulation, and finally to both cholesterol accumulation and oxidation, triggering together in-stent neoatherothrombosis. Our data indicate that these processes are likely initiated by an increased mechanical stress due to the compliance mismatch between the stent and the wall.

Acknowledgement/Funding: PRESTIGE grant agreement number 260309

3944 | BENCH
Inhibition of Coagulation factor Xa increases plaque stability and attenuates the onset and progression of atherosclerotic plaque in apolipoprotein e-deficient mice
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Background/Introduction: Atherosclerosis is a progressive chronic inflammatory vascular disorder, complicated by plaque rupture and subsequent thrombus formation. In vitro studies indicate that clotting proteases such as thrombin and Xa (FXa) promote an increase of cellular actions related to atherosclerosis - e.g. vascular permeability, inflammation, and apoptosis - presumably mediated through protease activated receptors (PARs).

Purpose: To elucidate the contribution of FXa in atherosclerosis, we investigated the effects of the direct FXa inhibitor rivaroxaban in atherosclerosis prone ApoE−/− mice.

Methods: In the first arm, female ApoE−/− mice (age 8–9weeks) received high-fat diet with or without rivaroxaban (12mg/gm chow) for 14 weeks (n=8/group). In the second arm, ApoE−/− mice received high-fat diet for 14 weeks, followed by either continuation with standard high-fat diet or high-fat diet supplemented with rivaroxaban (12mg/gm chow) for 6 weeks. (n=5/group). Extent of aortic arch atherosclerosis was assessed by haematoxilin & eosin immunohistochemistry (IHC); plaque vulnerability was examined by IHG against collagen, vascular...
Disruption of gut microbiota alters intestinal lipid metabolism and worsens atherosclerosis

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Purpose: Gut microbiota have been associated to metabolic diseases such as diabetes, NAFLD and atherosclerosis. Excessive use of antibiotics alters the composition of gut microbiota leading to so-called gut dysbiosis. The aim of this study was to investigate the impact of disruption of gut microbiota via long-term antibiotics treatment on atherosclerosis formation in ApoE−/− mice and unveil the underlying mechanisms.

Methods: To assess the impact of long-term antibiotics treatment on atherosclerotic lesion development ApoE−/− mice on a C57BL/6 background (n=12) were fed a chow diet and housed in a semi-sterile environment. Half of mice received oral largely non-absorbable antibiotic treatment in drinking water (vancomycin, ampicillin, neomycin sulfate, metronidazole) for 10 weeks prior to sacrifice at age of 22 weeks. Histological analysis of aortic roots was used to evaluate the extent of atherosclerosis. To gain insight into metabolic pathways, we performed state of the art metabolomics analysis of serum of untreated and antibiotics-treated ApoE−/− mice. We further performed RT-PCR and Western blot analyses of the intestine and liver to support our metabolomics findings.

Results: Histology of aortic roots showed that long-term antibiotics treatment significantly worsened atherosclerosis in ApoE−/− mice (+52±20%; p<0.01, n=6/group). Metabolomics analysis revealed fundamental changes between serum metabolites of untreated and antibiotics-treated mice with a predictive accuracy of 100% in separation of both groups by Random Forest classification. Using False Discovery approach (p<0.05, n=6/group), we found increased JNK activation in the liver shown by Western blot (p<0.05, n=6/group) and increased intestinal gene expression, FGFI5/FGR4 gut-nerve axis might be involved in reduction of CYP7A1 in the liver.

Conclusions: Our data implies that disruption of the gut microbiota via long-term antibiotics treatment has detrimental effects on atherosclerosis development. Further, we propose that modulation of intestinal lipid metabolism as well as biliary cholesterol removal by gut microbiota contributes to the observed phenotype.

3946 | BENCH Comprehensive metabolic profiling of statin therapy: longitudinal evidence and Mendelian randomization

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Objectives: Statins are first-line therapy for cardiovascular disease prevention, but their systemic effects across lipoprotein subclasses, fatty acids, and circulating metabolites remain incompletely characterized. We sought to determine the molecular effects of statin therapy on multiple metabolic pathways.

Methods: Metabolic profiles based on serum NMR metabolomics were quantified at 2 time points in 4 population-based cohorts from the UK and Finland. Concentration changes in 80 lipid and metabolite measures during follow-up were compared between 716 individuals who started statins and 4,874 persistent non-users. We further used Mendelian randomization to assess the corresponding metabolic associations of a genetic variant mimicking HMG-CoA reductase inhibition for 27,914 individuals.

Results: Starting statin therapy was associated with numerous lipoprotein and fatty acid changes including substantial lowering of remnant cholesterol (80% relative to LDL-C), but only modest lowering of triglycerides (25% relative to LDL-C). Among fatty acids, omega-6 levels decreased the most (68% relative to LDL-C); other fatty acids were only modestly affected. No robust changes were observed for amino acids, ketones, or glycolysis metabolites. The intricate metabolic changes associated with statin use closely matched the association pattern with rs129161 in the HMGCR gene (R2=0.94).

Conclusions: Statin use leads to extensive lipid changes beyond LDL-C and appears more efficacious for lowering remnant cholesterol than estimated based on triglyceride lowering. However, the metabolomics profiling suggested minimal effects on amino acids. The results exemplify how detailed metabolic characterization of genetic proxies for drug targets can inform indications, pleiotropic effects, and pharmacological mechanisms. The presentation will also include detailed etabonomic signatures for newer targets including PCSK9, APOC3, APOA5 and LPA, based on genetic evidence.
Academically, enrichment of these specific phospholipid have been recently corre-
related to enhanced cholesterol efflux capacity of HDL particles and may underlie the
improved HDL functionality after RYGB. Reduced sphingosine-1-phosphate
(S1P) content is a known mediator of HDL dysfunction. Indeed, S1P content was
also increased in small HDL-1Y after RYGB.

Conclusions: HDL subclasses analysis reveals that small size HDL levels are
increased and exhibit enhanced cholesterol efflux capacity in patients 1 year after
RYGB compared to the preoperative baseline.

Elevated content of small HDL in PC, PS, PA and their lyso-forms as well as
increased S1P levels may contribute to the improved athero-protective function of
HDL 1 year after RYGB.

Acknowledgement/Funding: The Swiss National Science Foundation Am-
bizione Grant; the Swiss Cardio-Onco-Grant - Alfriss and Annemarie von Sick
Grant; the Foundation Leduco.

3949 | BENCH

High-density lipoprotein bound surfactant protein B is associated with
outcome in patients with heart failure and preserved ejection fraction

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Introduction and aims: In advanced disease stages, heart failure with preserved
ejection fraction (HFpEF) is characterized by pulmonary congestion and impaired
gas exchange. Recently, circulating surfactant protein B (SP-B) has been sug-
gested as marker for lung damage in chronic heart failure. Excessive release of
SP-B into the circulation results in characteristic alterations in the high-density
lipoprotein (HDL) proteome with incorporation of SP-B into the HDL-associated
protein complex. Here, we hypothesized that impaired gas exchange resulting from
chronic pulmonary congestion is associated with increases in HDL-bound SP-B
(SP-B(HDL)) and assessed its value as potential prognostic marker in HF-
PEF.

Methods: Consecutive HFpEF patients (n=145) diagnosed according to current
ESC guidelines (1, signs and symptoms of heart failure, 2, left ventricular ejec-
tion fraction >50% and 3. evidence of abnormal left ventricular relaxation, fill-
ing or diastolic stiffness) were prospectively recruited and followed for a mean of
25.3 months. SP-B(HDL) levels at diagnosis were measured by ELISA assay, ex-
pressed as normalized values to a positive control on each plate and correlated
with functional and clinical parameters of the patients. Furthermore, the associa-
tion of SP-B(HDL) and prognosis considering a composite endpoint of hospital-
zation due to heart failure and/or cardiac death was assessed in a multivariate
regression model.

Results: HFpEF patients had significantly higher levels of SP-B(HDL) compared
to a pool of healthy controls (mean ± SEM HFpEF vs. mean ± SEM controls:
0.26±0.02 vs. 0.07±0.01, p<0.0001). SP-B(HDL) was inversely correlated with
carbon monoxide lung diffusion (r=-0.33, p=0.002), arterial oxygen saturation (r=
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NOAC compared to warfarin. The results were consistent when stratified for sex, age groups (0–65, 65–75, 75–89, ≥89 years), earlier TIA/ ischemic stroke, and earlier severe bleeds.

Conclusion: The main results indicate similar effectiveness and safety with NOAC and warfarin treatment in routine care including primary care in the Stockholm region. The secondary endpoints indicate a lower risk of intracranial bleeds, but a higher risk of gastrointestinal bleeding with NOAC compared to warfarin treatment.

Acknowledgement/Funding: Stockholm County Council

3988 | BEDSIDE

Predictors of thrombembolic events in left ventricular assist devices

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Introduction: Mechanical circulatory support system (MCS) such as left ventricular assist devices (LVAD) is gaining more and more acceptance in the treatment of end-stage heart failure (HF). Despite recent improvements, adverse complications still occur; however, convenient and safe solutions have not been developed to prevent thromboembolic events (TE events).

Methods: Data were reviewed retrospectively from patients receiving HeartMate or HVAD from 2012 to 2014 at a single center. A multi-variable analysis for TE events as primary endpoint including the variables atrial arrhythmia data and post LVAD implantation, surgical technique, VAD type, and baseline data was performed. Additionally, short and long term survival was evaluated.

Results: 381 consecutive patients underwent LVAD implantation from 2012 to 2014 (study group). Mean age 62.1±10.1 years, 88.4% were male, 44.2% had a dilatative cardiomyopathy, 124 received an HVAD and the main surgical implantation technique was the less invasive “Hannover” approach (60.22%). A total of 43 patients suffered from thromboembolic events. The 30-day and 1-year survival rates were 90% and 80%, respectively. Pump thrombosis developed in 123 patients (90.1%). The thromboembolic event rates in patients with AA (68.1%) were similar to those without (74.6%). Additionally, in comparing all LVAD patients and the effect of VAD model (Havard vs HeartMate) the thromboembolic event was not significantly different (p=0.228). Also there was no significant difference in adverse events comparing patients treated with NOAC and Warfarin.

Conclusions: Atrial arrhythmias do not appear to influence overall survival and the results suggest that only poor control of anticoagulation (INR <2) and off-pump surgery technique correlate significantly with the development of TE events.

Acknowledgement/Funding: none

3989 | BEDSIDE

Risk of thrombembolic events without oral anticoagulation in consecutive patients at 90 days after surgical aortic valve replacement with a bioprosthesis

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Background: Guidelines recommend that patients undergoing bioprosthetic aortic valve replacement receive at least 3 months of anticoagulation with warfarin because it is believed to reduce thromboembolic events. Purpose: We sought to determine the risk of thromboembolic events in such patients not treated with warfarin.

Methods: We performed a retrospective analysis of patients who had undergone bioprosthetic aortic valve replacement between 1984 and 2010; patients also undergoing surgery on other valves were excluded. We also excluded patients with a history of atrial fibrillation, mitral stenosis, deep venous thrombosis, pulmonary embolism, or a history of intracranial bleeding. According to these findings, there is no significant difference in adverse events through the VAD type, surgical approach and basic disease. The multivariate analysis showed that poor control of anticoagulation (INR <2) and off-pump surgery technique correlated significantly with the development of TE events.

Conclusion: Thromboembolic events without oral anticoagulation in patients at the end of the first 3 months after aortic valve replacement receive at least 3 months of anticoagulation with warfarin because it is believed to reduce thromboembolic events.
tiocoagulation was systematically chosen for these patients. Ninety-day outcome data were available for all patients.

**Results:** Mean age of patients not discharged on warfarin was 70±11 years; 68% were male, 12% had heart failure. Mean postoperative ejection fraction was 59%. There were 32 (1.4%) deaths in the 90 days after discharge. Mode of death was fatal pulmonary embolism in 2 patients, thromboembolism with stroke in 2, haemorrhage in 2, heart failure in 5, respiratory failure in 2, sepsis in 3, sudden death in 6, other causes in 10. The frequency of readmission was 3.9% and included pericardial/pleural effusion (2.2%), bleeding event (0.2%), endocarditis (0.4%), prosthesis dehiscence (0.1%), other (0.1%). Only 6 patients (0.3%) had a thromboembolic event in the 90 days after discharge (4 transient ischemic attacks and 2 major strokes which were fatal).

**Conclusion:** Patients undergoing surgical aortic valve replacement with a bio-prosthesis had a low risk of both major and minor bleeding complications in the 90 days after discharge when not anticoagulated.

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**DEVICE-BASED TREATMENTS FOR HYPERTENSION**

**3996 | BEDSIDE**

Controlling and lowering blood pressure with the MobiusHD device: first-in-man interim results (CALM-FIM study)

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**Objective:** To evaluate the safety and performance of the MobiusHD system in patients with resistant hypertension.

**Design and methods:** This is a multi-center (9 centers) non-randomized, first-in-man assessment of a nontoxic self-expanding, rectangular cuff implant (MobiusHD) designed to increase carotid sinus arterial wall strain without impacting home blood pressure. The subjects were randomized to one-year follow-up, and the primary endpoint was reduction in office systolic blood pressure (BP) measured during 1.5-year follow-up.

**Results:** So far 31 patients, mean age 52 (range 21–76) years, of the anticipated 36 patients were included and followed for one-year without re-angioplasty. For all patients, one- and two-year patency at PTA site was ascertained by duplex ultrasound examination. In 5 patients in whom there was reported DDD antihypertensive medications at the time of presentation, the European first-in-man study will have completed enrollment, and all 30 patients will have reached the 180-day safety endpoint. Moreover, 24 patients worldwide will have reached one-year follow-up.

**Conclusions:** So far, implanting the MobiusHD device in patients with resistant hypertension seem to be safe and shows promising results in BP lowering.

**Acknowledgement/Funding:** Vascular Dynamics, Inc.

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**3997 | BEDSIDE**

Effect of renal denervation on blood pressure levels and clinical course of obstructive sleep apnea in patients with resistant hypertension - 3 months outcomes of randomized trial

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**Objectives:** The aim of our study (NCT01366625) was to investigate the effect of renal denervation (RDN) for the treatment of resistant hypertension (RHTN) coexisting with obstructive sleep apnea (OSA). Here we report an analysis of the primary end point - blood pressure (BP) reduction at 3 months as well as an impact of OSA severity and glucose metabolism.

**Material and methods:** 60 patients (48M, 12F, mean age 55.3±9.3, range: 31–69yrs) with true RHTN (office systolic BP >140/90mmHg and daytime systolic BP average >135 mmHg on ≥3 antihypertensive drugs including a diuretic) co-existing with moderate-to-severe OSA (apnea/hypopnea index (AHI) ≥15) were randomly allocated to two groups: 30 patients (24M, 6F, mean age 55.9±9.4, range: 32–69yrs) and 30 patients (24M, 6F, mean age 54.5±9.2, range:31–68yrs) were assigned to control group. The primary endpoint was reduction of office systolic blood pressure (BP) at 3 months. Secondary endpoints included reduction of office BP and day/night SBP and DBP, and nighttime ambulatory ABP (ABP) on ambulatory blood pressure measurements (ABPM) as well as change in AHI and selected biochemical parameters at 3 months.

**Results:** There were no difference in age, gender, office or day/time ABPM levels between the groups. At 3 months, the number of patients on ≥3 antihypertensive drugs during that period. At 3 months, systolic BP levels in the RDN group were reduced by 22 mmHg (p<0.001), whereas they did not significantly differ from baseline in the control group (change +1.8 mmHg, p=0.123). Between-group differences in change were significant at 0.002 for systolic BP. Also diastolic BP levels decreased significantly (0.9 mmHg, p<0.001) in the RDN group, but not in the control group (-3.3 mmHg, p=0.176). 24h, daytime and nighttime ABP levels were reduced by 17.3/5.8 mmHg (p<0.001),11.1/2.6 mmHg (p<0.01), and 10.7/3.4 mmHg (p=0.01) in the RDN and control group, respectively. In the control group no significant changes in 24h, daytime and nighttime ABP were observed. Between-group differences in ABP were significant for daytime systolic and diastolic BP levels (p=0.008 and p=0.008, respectively) as well as 24h ABP levels (p=0.042 and p=0.037, respectively) but not for nighttime ABP levels. In the RDN group, 3 months after the procedure significant decrease in OSA severity measured with AHI (39.4±31.2 vs 3.1±0.051) was observed, whereas there was no difference in AHI in the control group (31.6±30.4, p=0.528). Between group differences in AHI change was significant at 0.05. Both in RDN and control group there were no differences in glycated hemoglobin, nor fasting glucose level 3 month after the procedure.

**Conclusions:** In keeping with our previous observations (Witkowski et alli Hypertension 2011; 58: 559–665), we now show in a randomized trial that RDN is associated with attenuation of BP and of OSA severity.

**Acknowledgement/Funding:** The study was supported by National Science Centre in Poland; Grant no. NN 402 491 140

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**3998 | BEDSIDE**

Effects of percutaneous transluminal renal angioplasty on office and home blood pressure and home blood pressure variability in hypertensive patients with renal artery stenosis

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**Background:** Renal artery stenosis (RAS) is associated with secondary hypertension, which is often resistant to antihypertensive medication. The most common cause of RAS is atherosclerotic RAS, and fibromuscular dysplasia (FMD) comprises most of the remaining causes. Percutaneous transluminal renal angioplasty (PTA) is one of the standard treatments for RAS, but its effect on blood pressure (BP) remained to be fully elucidated.

**Objectives:** We investigated whether the effects of PTA on BP control differ by its cause.

**Methods:** One hundred and twenty-six hypertensive patients with RAS (mean age 63 years; 31 female; 22.2% FMD) with 148 treated renal arteries were included and followed for one-year without re-angioplasty. For all patients, one-year patency at PTA site was ascertained by duplex ultrasound examination. In addition to office BP, home BP was self-measured via a validated semiautomatic device in the morning during the 7 consecutive days before and one-year after
PTA. Masked uncontrolled hypertension (MUH) was defined as an in-office BP of <140/90 mmHg and home mean BP of >135/85 mmHg. Day-by-day home BP variability was defined as the within-subject mean systolic BP and corresponding variability as estimated by standard deviation (SD), coefficient of variation (CV), maximum-minimum difference (MMD), variability independent of the mean (VIM), and average real variability (ARV).

**Results:** In total patients, office BP (157±26/82±15 to 132±16/74±12mmHg), home BP (147±18/79±14 to 134±15/73±9mmHg), and the number of antihypertensive medications (2.5±1.2 to 2.2±1.2) decreased significantly at one-year after PTA and ARAS, respectively. At baseline, the prevalence of MUH was not significantly different between ARAS and FMD patients (9.2 vs 10.7%); however, at one-year after PTA, that of MUH was significantly higher in patients with RAS than those with FMD (34.7% vs 14.3%, p < 0.01). Although the change in office BP was not different between FMD and ARAS (-32±24/-10±14 vs -23±28/-7±17mmHg), FMD patients showed a significantly greater decrease in home BP than those with ARAS (-23±19/-11±14 vs -10±20/-5±10mmHg; p < 0.01, respectively). In total patients, all systolic BP variability indices such as SD (10.2±4.6 to 8.5±3.5mmHg), MMD (28.0±13.4 to 23.4±10.2mmHg), VIM (10.2±4.5 to 8.5±3.5), ARV (11.1±5.7 to 9.3±4.7mmHg) (p < 0.01, respectively), and CV (7.0±3.1 to 6.3±2.6%; p < 0.05) decreased significantly at one-year after PTA. Compared with ARAS patients, FMD patients showed significantly greater decreases in SD (-3.8±6.1 vs -1.1±5.2mmHg), MMD (-12±19 vs -3±14mmHg), and ARV (-4.1±5.4 vs -1.2±3.7mmHg; p < 0.05, respectively), but not in CV (-3.2±6.4 vs -1.3±5.2%).

**Conclusion:** These results suggest that the effects of PTA on BP differ by its causes not only in BP reduction but also in some BP variability indices. Combined BP assessment of both office and out-of-office is important for the treatment success after PTA.

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**FUTURE DIRECTION FOR RESEARCH IN EXERCISE IN HEART FAILURE: DO WE KNOW IT ALL?**

**4026 | BEDSIDE**

**Five year follow-up results of 12 months of graded exercise therapy and intensive supervision in patients with chronic heart failure**

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**Background:** The positive effects of exercise therapy have unequivocally been proven in patients with Chronic Heart Failure (CHF). Retaining the improved exercise capacity though is difficult and requires behavioral change in which exercise becomes daily routine. This study describes the five year follow-up results of a care reform project for patients with CHF: Changing Leisure Time Physical Activity (LTPA) during and after Cardiac Rehabilitation (CR) by 12 months of guided with Standard Exercise Therapy (GET) was the focus.

**Purpose:** Reducing mortality and health care costs in patients with CHF by increasing LTPA.

**Methods:** Patients: Patients with CHF starting with CR in 2009–2010 were monitored and interviewed using regular health care based on known predictors of mortality in CHF (Age, LVEF, NYHA class, serum creat, DM, HFpEF/HFrEF, BMI, gender, smoking, use of ACE-i, use of Beta-blocker). We performed a 1 to 1 matched analysis without replacement on the basis of a propensity score of each patient. Mortality data of the patients’ follow-up were compared in both groups.

**Intervention:** ICD and pacemaker settings were optimized and a Cardio Pulmonary Exercise Test (CPET) was performed to determine maximal exercise capacity and the corresponding training protocol. Training consisted of two main goals: improving exercise capacity and muscular strength. Patients visited our outpatient clinic three times a week to train under supervision of a physiotherapist for 12 weeks. In addition, they received a GET protocol to train daily at home. Afterwards patients trained three times a week for 12 weeks with a physiotherapist nearby at home in order to make the transition from supervised training in an outpatient clinic to training at home as small as possible. In addition to these workouts, patients were stimulated to continue their personal GET protocol. The last six months patients trained at home unsupervised according to the GET protocol and the strength training exercises.

**Conclusion:** A maximal CPET was performed at the start, after three hours and six months and at the end of the program. Before all visits pacemaker and ICD settings were checked and if needed changed. Patients received feedback on the results from the exercise test and were able to talk about possible problems during training.

**Results:**

**Conclusion:** Our study showed, compared to usual care, significantly lower mortality rates five years after a cardiac rehabilitation program with 12 months of intensive supervision and Graded Exercise Therapy in patients with CHF.

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**4027 | BEDSIDE**

**Regular physical exercise enhances endothelial function in patients with heart failure with preserved ejection fraction**

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**Purpose:** To investigate the effects of regular physical exercise on the endothelial function, assess through changes of circulating blood markers of endothelial treatment of nitric oxide (NOx), dimethylarginine (ADMA), symmetric dimethylarginine (SDMA), Advanced Oxidation Protein Products (AOPP) and Xanthine Oxidase (XOD) in patients (pts) with heart failure with preserved ejection fraction (HFpEF).

**Methods:** A total of 57 pts with HFpEF were enrolled in the study. At baseline and 3 weeks later, in all pts values of NOx, ADMA, SDMA, AOPP and XOD were determined and exercise test was performed. After the initial study, pts were randomised to trained (T, n=35) and non-trained (NT, n=22) group. Non-trained group received usual community care while T group underwent a supervised 3 weeks physical exercise at residential center.

**Results:** After 3 weeks of physical exercise NOx increased significantly in T group (from 33.9±7.6 to 41.7±8.5 μmol/l, P<0.0001) and this value was higher than in NT group (P=0.0358). Value of ADMA as well as SDMA decreased in both groups after 3 weeks: ADMA in T group from 0.360±0.07 to 0.315±0.12 μmol/l (P=0.059) and in NT group from 0.325±0.09 to 0.305±0.07 μmol/l (ns); SDMA in T group from 0.290±0.09 to 0.250±0.14 μmol/l (by 13.7%; ns) and in NT group from 0.265±0.09 to 0.250±0.09 μmol/l (by 5.3%; ns). Higher decreased of ADMA in T group during exercise training (from 0.360±0.07 to 0.315±0.12 μmol/l, P<0.0001), resulted in significantly lower AOPP value in T group than in NT group at the end of the study (245.0±41.4 vs 280.0±28.4 μmol/l, P<0.001). Compared to the baseline, value of XOD after three weeks decreased in both groups (in T by 38.5% and in NT by 13.7%) and at the end of the study XOD was significantly lower in T than in NT group (190.5±33.0 vs 250.8±28.2, P<0.0001). After 3 weeks exercise capacity significantly increased in T group (P<0.001), and level and duration of exercise test were higher in T than in NT group (P<0.01 both).

**Conclusion:** In pts with HFpEF, regular physical exercise in addition to standard therapy, leads to an improvement in endothelial function, which is expressed through significant increase of NOx and decreased of ADMA, higher decreased of SDMA, AOPP and XOD than in pts with HFpEF who received usual community care and standard therapy. This improvement in endothelial function is associated with significant improvement in exercise capacity.

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**4028 | BEDSIDE**

**High intensity interval training improves clinical response after cardiac resynchronization therapy**

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**Introduction:** Cardiac rehabilitation (CR) is an established intervention in the comprehensive management of advanced heart failure patients. Modulation of the autonomic nervous system has been proposed as one of the responsible mechanisms, however the exact physiological processes whereby patients may benefit from CR are unclear. Aims: To evaluate the effect of CR with a high intensity interval training (HIIT) protocol on a population of advanced heart failure patients.

**Methods:** We randomly assigned consecutive patients with an indication for cardiac resynchronization therapy as per ESC guidelines to HIIT or no intervention in a 1:1 ratio. Patients were submitted to a comprehensive baseline evaluation including assessment of clinical parameters, functional capacity as assessed by cardiopulmonary treadmill exercise testing (CPET), endothelial dysfunction and cardiac denervation as assessed by miLB-123 scintigraphy. Patients were then submitted to CRT implantation and either underwent an 8 week CR protocol or standard care. Repeat assessment was performed at 1 month and at 3 months after inclusion. Statistical analysis was performed as intention-to-treat with the Wilcoxon rank-sum and signed-rank test where appropriate; an ordered logistic regression was used to study the effect of NIH on NYHA functional class. A 2-tailed p value <0.05 was considered statistically significant.

**Results:** 62 patients were included, of which 33 were randomized to CR, mean age 67±10.6 yrs, left ventricular ejection fraction (LVEF) 26±47.2%. No sig.
4036 | BEDSIDE
Mortality and morbidity in heart failure patients exposed to Digoxin: comprehensive data according to ejection fraction and atrial fibrillation in 41881 patients from the Swedish Heart Failure Register
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Background: Digoxin is authorized in European Union for the reduction of ventricular rate in patients with atrial fibrillation (AF) and for the management of heart failure with reduced ejection fraction (HFREF). However, data from randomized trials in HFREF with and without AF are limited, and a long-term assessment of mortality and HF hospitalization is lacking. The impact of digoxin on mortality in heart failure with preserved ejection fraction (HFPEF) is unknown. The aim of this research was to evaluate the association between digoxin and all-cause mortality, HF hospitalization and the composite of these outcomes in HFREF and HFPEF with and without AF.

Methods: We studied patients enrolled in the Swedish Heart Failure Registry between 2005 and 2012 and assessed the association between digoxin use and all-cause mortality, HF hospitalization and the composite of these outcomes in HFREF and HFPEF with and without AF.

Results: Baseline and post-treatment changes in cardio-pulmonary reserve

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Conclusion: In pts with HFPEF and abnormal diastolic response to exertion, improvement in exercise E/e' mediates the beneficial effect of spiro on exercise capacity. As functional limitation is a significant contributor to impaired wellbeing in pts with HFPEF, identification of exercise-induced increase in LVFP may define a subgroup with warranting trial of spiro.

4038 | BEDSIDE
Risk of long-term mortality associated with diuretic treatment in 17,519 heart failure outpatients was increased with 42% after adjustment for MAGGIC mortality risk predictors
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Background/Introduction: Diuretic treatment has previously been associated with increased long-term mortality in heart failure (HF) outpatients. However, objections have been raised that adjustment for confounders was insufficient and that diuretic use was a marker of disease severity rather than an independent risk factor of increased mortality. The MAGGIC meta-analysis from 2013 was based on 30 HF studies with a median follow-up of 2.5 years with the aim to identify independent risk factors for mortality in chronic HF. MAGGIC included patients with both reduced and preserved ejection fraction (EF) and identified 13 independent and 2 interaction predictors of mortality.

Purpose: To estimate the independent risk of long-term mortality associated with diuretic treatment in HF outpatients by adjusting for MAGGIC mortality risk predictors.

Methods: The Swedish HF registry (SwedeHF) is nationwide. All inpatients and outpatients with clinician-judged HF are eligible for inclusion. All outpatients (n=17,519) registered between 2004-2011 with known diuretic treatment (72%) and inpatient data (92%) at baseline were included in this study. Of these patients 83% had reduced EF and 17% had preserved EF. Median follow-up was 3.0 years. In SwedeHF over 80 variables are recorded at baseline, among them are the MAGGIC mortality risk predictors. Crude risk of all-cause long-term mortality associated with diuretic treatment and risk of all-cause long-term mortality associated with diuretic treatment after adjustment for MAGGIC mortality risk predictors were estimated in two separate cox regression models.

Results: Crude all-cause long-term mortality rate was increased in patients with diuretics when compared to patients without diuretics. Long-term risk of death remained increased after adjustment for MAGGIC mortality risk predictors (table 1).

Conclusions: In HF outpatients, risk of long-term mortality associated with
Aortic valve disease: don’t forget the aorta / New insights on peripheral circulation

AORTIC VALVE DISEASE: DON’T FORGET THE AORTA

4054 | BEDSIDE
Prospective analytical study of risk factors for valvular heart disease and disease of the ascending aorta - a nested population based case-control study

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Introduction: The risk factors for developing heart valve- and ascending aortic disease are mainly based on retrospective data. In order to elucidate these factors in a prospective manner, we have performed a nested case-referent study using data from large population based surveys.

Material and methods: 777 patients operated for heart valve disease or disease of the ascending aorta had previously participated in population based health studies in northern Sweden. The median time (IQR) from survey to surgery was 10.5 (9.0) years. The primary indication for surgery was aortic stenosis (41%), aortic regurgitation (12%), mitral regurgitation (23%), and dilatation/dissection of the ascending aorta (17%). For each case four age, gender and area matched referents were allocated.

Results: In multivariable models, hypertension, high cholesterol levels, diabetes and active smoking were associated with future surgery for aortic stenosis. Singerificance for aortic regurgitation was not predicted by traditional risk factors but high cholesterol level was associated with lower risk. A high cholesterol level predicted surgery for mitral regurgitation, whereas none of the other traditional risk factors were associated with mitral valve surgery. Hypertension, blood pressure and previous smoking predicted surgery for disease of the ascending aorta whereas diabetes was associated with reduced risk.

Conclusions: With a median time of almost 10 years, traditional risk factors predicted future surgery for aortic stenosis and disease of the ascending aorta whereas these risk factors did not predict surgery for aortic- or mitral regurgitation. Risk factor intervention may be warranted in early stages of aortic stenosis and disease of the ascending aorta. The unexpected associations between metabolic factors and aortic regurgitation and disease of the ascending aorta warrant further investigation.

Acknowledgement/Funding: Swedish Heart and Lung Foundation

4055 | BEDSIDE
Elastic properties of the ascending aorta in patients with a bicuspid versus tricuspid aortic valve and isolated severe aortic stenosis


Increased aortic stiffness has a negative impact on LV systolic and diastolic function in patients (pts) with severe aortic stenosis (AS). Bicuspid aortic valve (BAV) is associated with abnormal aortic elastic properties. There is no data regarding the impact of the presence of a BAV versus a tricuspid aortic valve (TAV) on the elastic properties of ascending aorta in pts with severe AS.

Purpose: The aim of our study was to assess the differences in the aortic stiffness between pts with BAVs and those with TAVs in a group of middle aged pts with severe AS and preserved LVEF (62±6%), in sinus rhythm, with no more than grade 2 aortic or mitral regurgitation. Patients were divided into two groups based on the presence of a BAV (26 pts) or TAV (25 pts). Aortic stiffness index (beta) was calculated using a validated formula based on ascending aorta diameters (measured by M mode echocardiography) and blood pressure values. Systemic arterial compliance (SAC) and valvulo-arterial impedance (Zva) were also determined.

Results: There were no significant differences between groups regarding age (p=0.2), gender (p=0.8), body mass index (p=0.2) and the presence of cardiovascular risk factors (diabetes, systemic hypertension, hyperlipidemia and smoking, p=0.1). The degree of systemic hypertension and the systolic and diastolic blood pressure values measured at the time of echocardiography were similar between groups (p=0.3). Parameters of AS severity (AVA, mean gradient, peak transvalvular velocity) were not different between groups (p=0.4 for all). Patients with BAVs had larger indexed LV end diastolic volumes (p=0.05) and a higher LV stroke volume index (p=0.04), although the degree of aortic regurgitation was similar between groups (p=0.9). The ascending aorta diameter was significantly larger (39±6 vs 33±6 mm, p=0.001) and beta index was significantly higher in the BAV group (13.5±4 vs 8.4±, p=0.005), while Zva and SAC were similar between groups (p=0.3 for both). Increased aortic stiffness was marginally correlated to larger aortic diameters (p=0.054). No significant correlations were found between beta index and indices of AS severity or LV function (including TDI derived parameters of systolic and diastolic function and global longitudinal strain).

Conclusions: Middle aged patients with isolated severe AS and a bicuspid aortic valve have an increased aortic stiffness when compared to patients of similar age, with the same degree of tricuspid aortic valve aortic disease. The impact of this finding on LV function, functional status and outcome needs to be determined.

Acknowledgement/Funding: Grant of the Romanian Ministry of National Education, CNCS – UEFISCUD, project number PN-II-ID-PCE-2012-4-0560 (contract 21/2013)

4056 | BEDSIDE
Genotype predicts aortic dissection risk in marfan syndrome

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Background: Risk assessment for aortic dissection in patients with Marfan syndrome is difficult. Aortic diameter is widely used, however the relationship between aortic diameter and occurrence of dissection is variable. Increasing evidence supports family history of dissection as an adverse prognostic predictor, suggesting that specific FBN1 mutations may carry increased risk for dissection.

Purpose: This study examined the relationship between FBN1 mutation type and dissection risk in Marfan syndrome.

Methods: The study group included all patients with Marfan syndrome and known FBN1 mutations collated from the clinic at our hospital, comprehensive literature search (PubMed) and review of published databases (ClinVar, UMD and HGMD). When patients were identified in published databases, the original clinical reports were reviewed whenever possible. Each mutation was included only once. Occurrence of aortic dissection with a mutation was recorded once, even when multiple dissections had occurred. Polymorphisms considered non-pathogenic were excluded. Mutations were grouped as missense (no cysteine affected), missense (cysteine affected), premature stop codon, frameshift and splice defects.

Results: A total of 2223 mutations were identified - 619 missense (no cysteine); 663 missense (cysteine); 611 stop; 152 frameshift and 178 splice. There were 196 (8.8%) mutations associated with aortic dissection. Aortic dissection was more frequently associated with stop/frameshift/splice mutations (99/941) than with missense mutations, with or without cysteine affected, 96/1282 (p=0.015). Missense mutations affecting cysteine were not associated with increased risk of dissection. Risk of dissection for patients with stop/frameshift/splice mutations was related to the position of the mutation within FBN1 (Table).

Genotype vs Risk of Dissection

<table>
<thead>
<tr>
<th>Mutation location</th>
<th>Risk of Dissection</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Missense + cysteine</td>
<td>Stop/Frameshift/Splice</td>
<td>Ref.</td>
</tr>
<tr>
<td>Exons 1–10</td>
<td>9/145 (0.06)</td>
<td>22/155 (0.142)</td>
</tr>
<tr>
<td>Exons 11–18</td>
<td>19/385 (0.06)</td>
<td>44/239 (0.08)</td>
</tr>
<tr>
<td>Exons 1–30</td>
<td>39/602 (0.06)</td>
<td>53/447 (0.119)</td>
</tr>
<tr>
<td>Exons 1–40</td>
<td>51/799 (0.06)</td>
<td>67/593 (0.113)</td>
</tr>
<tr>
<td>Exons 1–50</td>
<td>67/1000 (0.07)</td>
<td>78/716 (0.109)</td>
</tr>
<tr>
<td>Exons 1–65</td>
<td>96/1282 (0.07)</td>
<td>99/941 (0.105)</td>
</tr>
</tbody>
</table>

Conclusions: FBN1 mutations of stop/splice/frameshift type are associated with greater risk of aortic dissection, particularly when occurring towards amino terminus of the encoded protein.

NEW INSIGHTS ON PERIPHERAL CIRCULATION

4058 | BEDSIDE
Cardiovascular outcome in patients with peripheral artery disease (PAD) as initial manifestation of atherosclerotic disease compared with patients with pad as subsequent diagnosis after coronary heart disease


Objective: The purpose of this study was to evaluate cardiovascular outcome in patients (pts) with peripheral artery disease (PAD) as initial manifestation of atherosclerotic disease compared with pts with PAD as subsequent diagnosis after coronary heart disease (CHD).

Methods: A total of 2223 mutations were identified - 619 missense (no cysteine); 663 missense (cysteine); 611 stop; 152 frameshift and 178 splice. There were 196 (8.8%) mutations associated with aortic dissection. Aortic dissection was more frequently associated with stop/frameshift/splice mutations (99/941) than with missense mutations, with or without cysteine affected, 96/1282 (p=0.015). Missense mutations affecting cysteine were not associated with increased risk of dissection. Risk of dissection for patients with stop/frameshift/splice mutations was related to the position of the mutation within FBN1 (Table).
lern, with an estimated 20% prevalence among the elderly in Sweden. PAD confers a risk for subsequent major cardiovascular events. However, contemporary nationwide real-life data on cardiovascular outcome in patients with PAD as initial atherosclerotic manifestation is scarce.

**Purpose:** To describe cardiovascular risk and drug therapy in patients with incident PAD as initial atherosclerotic diagnosis versus patients diagnosed with PAD as subsequent diagnosis following coronary heart disease (CHD) or ischemic stroke (IS) in Sweden.

**Methods:** This observational cohort study linked morbidity, mortality, and medication data from Swedish national registries for patients hospitalized with a diagnosis of PAD from 2006–2014. The study included patients with incident PAD diagnosis only and incident PAD patients with a history of CHD, IS, or both CHD and IS. Cardiovascular outcome was defined as a composite of MI, IS, and cardiovascular death. The risk and relative risk in the different patient groups were assessed by Kaplan-Meier analysis and Cox proportional hazards modelling, respectively. Patients were followed for up to 8 years.

**Results:** In total, 66,189 patients were diagnosed with PAD, 40,136 with PAD as single recorded atherosclerotic diagnosis, 16,786 with a prior history of CHD, 5803 with a history of IS, and 3464 with a history of both CHD and IS. Patients with PAD only were younger (mean age, 74.6 years vs. 77.1 years) and more often women (51.6% vs. 41.8%) compared with the multi-vessel affected group. Fewer patients with incident PAD received secondary preventive drug therapy: antplatelet therapy (62% vs. 80%), statins (47% vs. 61%), and anti-hypertensives (77% vs. 94%) compared to the multi-vessels affected. One-year cumulative incidence rate of cardiovascular outcome was 11.7% in patients with PAD only compared with 24.2% in the multi-vessel affected group (Figure 1). The corresponding number for all-cause mortality was 16.2% vs. 25.1%. History of stroke among PAD subjects increased risk for a cardiovascular event one year after PAD diagnosis whereas CHD did not (Hazard ratio (HR) 1.35 (95% CI 1.22–1.49, p < 0.001 and HR 1.06 (98.1–1.4), p=0.145). The multi-vessel affected group (PAD+CHD+IS) had highest risk (HR 1.40 (1.26–1.55); p<0.001).

**Conclusions:** PAD as initial manifestation of atherosclerotic disease confers a high risk for cardiovascular events; more than one of ten patients suffer a major cardiovascular event within a year while almost one in five patients die within a year. Adoption of a higher incidence risk, whereas history of CHD did not. Despite substantial risk for cardiovascular events, many PAD patients did not receive secondary preventive drug therapy.

**Acknowledgement/Funding:** AstraZeneca funded this study.

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**4060 | BEDSIDE**

**Resting heart rate is an independent predictor of mortality in patients with peripheral artery disease**

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**Background:** Resting heart rate has been increasingly identified as a marker of cardiovascular risk, and has been extensively studied as a predictor of coronary artery disease progression. In peripheral artery disease (PAD), the prognostic impact of resting heart rate impact remains unknown.

**Purpose:** To assess the association between resting heart rate and mortality in patients with PAD.

**Methods:** In this non-concurrent prospective cohort study, consecutive patients undergoing invasive peripheral procedures because of Fontaine IIb–IV symptoms of PAD were included. Data were collected from a dedicated, mandatory fill-in clinical pathway, which includes resting heart rate determination by averaging 3 manual radial pulse palpation measurements taken 24 hours after an invasive peripheral procedure as part of periprocedural monitoring. Multivariable Cox proportional hazards were developed to predict all-cause mortality, even after adjusting for age, gender, other traditional risk factors, preventive medication, presence of coronary or cerebrovascular disease, atrial fibrillation and heart rate-lowering medication (odds ratio 1.018; 95% confidence interval 1.007–1.030; P = 0.008).

**Results:** A total of 1727 patients were included (mean age 64±18 years, 38% were female, 38% had critical limb ischemia). During a median follow-up of 371 (interquartile range 188–543) days, 394 (22.8%) patients died. On multivariable Cox analysis, resting heart rate emerged as an independent predictor of mortality, even after adjusting for age, gender, other traditional risk factors, preventive medication, presence of coronary or cerebrovascular disease, atrial fibrillation and heart rate-lowering medication (odds ratio 1.018; 95% confidence interval 1.007–1.030; P = 0.008).

**Conclusions:** Resting heart rate is an independent predictor of mortality in patients with PAD; our findings extend heart rate as a marker for prognosis of non-corony vascular disease.

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**4061 | BEDSIDE**

**Impact of ACE inhibitor and ARB use on long-term limb outcomes in patients with established peripheral artery disease: Insights from the REACH Registry**

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**Background:** The role of angiotensin converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARB) in patients with peripheral artery disease (PAD) is inconclusive, particularly after the retraction of a large trial of ACEi in intermittent claudication (IC).

**Purpose:** We sought to study the impact of ACEI/ARB on adverse limb outcomes in patients with established PAD enrolled in the international REACH registry.

**Methods:** Differences between users of ACEI/ARB at study enrollment were accounted for with propensity score matching. All-cause mortality and major adverse CV events (MACE, including mortality, myocardial infarction, stroke and lower limb major amputation) up to 15 years (mean 11.8±2.3 years) were compared between 3 groups of patients according to baseline ABI: normal (1.00 to 1.40), borderline (0.91 to 0.99) and PAD (<0.90). Multivariable Cox proportional hazards regression was used to evaluate long-term mortality risk of borderline ABI.

**Results:** Of 689 patients (70.1±11.8 years, 58.6% men), 70.8% (n=488), 9.0% (n=62) and 20.2% (n=139) had normal, borderline ABI and PAD, respectively. Cumulative incidence of all-cause mortality was higher in patients with PAD (74.4%) and borderline ABI (71.0%) than in patients with normal ABI (54.7%; p=0.011). Adjusted mortality risks were significantly higher in patients with PAD (Hazard Ratio (HR) 1.60; 95% CI: 1.24–2.08; P < 0.001) and borderline ABI (HR: 1.59; 95% CI: 1.09–2.31; P=0.02) compared to those with normal ABI. The risks of MACE were significantly higher in patients with PAD (HR: 1.90; 95% CI: 1.49–2.42; P < 0.001) and borderline ABI (HR: 1.67; 95% CI: 1.18–2.37; P=0.004) than in those with normal ABI.

**Conclusion:** Patients with borderline ABI was associated with significantly higher risks of long-term mortality and MACE that are comparable to patients with PAD.
4062 | BEDSIDE

Transradial approach for carotid artery stenting in high-risk patients

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Background: Carotid artery stenting (CAS) is an alternative to carotid endarterectomy (CEA). CAS from the radial approach is gaining experience in high volume transradial centers. The purpose of this study was to evaluate the safety and efficacy of CAS using transradial approach in high risk patients.

Methods: Transradial selective approach was performed in 150 patients who had undergone transradial CAS in a high volume transradial center. A separate analysis with all previously defined high risk patients with TRA CAS was performed.

Results: TRA CAS was done in 758 patients (mean age 66, 70% male). CAS was successful in 758 (100%) patients; 367 (48%) patients were defined as high risk patients (<2 high-risk criteria according to SAPPHIRE classification). CAS was performed in 403 (65.9%) cases with filter time of 5±2 minutes. Fluoroscopy time was 8 minutes (5-35 minutes) and contrast volume was 150 ml (150-350ml). Adverse events included 2/367 major strokes (0.5%) with mortality 0.5%, 3/367 minor strokes (0.8%), and 4/367 intraprocedural TIA (1%). There were no major bleeding complications. Minor bleeding access site complications were present in 15/367 (4%) patients. Hospital stay was 1±1 day in 97% of high risk patients after the procedure. At 30 days follow up there were no additionally registered ischemic events.

Conclusion: The transradial CAS is safe and feasible in high risk patients when done by experienced transradial CAS operators.

4063 | BEDSIDE

Usefulness of ultrasonography in endovascular therapy for chronic total occlusion of femoro-popliteal arteries


Background: The success rate of endovascular therapy (EVT) for long chronic total occlusion (CTO) of femoro-popliteal (FP) arteries has improved because of devices development. However, patency rate after EVT has not been improved remarkably. We have used ultrasonography (US) in EVT for FP CTO lesions.

Purpose: Our aim was to investigate the usefulness of the US guided wiring in EVT for long CTO lesions of FP.

Method: In 2720 consecutive cases which underwent EVT between May 2007 and December 2014, we focused on 186 cases for long CTO (length >150mm). Comparing investigation about procedure results, intravascular ultrasound (IVUS) findings and patency rate was performed between O group and N group. In O group, we used old US machine which was set as default preset. In N group, US was performed by 1 MHz linear transducer which was set as our original preset for EVT, and we performed wiring with our original method.

Results: Mean age was 73±10 year.o, and female was 78 cases (41.9%). No significant difference was detected in patient and characteristics. Technical success rate was 67% in O group and 88.8% in N group. Only antegrade approach case in N group was higher than N group (85.7% vs. 46.6%; p<0.0001). Dose of radiation in N group was lower than O group (191±167 mGy vs. 275±421±167 mGy; p<0.01). Dose of contrast media in N group was less than O group (139±67±2 ml vs. 218±97±2 ml; p<0.01). Primary patency at two years in N group was higher than O group (72.6% vs. 54.1%; p<0.03). In IVUS findings, rate of all true lumen tracking in N group was higher than O group (true lumen: 50.0% vs. 3.8%, subintimal length<5cm: 10.0% vs. 5.8%; p<0.01). Primary patency of all true lumen tracking was the highest (all true: 81.1%, subintimal length<5cm: 62.5%, >5cm: 47.8%; p<0.01).

Conclusion: The US guided wiring with our original method was less invasive treatment and improved primary patency in EVT for long FP CTO lesions.

4064 | BEDSIDE

Effect of carotid stenting on the lipid core of atherosclerotic carotid stenosis assessed by near-infrared spectroscopy and intravascular ultrasound

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Background/Introduction: Atherosclerotic carotid artery disease is a common determinant of thromboembolic stroke. However, limited insights in vivo into the composition of carotid stenosis are available. Prediction of lesion-related atheroembolic potential and selection of patients who would benefit most from carotid endarterectomy or carotid stenting (CAS) is challenging.

Purpose: To describe size and distribution of lipid core plaques in atherosclerotic internal carotid artery (ICA) stenoses and changes of LCP after CAS using near-infrared spectroscopy (NIRS) and intravascular ultrasound (IVUS).

Methods: We performed NIRS-IVUS during 77 CAS procedures in 73 patients (men 66%, age 67±8±3 years) with ICA stenosis >65% on angiography. We measured minimal luminal area (MLA), plaque burden (PB), lipid core burden index (LCBI), maximal lipid core burden index in any 4mm segment of the artery (LCBImax) and lipid core burden index in 4mm segment at the site of MLA (LCBImax). Three NIRS-IVUS pullbacks were performed: at baseline, after stent implantation and after balloon postdilatation.

Results: The IVUS cross-sectional frame with the maximal LCBI was localized 2.87±7.9mm (95% CI: 5.01±1.72) proximally from the site of MLA (Figure). Plaque burden at the site of MLA was 48.8±10.7% compared to 62.8±20.4% at the site of maximal LCBI (p<0.01). Lipid rich plaques were significantly more frequent elsewhere than at the site of MLA (LCBImax at baseline 346±62±90.0 vs. LCBImax at baseline 219±62±37.5, p<0.01). Minimal luminal area increased significantly both with stent implantation and postdilatation (Table) but the effect of postdilatation on LCP was not significant. Postdilatation of the stented segment had no further significant effect on LCBImax and LCBImax (Table).

Conclusions: The highest lipid pool of the plaque was localized proximally from the site of MLA. Implantation of the self-expandable carotid stent alone led to significant decrease of lipid core size. On the contrary, postdilatation of the stent led to larger acute lumen expansion.

Acknowledgement/Funding: The study was supported with institutional grant no. 6007.

4065 | BEDSIDE

Patients with high carotid heart rates bilaterally show increased cardiovascular event rate

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1 Hippokration Hospital, University of Athens, 1st Department of Cardiology, Athens, Greece. 2 University Hospital of Patras, Department of Cardiology, Patras, Greece. 3 University of Bolton, Centre for Material Research and Innovation, Bolton, United Kingdom

Background: Inflammation is a recognized characteristic of vulnerable atherosclerotic plaque. Recently, evidence emerged about the role of microwave radiometry (MWR) for the evaluation of arterial inflammation in atherosclerotic patients by measuring temperatures.

Purpose: The aim of the present study was to evaluate in patients with documented coronary artery disease (CAD) the change in carotid morphological and functional characteristics and b) whether increased carotid temperatures are associated with a reduction in self-reported claudication, while ARB use was also associated with a reduction in future revascularization procedures and ischemic amputations.

Methods: Consecutive patients with significant CAD were included in the study. Common carotid intima media thickness (cIMT) and maximum carotid plaque thickness (MPT) were assessed in all carotids by ultrasound, according to Mannheim consensus document. By MWR was assigned as the temperature difference (maximum minus minimum) along the carotid artery. AT <0.9°C was assigned as high AT. Major cardiovascular event (MACE) was defined as death, stroke, myocardial infarction or revascularization. All patients were followed-up for
one year. Patients without events underwent new MWR and ultrasound measurements at one year.

Conclusion: CAS performed according to the ‘tailored’ algorithm prior to cardiac surgery is a low risk procedure and might be an option to prevent possible perioperative neurological complications of ICA stenosis. Patients requiring urgent cardiac surgery have slightly increased risk of the procedure.

STABLE MYOCARDIAL ISCHAEMIA: FROM SUSPICION TO INTERVENTION

4067 | BEDSIDE
Prevalence and prognosis in patients with known or suspected myocardial ischemia but no obstructive coronary artery disease
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Background: The knowledge of patients with no obstructive coronary artery disease (CAD) is limited.

Purpose: To evaluate the prevalence of nonobstructive and obstructive CAD. The knowledge of patients with no obstructive coronary artery disease (CAD) is limited.

Methods: We searched current literature for studies reporting prevalence or prognosis of patients with no obstructive CAD (<50% stenosis) among those with known or suspected CAD but not identified as acute STEMI. The patients with no obstructive CAD were further grouped as non-obstructive CAD (0%–99%) and nonobstructive CAD (1%–50%). Impact of ischemia among these patients was also assessed.

Results: Fifty six studies with 1,396,585 subjects were included in this analysis. The prevalence of patients with no obstructive CAD was 66% (95% CI: 62% to 70%) in patients with stable angina and 13% (95% CI: 11% to 16%) in patients with NSTE-ACS. The prevalence varied depending on sex, clinical setting, and risk profile of the population investigated. The risk of hard cardiac events (cardiac death or MI) in patients with nonobstructive CAD was 71% lower compared with patients with obstructive CAD (RR: 0.29, 95% CI: 0.21 to 0.40), but was 83% higher compared with those with no CAD (RR: 1.83, 95% CI: 1.52 to 2.20). The annualized event rate of hard cardiac events among subjects with no, nonobstructive and obstructive CAD were 0.3%, 0.7% and 2.5% respectively in stable chest pain patients and 1.2%, 4.1% and 17.0% in NSTE-ACS patients. The correlation between CAD severity and prognosis is consistent across the effects on all-cause death, MI, total cardiovascular events and revascularization. Among patients with no obstructive CAD, myocardial ischemia identified by noninvasive functional testing predicted a higher risk of total cardiovascular events (RR: 2.55, 95% CI: 1.72 to 3.77).

Conclusions: Nonobstructive CAD is associated with a favorable prognosis compared with obstructive CAD, but is not benign. The high prevalence and impaired prognosis of this population warrants further research to improve the risk stratification and management among these patients.

Patient and procedure characteristics

<table>
<thead>
<tr>
<th>Procedure</th>
<th>HP (n=51, 56%)</th>
<th>SP (n=40, 44%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>69±9±5.7</td>
<td>67±6.8±5.5</td>
<td>0.09</td>
</tr>
<tr>
<td>Ipsilateral stroke/TIA</td>
<td>16 (31%)</td>
<td>21 (52.5%)</td>
<td>0.2</td>
</tr>
<tr>
<td>ICA stenosis</td>
<td>85.5±10%</td>
<td>85.6±8%</td>
<td>0.9</td>
</tr>
<tr>
<td>Proximal neuroprotection device</td>
<td>24 (47%)</td>
<td>20 (50%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Closed-cell/mesh-covered stent</td>
<td>48 (94%)</td>
<td>35 (87.5%)</td>
<td>0.8</td>
</tr>
<tr>
<td>Left main stenosis</td>
<td>16 (31%)</td>
<td>32 (10%)</td>
<td>1.0</td>
</tr>
<tr>
<td>euroSCORE II</td>
<td>2.8±1.3%</td>
<td>1.9±1%</td>
<td>0.008</td>
</tr>
<tr>
<td>Isolated CABG</td>
<td>46 (90%)</td>
<td>35 (87.5%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Isolated valve surgery or CABG</td>
<td>5 (10%)</td>
<td>5 (12.5%)</td>
<td>0.7</td>
</tr>
</tbody>
</table>

*Valve/aortic surgery/left ventricle aneurysmectomy/left atrial appendage closure.
4068 | BEDSIDE
European society of cardiology guidelines over-estimate the probability of coronary artery disease in patients with suspected angina. Results from the Scottish Computed Tomography of the HEART trial


Methods: We categorized 1,778 patients (mean age 58±9 years) who had undergone computed tomography coronary angiography (CTCA) who underwent CCTA between January 2008 and December 2012 at 10 Danish hospitals. CTCA was evaluated by at least two independent accredited assessors to determine the presence of CAD 70. ESC guideline-defined pre-test probabilities of obstructive coronary artery disease were compared with the observed prevalence of disease defined by CTCA.

Results: The observed prevalence of CAD 70 was on average 2-fold lower than that predicted by the ESC guidelines across all age, sex and symptom categories (Figure 1). The pre-test probability contributed considerably to the observed differences between modalities in the pooled AER after a negative test result.

Conclusions: Current ESC guidelines markedly overestimate the probability of coronary artery disease. This may lead to unnecessary investigation of a large number of patients in current contemporary practice.

Acknowledgement/Funding: This work was supported by a Collaboration Grant from the Netherlands Heart Foundation (2014T051).

4069 | BEDSIDE
Prognostic value of all noninvasive cardiac imaging modalities in patients with suspected or known coronary artery disease - a meta-analysis


Methods: A meta-analysis was performed to explore the effects of pre-test probability and baseline presence of CAD on AER after a negative test result.

Conclusion: This meta-analysis provides a strong level of evidence that a negative test result, regardless of the selected non-invasive cardiac imaging modality, conveys a good prognosis for patients with suspected or known CAD. Variation in prognosis between modalities is highly influenced by differences in pre-test probability and baseline presence of CAD.

Acknowledgement/Funding: Grant from the Netherlands Heart Foundation (2014T051).

4070 | BEDSIDE
Prognostic assessment of stable coronary artery disease using computed tomography angiography: a danish multicenter cohort study

L. Huche Nielsen1, H.E. Boetker2, H. Toft Soerensen2, M. Schmidt2, L. Pedersen1, B.L. Norgaard2 on behalf of Western Denmark Heart Registry-CT study group.

Conclusion: The impact of age, sex and comorbidity on the prognostic value of coronary computed tomography angiography (CCTA) in real-world patients suspected of stable coronary artery disease (CAD) have not been investigated.

Purpose: To examine the 3.5-year real-world prognosis of stable CAD as assessed by CCTA; and to examine the prognostic impact of age, sex and, comorbidity.

Methods: This registry study is based on 16,949 consecutive patients (median age 57 years; 57% women) with suspected CAD (angina/dyspnea symptoms) who underwent CCTA between January 2008 and December 2012 at 10 Dan-

Figure 1. Comparison of ESC Guideline-defined Pre-test Probabilities (PTP) and Computed Tomography Coronary Angiography-defined Obstructive (≥70% Stenosis) Coronary Artery Disease. A. Male. B. Female.

AER for cardiac death/MI negative test

Conclusion: This meta-analysis provides a strong level of evidence that a negative test result, regardless of the selected non-invasive cardiac imaging modality, conveys a good prognosis for patients with suspected or known CAD. Variation in prognosis between modalities is highly influenced by differences in pre-test probability and baseline presence of CAD.

Acknowledgement/Funding: Grant from the Netherlands Heart Foundation (2014T051).
ISH hospitals. The endpoint was a composite of late revascularization procedures >90 days after CCTA, myocardial infarction (MI) and all-cause mortality. We used the Kaplan-Meier estimator to compute 91-day to 3.5-year risk according to CAD severity. Comparisons between patients with and without CAD were based on Cox regression adjusted for age, sex, comorbidity burden according to Charlson Comorbidity Index, cardiovascular risk factors, concomitant cardiac medications, and post-CCTA treatment within 90 days. Analyses were repeated stratified by age groups (<55, 56–64, and ≥65 years), sex and comorbidity burden, respectively.

**Results:** The composite endpoint occurred in 486 patients (overall: late revascularization, n=173; MI, n=105; death =261) during follow-up. Risk of the composite endpoint ranged from 1.5% to 6.8% and 15% for patients without CAD, obstructive CAD and 3- vessel/left main disease, respectively. Compared with patients without CAD, patients with obstructive 1-vessel CAD (hazard ratio [HR]: 1.13; 95% confidence interval [CI]: 1.37–2.44), 2-vessel CAD (HR: 2.97; 95% CI: 2.09–4.22), and 3-vessel/left main CAD (HR: 4.41; 95% CI: 2.90–6.69), as well as those with non-obstructive CAD (HR: 1.28; 95% CI: 1.01–1.63) experienced higher relative risk of the composite endpoint. This pattern remained after stratification by age, sex, or comorbidity.

**Conclusion:** CAD severity determined by CCTA predicts the composite endpoint comprising late revascularization, MI and all-cause mortality (up to 3.5 years) independent of age, sex, or comorbidity burden. These findings support the diagnostic value of CCTA in an ageing population with comorbidity in real-world clinical practice.

### 4071 | BEDSIDE

**Canadian Cardiovascular Society (CCS) angina classification extracted from clinical notes by natural language processing: validation and association with healthcare utilization in an integrated health network**

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Background: Canadian Cardiovascular Society (CCS) angina classification has been positively associated with revascularization, myocardial infarction, and mortality in clinical trials among patients with obstructive CAD, but the rates of events largely varied across single studies. We carried out a meta-analysis to compare the clinical presentation and prognosis of NObCAD and ObCAD.

### Methods:
We identified Veterans with incident stable ischemic heart disease (SIHD) between 1/1/2006 and 12/31/2013 and used NLP to extract CCS classifications from medical notes. NLP-extracted values were validated against those obtained by three human chart annotators in 500 documents and positive predictive value and sensitivity were quantified. Multivariable-adjusted regression models were used to calculate risks for revascularizations, hospitalizations, emergency department (ED) visits, outpatient visits, and total costs at one-year follow-up.

### Results:
Over 214 million clinical documents were processed for 6,556,919 Veterans, and 6,689 NObCAD and 5,262 ObCAD patients were included in the analysis. Multivariable regression models showed that NObCAD patients had significantly higher risk of revascularization, hospitalization, emergency department visits, outpatient visits, and total costs at one-year follow-up.

### Incidence of healthcare utilization and changes in CCS class by initial CCS angina classification among new diagnosis of SIHD during a one-year follow-up period

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Initial CCS angina classification</th>
<th>P for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICG %</td>
<td>(n=4,825)</td>
<td>(n=6,689)</td>
</tr>
<tr>
<td>PGC, %</td>
<td>13.5%</td>
<td>22.7%</td>
</tr>
<tr>
<td>CABG, %</td>
<td>4.7%</td>
<td>8.5%</td>
</tr>
<tr>
<td>All-cause hospitalizations, %</td>
<td>36.8%</td>
<td>43.9%</td>
</tr>
<tr>
<td>ER visits, count, mean (SE)</td>
<td>5.8±0.087</td>
<td>5.3±0.17</td>
</tr>
<tr>
<td>Outpatient visits, mean (SE)</td>
<td>30.1±0.08</td>
<td>32.0±0.07</td>
</tr>
<tr>
<td>Total costs, mean (SE)</td>
<td>$28,146</td>
<td>$31,008</td>
</tr>
</tbody>
</table>

Conclusion: NLP is an effective method for identifying CCS class in the EHR. Worse initial CCS class is associated with increased healthcare utilization at one year.

**Acknowledgement/Funding:** Investigator Sponsored Research Grant from Gilead Sciences, Inc.

### 4072 | BEDSIDE

**Influence of national guidelines on the investigation of patients with suspected angina in a district hospital rapid access chest pain clinic**

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**Background:** The Rapid Access Chest Pain Clinic (RACPC) is a "one-stop" clinic which is designed to identify patients with stable chest pain due to coronary artery disease (CAD) and reassure those with non-cardiac pain. Historically, patients were offered exercise testing (ETT) or coronary angiography (EHT) however in March 2010 the National Institute of Clinical and Healthcare Excellence (NICE) published guidelines recommending assessment of likelihood of CAD based on age, gender, chest pain type and risk factors followed by further assessment with either CT scanning or functional imaging (angiography). This guideline has encouraged the use of ETT in patients without known CAD. The current study investigated temporal trends in the investigation of patients referred to a district hospital RACPC before and after publication of the NICE guideline.

**Methods:** We performed a retrospective analysis of consecutive patients referred to our RACPC (Sep 08-Oct 15). We assessed likelihood of CAD according to NICE guideline which defined high risk as likelihood of CAD: >60%, intermediate risk: 30–60%, low risk: 11–29% and very low risk: <10%. We recorded choice of initial and any subsequent investigation requested from clinic and performed economic analysis using current UK tariff.

### Results:
Our cohort comprised 6815 patients; 28% had high likelihood of CAD, mandating ICA; 10.2% intermediate likelihood, mandating functional imaging; 11.5% low likelihood, mandating CT and 50.3% very low likelihood. We divided patients into chronological cohorts (each of whom was composed of consecutive patients referred with a diagnosis of angina). From the inception of the National Institute of Clinical and Healthcare Excellence (NICO) guidelines which spanned periods prior to, and after publication of the NICE guideline. Prior to the NICE guideline 86% patients had an ETT which reduced to 72% post-NICE. Similarly, more patients were discharged without investigation (12% pre-NICE vs 25% post). There was an increase in the overall number of patients referred for ICA (17% pre-NICE, 19% post), CT (0.4% pre-NICE to 4.4% post) and functional imaging (3.2% pre-NICE to 7.5% post). Overall the number of tests increased from 1.24 to 1.34 per patient post-NICE and average cost per patient from £262 ($338) to £360 ($461). If the NICE guidelines were strictly applied to our population the average cost would have decreased by 39% to £172 ($222) per patient.

### Conclusion:
This is the largest study reporting temporal trends in assessment of likelihood of CAD in a RACPC. Since the NICE guidelines were first published, we have performed a head-to-head comparison of patients referred with a diagnosis of angina, and the average cost per patient reducing by 39%. This demonstrates that the NICE guidelines are likely to show NST-segment elevation ACS (N-STACS) rather than STACS.

**Non-obstructive versus obstructive coronary artery disease in acute coronary syndrome: a meta-analysis**

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**Background:** Differences in prognosis and baseline clinical presentation have been described among patients with non-occlusive coronary artery disease (NObCAD) and obstructive CAD (ObCAD), but the rates of events largely varied across single studies. We carried out a meta-analysis to compare the clinical presentation and prognosis of NObCAD versus ObCAD ACS patients, as well as of the subjects with zero versus mild occlusion.

**Methods:** Searches were made in Medline, Embase, Cochrane databases, and proceedings of international meetings up to June 30, 2015. Both raw data and adjusted or propensity score matched estimates were extracted at any time-point. The primary, pre-specified hypothesis of the study was that clinical outcomes (as defined by the authors) were less frequent in NObCAD vs ObCAD patients. Two secondary hypotheses were investigated: (1) among ObCAD subjects, those with angiographic stenosis (≥50% stenosis) have a lower risk of events than patients with 1%–49% stenosis; (2) at baseline, ObCAD subjects are more likely to show NST-segment elevation ACS (N-STACS, rather than STACS) than ObCAD patients. We used both random-effect direct comparison (head-to-head) and proportion meta-analyses to estimate yearly or monthly outcome rates.

**Results:** In 33 studies, published between 2003 and 2015, 51,548 participants, evaluated the clinical outcomes of ObCAD or NObCAD patients (mean follow-up 24m; range 1–126m). In NObCAD and ObCAD patients, respectively, the combined yearly rates were: 2.4% vs 10.1% (all-cause mortality); 1.4% vs 6.0% (myocardial infarction); 4.0% vs 12.8% (all-cause mortality plus myocardial infarction); 1.4% vs 5.9% (cardiac death), and 9.2% vs 16.8% (major cardiovascular events - MACE). In direct-comparison meta-analyses, all of the above outcomes were significantly less frequent in NObCAD subjects with risk ratios ranging from 0.33 to 0.66. No differences in any outcome rate were observed between mild occlusion (1%-49% stenosis) and zero occlusion patients. At baseline, the combined proportion of STACS were 14.7% and 73.8% in NObCAD and ObCAD patients, respectively (summary RR=0.20; p<0.001).
**Interpretation:** NObCAD patients have a significantly lower cardiovascular risk at baseline and a subsequent lower likelihood of death or main cardiovascular events. However, NObCAD subjects are still at high risk for cardiovascular mortality and morbidity, suggesting a potential under-treatment and claiming for a specific management.

**Conclusions:** NObCAD patients have a significantly lower cardiovascular risk at baseline and a subsequent lower likelihood of death or main cardiovascular events. However, NObCAD subjects are still at high risk for cardiovascular mortality and morbidity, suggesting a potential under-treatment and claiming for a specific management.

**4074 | BEDSIDE**

**Twenty-five year follow-up of patients with chest pain and smooth, unobstructed epicardial coronary arteries**

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**Background:** Recent evidence suggests that the prognosis of patients with chest pain and unobstructed epicardial coronary arteries/microvascular angina may be a cause for concern. The maximum follow-up period that has been documented in the literature for a group of patients with this condition is 14 years. Unanswered questions include whether these patients consistently develop obstructive ischaemic heart disease, what their life expectancy is, and whether they die from cardiovascular causes. Over 25 years ago, our group exhaustively characterised a group of patients with, what was then termed, cardiac syndrome X – a triad of angina pectoris, a positive exercise test for myocardial ischaemia and smooth, unobstructed epicardial coronary arteries.

**Purpose:** To investigate the life expectancy and cause of death in patients with well-characterised cardiac syndrome X followed up for 25 years.

**Methods:** Using information from hospital databases, local registry offices, general practitioners and national databases, we tracked alive or dead status of 99 patients with cardiac syndrome X enrolled in a study over 25 years. Cause of death was established from the death certificate.

**Results:** We collected data on 90 patients - 9 were lost to follow-up. Fourteen patients had died (15%; 6 women, 8 men; mean age at death 75±10 years, range 61–91 years). Primary cause of death was documented as myocardial infarction with chronic atheromatous occlusion of coronary arteries (1 patient), cancer (6), ruptured aortic aneurysm (1), pneumonia (3), multi-organ failure, ischaemic heart disease, dementia (1), multi-organ failure, upper Gl bleed, duodenal ulcer (1), and end-stage dementia (1). In one patient who died of cancer, ischaemic heart disease was listed as a secondary cause of death.

**Conclusions:** In our cohort of exhaustively characterised patients with chest pain and smooth, unobstructed epicardial coronary arteries, 3 patients had ischaemic heart disease listed on the death certificate, and one of these died from a myocardial infarction. This study is the longest follow-up reported, showing that in this particular type of patient, progression to coronary disease and fatal myocardial infarction is uncommon.

**4075 | BEDSIDE**

**Gender differences in non-culprit coronary plaque microstructures on frequency-domain optical coherence tomography in stable coronary artery disease**


1Medical Research Institute, Heart Health, Adelaide, Australia; 2Cleveland Clinic, Department of Cardiovascular Medicine, Cleveland, United States of America; 3South Australian Health & Medical Research Institute, Heart Health, Adelaide, Australia

**Background:** Numerous studies have shown different features of culprit plaques between men and women. This observation suggests a potentially distinct form of pathophysiology of atherosclerosis between genders. Given the systemic nature of coronary atherosclerosis, we hypothesized that non-culprit plaques in women undergoing percutaneous coronary intervention (PCI) might also exhibit distinct plaque features.

**Purpose:** To determine gender differences in non-culprit plaques by using frequency-domain optical coherence tomography (FD-OCT) imaging.

**Methods:** Non-culprit plaques were evaluated by FD-OCT imaging in patients with stable CAD (n=320) requiring PCI. FD-OCT measures were compared between genders.

**Results:** Women were more likely to have a history of hypertension (79.6 v. 67.7%, p=0.02), diabetes (41.7 v. 31.3%, p=0.03) and metabolic syndrome (53.4 v. 36.8%, p=0.02). Non-culprit plaques in women were less likely to exhibit plaque rupture and more likely to demonstrate plaque erosion (Table). Furthermore, women were less likely to harbor cholesterol crystal and calcification, and more likely to have a smaller lipid arc (Table). These differences persisted after adjusting clinical demographics (plaque rupture: p=0.03, plaque erosion: p=0.03, cholesterol crystal: p=0.02, calcification: p=0.02, lipid arc: p=0.04). There were no significant differences in fibrous cap thickness, TCFA and microchannel.

**Conclusions:** Despite more comorbid risk factors in women, their non-culprit plaques exhibited more plaque erosion and less cholesterol and calcium content. This distinct phenotype suggests potential gender-related differences in the pathophysiology of atherosclerosis.

**4076 | BEDSIDE**

**Impact of diabetes mellitus on 5-year clinical outcomes in patients with chronic total occlusion lesions**


1Korea University Guro Hospital, Seoul, Korea Republic of; 2Soon Chun Hyang University Gumi Hospital, Gumi, Korea Republic of; 3Eulji General Hospital, Cardiology Department, Seoul, Korea Republic of; 4Soon Chun Hyang University Gumi Hospital, Gumi, Korea Republic of; 5Kangwon National University Hospital, Chuncheon, Korea Republic of

**Background:** Diabetes Mellitus (DM) can lead to cardiovascular morbidity and mortality. However, there are limited data regarding the impact of DM in patients who have chronic total occlusion (CTO) lesion on long-term clinical outcomes.

**Methods:** A total of 822 consecutive CTO pts who underwent diagnostic coronary angiography and received percutaneous coronary intervention (PCI) or optimal medical treatment (OMT) were enrolled. Pts were divided into two groups according to the presence of DM: 1) the DM group (n=363) and 2) Control group without DM (n=459). To adjust for potential confounders, a propensity score matching (PSM) analysis was performed using the logistic regression model. Major adverse cardiac events (MACE), the composite of total death, myocardial infarction, stroke and revascularization, were compared between the two groups up to 5 years.

**Results:** After PSM analysis, two propensity score-matched groups (298 pairs, n=596, C-statistic=0.655) were generated and the baseline characteristics were balanced. Up to 5 years, there was a trend toward higher incidence of any revascularization, particularly non-target vessel revascularization and total MACE in the DM group compared with the control group (Table). However, there was no significant difference in the incidence of mortality and myocardial infarction between the two groups up to 5 years.

**Table.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total death</td>
<td>0.01</td>
</tr>
<tr>
<td>Cardiac death</td>
<td>0.02</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0.02</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.02</td>
</tr>
<tr>
<td>Revascularization</td>
<td>0.02</td>
</tr>
<tr>
<td>Target lesion (CTO vessel)</td>
<td>0.02</td>
</tr>
<tr>
<td>Target vessel (CTO vessel)</td>
<td>0.02</td>
</tr>
<tr>
<td>Non-target vessel (Non-CTO vessel)</td>
<td>0.02</td>
</tr>
<tr>
<td>Total MACE</td>
<td>0.02</td>
</tr>
</tbody>
</table>

**Conclusions:** This study implies that diabetic pts with CTO should be managed more carefully in clinical follow-up as they were associated with higher trend of revascularization and total MACE rates up to 5 years.

**NEW DEVELOPMENTS IN CARDIOVASCULAR SPECT AND PET**

**P4077 | BEDSIDE**

**SPECT myocardial perfusion imaging adds incremental prognostic value over cardiorespiratory fitness**

M. Al-Mallah1, A. Ahmed1, W. Qureshi2, 1King Abdul Aziz Medical City, King Saud bin Abdulaziz University for Health Sciences, King Abdullah International Medical Research, Riyadh, Saudi Arabia; 2Wake Forest University, Winston-Salem, United States of America

**Background:** Cardiorespiratory fitness (CRF) has been shown to be a strong predictor of outcomes. However, it is not clear whether myocardial perfusion imaging (MPI) adds incremental prognostic value over CRF across the spectrum of fit-
ness. We examined the incremental prognostic value of the single Photon Emission Computed Tomography – Myocardial Perfusion Imaging (SPECTMPI) over CRF.

Methods: We retrospectively studied 3,216 patients referred for an exercise SPECT MPI between April 2004 and May 2009. Patients were followed up for the primary end point of cardiac death and nonfatal myocardial infarction (CD/MI). The incremental prognostic value of SPECT-MPI was examined over the CRF in nested adjusted Cox regression models.

Results: A total of 3,216 (mean age 60±11 years, 60% males) were included in this analysis. Over a median follow-up of 5.5 years (25th to 75th percentiles, 3.7–6.9 years), 150 (4.7%) patients experienced CD/MI. Using Cox regression, both CRF and MPI were independent predictors of outcomes (figure). In addition, both CRF (model area under the curve 0.733, (95% CI, 0.693–0.772) vs 0.705, (95% CI, 0.663 – 0.746), p=0.049) and SPECTMPI (0.741, (95% CI, 0.699 – 0.783) vs 0.704, (95% CI, 0.662 – 0.746), p=0.002) improve prediction of CD/MI beyond conventional risk factors. However, SPECTMPI added incremental prognostic value over CRF in predicting CD/MI (0.732, (95% CI, 0.693–0.772) vs 0.757, (95% CI, 0.716 – 0.797), p=0.0114) while CRF did not add over MPI.

Conclusions: While both SPECT-MPI and CRF are independent predictors of major cardiac event, SPECT MPI adds incremental prognostic value of the CRF.

P4078 | BEDSIDE
Known coronary artery disease modifies the prognostic significance of mild stress-induced myocardial ischemia: insights from the BASEL VIII study
N. Schaerli1, C. Puelacher1, U. Honegger1, R. Twenerbo1,2, M. Wagener1, G. Pretre1, M. Zellweger2, D. Wild3, S. Osswald2, C. Mueller2. 1 University Hospital Basel, Cardiovascular Research Institute, Basel, Switzerland; 2University Hospital Basel, Department of Cardiology, Basel, Switzerland; 3University Hospital Basel, Division of Nuclear Medicine, Basel, Switzerland

Introduction: Myocardial perfusion imaging (MPI) is used to detect and determine the extent of stress-induced myocardial ischemia. Patients are referred to MPI for varied reasons, including clarification of suspected coronary artery disease (CAD), risk stratification ahead of large operations and evaluation of Known CAD ahead of possible interventions. Clinical decisions are partly based on the MPI results, especially the so-called summed difference score (SDS). But there is no consensus on the SDS cut-off to differ between clinically relevant and non-relevant stress-induced myocardial ischemia. It is unclear if the same cut-off is applicable to patients with and without known CAD. Therefore, we compare two commonly used cut-offs, by demonstrating patient characteristics and outcomes.

Methods: In this prospective observational study, we enrolled consecutive patients referred to single-photon emission computer tomography (SPECT) myocardial perfusion imaging (MPI) to detect stress-induced myocardial ischemia. The images were scored semi quantitatively using a 17-segment model with a 5-point scale. Summed stress score (SSS) and summed rest score (SRS) were calculated by adding the scores of the 17 segments in the stress and rest images. SDS was derived as the difference between stress and rest scores. Depending to the SDS, we assigned all the patients in one of three groups: SDS 0 to 1 (no ischemia), SDS 2 to 3 (mild ischemia), SDS 4 or higher (moderate ischemia). Patients were followed for 720 days for the occurrence of acute myocardial infarction (AMI) and death.

Results: We included 3052 patients into this analysis. 1911 (62.6%) patients met the criteria for the no, 296 (9.7%) for the mild, and 845 (27.7%) for the moderate ischemia group. In the no ischemia group 101 (5.3%) reached the combined endpoint (all-cause death and AMI), in the mild ischemia group 29 (9.5%) reached the combined endpoint. In the moderate group 115 (13.6%) reached the combined endpoint. Multivariate cox-regression analysis showed an interaction of SDS group and known CAD (p=0.015). In the following subgroup analysis, in patients without known CAD, mild ischemia was associated with a hazard ratio (HR) of 2.94 (1.35–6.38; p=0.006) compared to no ischemia for the combined endpoint but a similar HR as moderate ischemia (HR 2.94 vs HR 3.18, p=0.837). In patients with known CAD, mild ischemia was associated with a non-significant HR compared to no ischemia for the combined endpoint (HR 1.22 [0.73–2.02], p=0.448) but a significant HR of 1.86 (1.13–3.06; p=0.015) compared to moderate ischemia.

Conclusions: While both SPECT-MPI and CRF are independent predictors of major cardiac event, SPECT MPI adds incremental prognostic value of the CRF.

P4079 | BEDSIDE
Diagnostic performance of the cadmium-zinc-telluride SPECT system using low-dose technetium-99m with a short-scan time as assessed by fractional flow reserve
S. Hida, T. Chikamori, J. Yamashita, H. Koshino, N. Murata, Y. Igarashi, C. Shibata, T. Saitoh, K. Hirose, A. Yamashina, Tokyo Medical University, Tokyo, Japan

Background: Although low-dose stress myocardial SPECT using the cadmium-zinc-telluride (CZT) camera is reported to show adequate image quality, few studies evaluate its diagnostic accuracy with short-scan time as assessed by fractional flow reserve.

Methods: We prospectively evaluated 103 consecutive patients with suspected or known CAD with low-dose stress/rest (technetium-99m radioisotopes 185/370MBq) SPECT using Discovery NM 530c. Image scan time was 10 min for stress and 6 min for at rest (Image-1). Subsequently, images were reconstructed to evaluate shorter scan time (Image-2: 6 min for stress and 4 min for at rest). Each SPECT image was assessed with a 17 segment model using a 5-point scoring system. For each coronary territory, a regional stress score, rest score and difference score (DS) were calculated, and regional DS >1 was defined as myocardial ischemia. Within 3 months, CAG was performed; FFR was measured if intermediate coronary stenosis was observed. A significant stenosis was defined as ≥90% diameter narrowing on visual estimation, or as a lesion with <90% and ≥50% stenosis and FFR <0.80.

Conclusion: A different SDS cut-off should be considered for patients with CAD compared to patients without previously known CAD.

Acknowledgement/Funding: Swiss National Science Foundation, Swissheart Foundation, University Basel, University Hospital Basel
Results: Among 103 patients, 59 patients (57%) had intermediate lesions in at least one of the 3 major coronary arteries. As for per-vascular analysis, 94 coronary vessels out of the 309 coronary arteries were regarded to have intermediate lesions and were measured with myocardial FFR. To detect individual coronary stenosis, Image-1 showed respective sensitivity, specificity and accuracy of 83%, 71%, 79% for LAD, 71%, 71% for LCX, 82%, 70%, 75% for RCA stenosis, whereas Image-2 had higher sensitivity and accuracy without loss of specificity (relative specificity, sensitivity and accuracy of 91%, 68%, 83% for an LAD, 74%, 72%, 73% for an LCx, and 90%, 78% for an RCA stenosis, respectively).

Conclusions: These results suggest that further reduction of scan time such as 6-min for stress and 4-min for at rest, may be possible, even using low-dose technetium-99m of 555 MBq.

P4080 | BEDSIDE
Sensitive detection of relapsing cases in Takayasu arteritis by 18F-fluorodeoxyglucose-positron emission tomography/computed tomography
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Background: The clinical value of 18F-fluorodeoxyglucose (FDG)-positron emission tomography (PET) /computed tomography (CT) for diagnosing Takayasu arteritis (TA) has been elucidated. However, clinical evaluation of disease activity is often difficult in TA patients with receiving immunosuppressive treatment.

Purpose: The aim of this study is to evaluate whether the maximum standard-impacted value (SUVmax) of FDG-PET/CT provides a quantitative indication of disease activity in TA cases.

Methods: Seventy-three TA patients and 40 control subjects without arteritis who underwent FDG-PET/CT were enrolled. Active patients with or without corticosteroid or immunosuppressive therapy and inactive patients were defined according to National Institutes of Healthcare criteria. Active patients under the therapy were defined as relapsing cases. Biomarkers including C-reactive protein (CRP) and Erythrocyte Sedimentation Rate (ESR) were measured. Focal uptake lesions in arterial wall of aorta and its major branches were assessed and SUVmax was measured. SUV-mean in inferior vena cava was also measured for calculating target to background ratio (TBR).

Results: Positive FDG uptake in arterial wall was seen in 78.7% of TA patients and 66.1% lesions with the positive uptake was observed in ascending aorta, aortic arch or left subclavian artery. The SUVmax was significantly higher in active than inactive cases and controls (active (n=58), 2.8±0.7 vs. inactive (n=18), 1.9±0.2; control (n=40), 1.8±0.2; p < 0.001 each). Given a SUVmax cut-off of 2.1, sensitivity for active-phrase TA was 90.9%, specificity 87.9%, positive predictive value 87.7%, and negative predictive value 91.1%. Area under the curve (AUC) of CRP and ESR were 81.8% and 76.0% respectively, on the other hand, AUC of SUVmax and TBR were 91.0% and 88.7%. The SUVmax in relapsing cases was also higher than inactive and control cases (relapsing (n=31), 2.7±0.7 vs. inactive, control; p < 0.001 each). In relapsing cases, AUC of CRP was 74.7%, however SUVmax was 90.1%.

Conclusion: The SUVmax is useful for assessing disease activity of TA with high sensitivity. FDG-PET-CT plays a crucial role for detection of active inflammation in not only patients with active TA before treatment, but also in relapsing patient under receiving immunosuppressive agents.

P4081 | BEDSIDE
Analysis of left ventricular synchrony and coronary flow reserve in myocardial ischaemia: a study with 13N-ammonia gated PET
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1 National Institute of Cardiology Ignacio Chavez, Mexico City, Mexico; 2 University Medical Center Groningen, Groningen, Netherlands

Background: Intraventricular dysynchrony of the left ventricle (LV) can lead to impaired systolic function and increased wall stress. Gated positron emission tomography (PET) constitutes a validated tool to evaluate ventricular synchrony based on phase analysis. Standard deviation (SD) and entropy (E) have shown the best reproducibility and a relationship with perfusion status has been proposed. Moreover, PET allows for improved image acquisition along with absolute quantification of coronary blood flow (CBF) and flow reserve (CFR). Therefore, the aim of this study was to evaluate the relationship between PET-measured LV synchrony and myocardial perfusion through semi-quantitative and quantitative analysis with 13N-ammonia gated PET in patients with ischaemic heart disease.

Methods: 175 consecutive patients who underwent rest/stress 13N-ammonia PET for suspected myocardial ischaemia were included. Change in SD and E between rest and stress, as well as a stratified comparison according to the severity of myocardial ischaemia determined by summed stress score (semi-quantitative analysis) and CFR (quantitative) was made through parametric statistical testing.

Results: Results are summarized in Table 1. We found an increase in SD between rest and stress with severe ischaemia (p < 0.008). On the other hand, E showed significant differences between rest and stress in all groups, showing that ventricular synchrony deteriorates as ischemia worsens, with an inverse correlation with the CFR. This suggests that Entropy may partially reflect myocardial stunning during induced ischaemia in gated PET-MPI.

Conclusion: Phase analysis of gated PET-MPI allows the evaluation of LV global dys synchrony. Phase Entropy is significantly different between rest and stress, this difference increases with increasing severity of ischaemia, with an inverse correlation with the CFR. This suggests that Entropy may partially reflect myocardial stunning during induced ischaemia in gated PET-MPI.
Atherosclerotic plaque molecular imaging with 18F-sodium fluoride (NaF) in positron emission tomography with computed tomography (PET-CT) provides insight on its calcification activity. In particular, there is potential discrimination between active unstable microcalcification (spotty calcification targeted by 18F-NaF) and established dormant calcification (macrocalcification on CT).

We aimed to study 18F-NaF atherosclerotic plaque uptake in high cardiovascular (CV) risk subjects and its association to standard risk factors and coronary artery calcium score.

**Methods:** High CV risk hypertensive individuals according to the European Society of Cardiology Guidelines from a single centre were prospectively selected and scanned with 18F-NaF-PET-CT in the coronary, aortic and carotid arteries. Atherosclerotic plaque 18F-NaF uptake was assessed as Corrected Uptake Per Lesion (CUL): maximum standard uptake value in each vascular territory subtracted by mean pool activity in the superior vena cava. We studied 18F-NaF uptake distribution per vascular territory and its association with coronary artery calcium score. Data is expressed as mean ± standard deviation or median (interquartile range) according to the normality of the distribution.

**Results:** Mean age is 64 years, 56% male and 96% Caucasian (n=25). All patients are hypertensive. 72% with hyperlipidaemia, 52% obese and 24% with chronic kidney disease. Ninety six per cent of the subjects show 18F-NaF uptake in the aorta (CUL 0.85±0.30), 40% in the carotid arteries (CUL 0.00, 0.00–0.73) and 64% in the coronary arteries (CUL 0.44, 0.00–0.63). Individuals with five or more CV risk factors (60%) have increased overall 18F-NaF uptake (CUL 1.05±0.31 vs 0.68±0.28, p<0.01). Furthermore, there is a positive correlation between maximum 18F-NaF uptake and 10-year expected CV risk assessed by SCORE (r=0.49, p<0.01). Median coronary calcium score is 0.0 (0.0–11.0). Of the 16 individuals with calcium score between 0 and 10 (17 with score <0), 13 feature significant 18F-NaF uptake in the coronary arteries. Three of the five subjects with calcium score between 11 and 100 have significant 18F-NaF uptake. Only one of the remaining two individuals with calcium score over 100 shows 18F-NaF uptake. Thus, there is no correlation between 18F-NaF uptake in the coronary arteries and calcium score (p=0.87) in an original study in a high CV risk population.

**Conclusion:** In a high CV risk group without manifest CV disease, 18F-NaF atherosclerotic plaque uptake is related to the burden of CV risk factors but there is no association between coronary artery uptake and calcium score, possibly due to the identification of different pathophysiological stages in the atheroma calcification process.

**COMPLICATIONS OF HYPERTENSION**

**P4084 | BEDSIDE**

Low testosterone and high C-reactive protein are complementary determinants of global arterial function and early structural changes in men with arterial hypertension

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**Purpose:** Arterial functional and structural characteristics are important determinants of cardiovascular performance and predictors of risk in patients with arterial hypertension. Low androgen level and low-grade inflammation may be contributing factors to atherosclerosis process and cardiovascular disease. We investigated whether low testosterone and high C-reactive protein (CRP) levels are complementary determinants of global arterial function and early structural changes in hypertensive men.

**Methods:** We evaluated arterial structural and functional characteristics (carotid-femoral pulse wave velocity (PWV), augmentation index (AIx), flow-mediated dilation (FMD) of the brachial artery and penile peak systolic velocity (PSV)) and we measured high sensitivity CRP and total testosterone (TT) levels in 167 men (mean age 56±7 years) without manifest cardiovascular/atherosclerotic disease. Low penile PSV indicates severe penile vascular disease and increased risk of major cardiovascular events.

**Results:** In multivariable models, both CRP and TT are significantly correlated with brachial FMD, penile PSV, carotid-femoral PWV and AIx. The distribution of CRP was split by the median (1.85 mg/l) and accordingly subjects were stratified into those with high and low level. All patients were then categorized by CRP level and further subdivided according to presence/absence of testosterone deficiency (TT <3.5 ng/ml). The subgroup of hypertensive patients with high CRP/low TT (n=41) exhibited significantly lower age and systolic blood pressure-adjusted brachial FMD and penile PSV (figures A-B) and higher PWV, AIx (figures C-D) as compared with the subgroups of high CRP/high TT, low CRP/low TT and low CRP/high TT (overall P<0.01, by ANCOVA).

**Conclusions:** The association between the arterial stiffness and serum calcium levels compared with age. Pathophysiological abnormalities related to increased serum calcium levels appeared to be associated with accelerated progression of arterial stiffness with age.

**P4085 | BEDSIDE**

Longitudinal changes of the serum calcium levels and accelerated progression of arterial stiffness with age

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**Background and aims:** The progression of arterial stiffness is accelerated by aging, although the underlying mechanisms have not yet been clarified. This prospective observational study was conducted to clarify whether longitudinal changes in the serum calcium/phosphate levels are associated with the accelerated progression of arterial stiffness with age.

**Methods:** In a cohort of employees at a construction company (1507 middle-aged Japanese men), the serum calcium/phosphate levels and brachial-ankle pulse wave velocity (baPWV) were measured at the start and at the end of a 3-year study period.

**Results:** A general linear model multivariate analysis revealed a significant interaction of the 2 factors (age and longitudinal changes of the serum calcium levels) on increasing progression of arterial stiffness (measured by baPWV) during the study period (dePWV). The deCa was significantly correlated with the delPWV even after adjustments for covariates in subjects aged >48 years. The delPWV in subjects aged <48 years with the delCa in the upper tertile (69±137 cm/sec) was significantly larger than in the other groups even after adjustments for covariates (e.g., del PWV in subjects aged <48 years with the delCa in the lower tertile was 1±94 cm/sec) (p<0.01).

**Conclusions:** In essential hypertensive men pronounced subclinical inflammation in conjunction with low androgen level exert an additive unfavourable effect on arterial function and structure. This finding underlines the important role of TT and CRP as markers of arterial damage, and implies a synergistic role of these compounds to the pathophysiology of cardiovascular disease in hypertensive males.
P4086 | BEDSIDE

Angiotensin receptor-1 antagonists improve endothelial glycocalyx and aortic stiffness after 2 years successful treatment in untreated patients with essential hypertension

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Background: Aortic stiffness is considered a valuable index of subclinical damage in hypertensive patients offering to cardiovascular risk estimation. The integrity of endothelial glycocalyx plays a vital role in vascular permeability, inflammation and elasticity. We aimed to explore any changes in aortic stiffness as well as in endothelial glycocalyx during repeated evaluations in controlled patients with essential hypertension.

Methods: We studied 78 patients with newly diagnosed and never treated essential hypertension (mean age 48±10 years, 59 males). At baseline, we performed carotid-femoral artery pulse wave velocity (PWV) in order to evaluate aortic stiffness. Increased perfusion boundary region (PBR) of the sublingual microvessels (ranged from 5-25 micrometers) using Sideview Darkfield imaging was measured as a non-invasive accurate index of reduced endothelial glycocalyx thickness. All patients started antihypertensive treatment with calcium blockers (CaB), sartans (ARBs) or their combination (Combo) and they repeatedly re-evaluated at 3 months intervals in a period of 24 months. Each patient had two four-evaluations, totally.

Results: Thirty-four patients (44%) were re-evaluated at 6, 12, 18 months (Group 1), 17 patients (22%) at 12, 18, 24 months (Group 2), 8 patients (10%) at 18 and 24 months and finally 15 patients were evaluated at 24 months (Group 4). Blood pressure (BP) was controlled, defined as <140/90 mmHg, in 20 (59%), 31 (80%), 27 (75%) and 32 (78%) patients at 6, 12, 18, 24 months, respectively. Regarding patients with controlled BP and compared to baseline evaluation, we found that: a. at 6 months re-evaluation, PWV (10.8±2 vs. 11.7±2.4 m/sec, p<0.05), PBR 5-25 (1.9±0.2 vs. 2.1±0.3 mm, p<0.05) and PBR 20-25 (2.3±0.4 vs. 2.7±0.5 mm, p=0.02) decreased, b. at 12 months re-evaluation: PWV (10.5±2 vs. 11.7±2 m/sec, p=0.006) decreased and c. at 24 months re-evaluations: PWV (10.9±3 vs. 11.9±3 m/sec, p<0.05), PBR 5-25 (1.9±0.3 vs. 2.1±0.2 mm, p<0.05), PBR 10-19 (2.1±0.2 vs. 2.2±0.3 mm, p<0.05), PBR 20-25 (2.4±0.4 vs. 2.6±0.3 mm, p<0.01) decreased. Finally, we concluded that the ARBs (alone or combined with CaB) compared with CaB, better improved PWV (p<0.04), PBR 20-25 (p<0.05), PBR 10-19 (p<0.05) and PBR 20-25 (p<0.05) at 24 months in controlled hypertensive patients.

Conclusions: Cardiovascular risk reduction in hypertensives is based not only in blood pressure decrease but also in target organ damage improvement. This is the first study showing the parallel improvement of aortic stiffness and endothelial glycocalyx in well controlled hypertensives under ARBs in sequential evaluations lasting for two years. Further studies are needed to confirm our results and possibly establish endothelial glycocalyx measurement as a novel index regarding cardiovascular risk estimation.

P4087 | BEDSIDE

Evaluation of coronary flow velocity by Doppler echocardiography in the treatment of hypertension with the ACEI/ARB: correlation to the histological cardiac fibrosis

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Background: Coronary flow velocity (CFV) is markedly reduced in cardiac hypertrophy and believed to reflect cardiac fibrosis. However, the clinical reliability of CFV by pulsed-wave Doppler echocardiography in the evaluation of patients with hypertensive cardiomyopathy remains indeterminate.

Purposes: In this translational study, we investigated the applicability of CFV in both human and murine hearts under pressure overload.

Methods: In this longitudinal, prospective study, we enrolled hypertensive patients with no evidence of coronary artery disease. Before and after 12 weeks of ACEI/ARB treatment, Doppler echocardiography derived CFVs were calculated. Also, using aortic banding, we developed pressure overload model in 8-10 week old male C57BL/6 mice. Post 7 days, the banding was performed to mimic the treatment. Serial echocardiography including CFV was followed.

Results: Post treatment, the average CFV and diastolic filling pressure (E/e') in hypertensive patients improved significantly but remained lower compared with the CFV in normotensive subjects. The changes were not observed in left ventricular ejection fraction, left ventricular mass index or left ventricular end diastolic volume. Likewise, compared with the CFV in aortic banded mice, the CFV increased significantly post banding. In addition, the systolic/diastolic flow ratio immediately increased after surgery but returned to the baseline post banding, similar to the change of fibrosis areas under Masson Trichrome stain.

Conclusions: These results indicate that hypertensive patients at the early stage show decreased CFV despite having normal resting flow. Treatment with an ACEI/ARB for 12 weeks improved CFV. CFV is a reliable parameter to evaluate the early cardiac dysfunction and the subsequent cardiac fibrosis.

P4088 | BEDSIDE

Testosterone loss as essential parameter of silent target organ damage in primary hypertension

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Background: Testosterone levels lessen in essential hypertension male patients (normotension as a control group) on a similar age. Assessment of hypotension related asymptomatic target organ damage (TOD) is fundamental for any further therapeutic decision.

Purpose: To investigate any association between testosterone levels and TOD in hypertensive male population.

Methods: 127 hypertensive men (aged 55±9 years) without any history of cardiovascular disease underwent 2D echocardiography evaluation of left ventricle mass index (LVMI), ultrasound carotid intima–media thickness (IMT) and carotid-femoral pulse wave velocity measurement (PWV). All patients were screened for microalbuminuria defined as urinary albumin/creatinine ratio >3.9 mg/g on 24 hours urine collection specimen. Total testosterone (TT) levels were measured in all patients. Testosterone deficiency (TD) is considered when TT <3.5 ng/ml.

Results: 33 (26%) patients were identified with TD. Compared to patients with normal TT levels, they were older (59±5 vs 53±7 years), with higher systolic blood pressure (140±15 mmHg vs 132±10 mmHg) and a greater prevalence of diabetes (35 vs 18%), (all P<0.05). Furthermore, TD patients had higher LVMI index, carotid IMT, PWV and a greater prevalence of microalbuminuria (Table). The association remained significant in multivariate analysis after adjustment for age and BP level.

Conclusion: Testosterone deficiency is associated with indices of target organ damage in asymptomatic hypertensive males. These findings may provide clinical information and insights into pathophysiology of low testosterone and its prognostic role in essential hypertension.

P4089 | BEDSIDE

The association between cognitive decline and blood pressure in elderly patients with controlled hypertension

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Introduction: Structural and functional brain alterations are associated with normotensive studies in animal models of hypertension (HT) and in hypertensive patients indicate that HT could accelerate brain aging. Although there has been considerable research with regards to the impact of HT on cognition, these studies usually compare untreated-HT subjects to treated-HT subjects. While untreated-HT subjects have been reported to perform worse in cognitive tests than treated-HT, data comparing treated-HT and normotensive subjects are still scarce. Therefore, there is a need to understand better how blood pressure (BP) below the actual hypertensive threshold, affects specific cognitive processes like executive functions, to determine whether HT subjects can perform as well as normotensive subjects, while treated.

Purpose: The objective of this study was to assess cognitive performance in older adults treated and controlled for blood pressure when compared to untreated normotensive subjects, and to determine whether blood pressure still correlates with poorer cognitive performance.

Methods: Forty-eight older adults aged between 65 and 85 years were recruited in the community and divided into two groups: normotensive (n=26) and controlled hypertensive (n=22). Each participant underwent a neuropsychological assessment that targeted memory, attention, language and executive functions. Ambulatory blood pressure monitoring (24 hours) as well as a blood test (Na+, K+, Ca++, blood creatinine, glucose, triglycerides, thyroid function) were performed. One-way ANOVAs were conducted on each neuropsychological measure with group (normotensive vs. hypertensive) as a between-subject factor. Pearson correlations were also performed to examine the relationship between blood pressure parameters and cognitive performance.

Results: Results from the ANOVAs revealed a significant difference between groups on response times in the switching condition of the Colour-Word Interference Test (CWIT), with controlled hypertensive patients performing worse than their normotensive counterparts. The analysis also demonstrated significant positive correlations (p<0.05) between the percentage of systolic blood pressure
SBP day values over 135 mmHg (% SBP day > 135 mmHg), and a number of conditions like, the switching cost from the CWIT, and the Trail Making Test Part B (TMTB). The switching conditions (e.g., TMTB), as well as the switching cost (difference in the reaction time between repetitive, and switching tasks), both assess cognitive flexibility, which is an executive function that relies heavily on prefrontal lobe integrity. Incidentally, these mechanisms have been reported as good predictors of cognitive decline and dementia in older adults.

The goodness-of-fit of the linear relationship between BP and hypertensive cardiovascular damage induced by progressively adding sitting, awake, nighttime home, and ambulatory blood pressures.

Table 2. The change in the goodness-of-fit of the linear relationship between BP and hypertensive cardiovascular damage induced by progressively adding sitting, awake, nighttime home, and ambulatory blood pressures.

<table>
<thead>
<tr>
<th>Group</th>
<th>Change in SBP</th>
<th>Change in DBP</th>
<th>Change in Sitting</th>
<th>Change in Wake</th>
<th>Change in Peak</th>
<th>Change in Mid</th>
<th>Change in Night</th>
<th>Change in Home</th>
<th>Change in Amb</th>
<th>Change in P value for the Change in Model</th>
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<td>SBP</td>
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<td>LAVI</td>
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P4090 | BEDSIDE
Home versus ambulatory blood pressure in prediction of the risk of hypertensive cardiovascular damage

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Background: Home (HBP) and ambulatory blood pressure (ABP) are better predictors of target organ damage (TOD) than clinic BP measurement. We evaluated whether home BP monitoring was associated with hypertensive TOD more closely.

Methods: Taiwan hypertension associated cardiac disease consortium included 11 Taiwan medical centers and enrolled hypertensive patients with/without previous medical treatment. For the 740 participants with cardiovascular risk factors, we measured clinic BP, ABP monitoring (24-h) and HBp monitoring during daytime and night-time (automated asleep measurements, three nights, 3-hourly measurements/night). Target organ damage was assessed by echocardiographic left ventricular mass index (LVMI), left atrium volume index (LAVI), and carotid-femoral pulse wave velocity (PWV).

Results: Complete data were collected in a total 561 study participants (mean age 65.0±10.8 years; men 61.3%). Daytime and night-time HBP were slightly higher than the respective ABP values (difference for systolic daytime/night-time 7.3±14.2/11.3±18.5 mmHg, P < 0.001; for diastolic 5.4±9.7/4.7±12.1, P < 0.001).

The goodness of fit of the association between SBP and LVMI was significant greater than that for relation between ABP and PWV (p=0.045). Complete revascularization was not associated with mortality using Cox regression and inverse probability treatment weighted (IPTW) analyses.

Complications of hypertension / New aspects on PCI

P4091 | BEDSIDE
Prognostic significance of incomplete revascularization and bystander coronary anatomy following percutaneous coronary intervention: an observational study of 6,751 patients with multivessel disease

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Background: More than 50% of patients undergoing percutaneous coronary intervention for all indications have angiographic evidence of multivessel disease. Whether or not complete revascularisation impacts long-term mortality, or whether select patient subgroups or patients with specific coronary anatomy may derive benefit from complete revascularization is unclear.

Methods: A total of 14,452 patients underwent PCI between 2004–2015 at Harefield Hospital, UK. Of these, 7,076 patients had multivessel disease (defined as coronary stenoses ≥70% in ≥2 epicardial coronary arteries), and 337 patients had left main-stem stenosis ≥50% were excluded. A total of 6,751 patients were included in the final analysis. We analyzed all-cause mortality at 3 years and performed stratified analyses for untreated coronary anatomy using Cox regression and inverse probability treatment weighted (IPTW) analyses.

Results: Of the 6,751 patients, 2336 patient had STEACS, 1,295 patients had NSTEMACS, and 3,127 patients had stable disease. A total of 936 patients had complete revascularisation. Patients undergoing complete revascularization were younger; more likely to have stable disease; less likely to present with STEACS; less likely to have diabetes; and less likely to have severe left ventricular function. In the 5,819 patients who had complete revascularisation, 3,486 patients (60%) had bystander LAD disease; 1,791 patients (31%) had bystander proximal LAD disease; 2,695 patients (46%) had bystander LCX disease; and 2,550 patients (44%) had bystander RCA disease. The unadjusted 3-year mortality rates were lower with complete revascularization (10.8% vs. 13.1%, p=0.047).

Complete revascularization was not independently associated with mortality using Cox regression analyses (HR=1.01, 95% CI 0.78–1.31, p=0.939) and IPTW analyses (HR=1.01, 95% CI 0.77–1.33, p=0.950). Complete revascularization was not associated with mortality in subgroup analyses for age, diabetes, cardiogenic shock and indication for procedure. When performing stratified analyses within anatomical subsets of bystander coronary disease, there was no association with the presence of untreated LAD disease (HR=0.90, 95% CI 0.77–1.17, p=0.482) and untreated LCX disease (HR=0.90, 95% CI 0.74–1.10, p=0.999). However, the presence of untreated proximal LAD disease (HR=1.23, 95% CI 1.06–1.51, p=0.045) and untreated RCA disease (HR=1.36, 95% CI 1.08–1.65, p=0.007) was independently associated with increased mortality. These findings were confirmed in IPTW analyses.

Conclusions: In this real world all-comers analysis of patients undergoing PCI, incomplete revascularisation was not associated with long-term mortality. However, the presence of untreated proximal LAD and RCA disease was an independent predictor of long-term mortality. This study suggests that complete revascularisation may be more effective for select patient groups with anatomical subsets of coronary disease.
P4093 | BEDSIDE
Outcomes of a novel abluminal bioabsorbable versus durable polymer-coated everolimus-eluting stent in complex patients and coronary artery disease

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Background: There are currently no reports of outcomes in patients with coronary artery disease (CAD), presenting with complex clinical and angiographic characteristics, treated with Synergy, a newer generation bioabsorbable polymer-coated everolimus-eluting stent.

Aim: To investigate the impact of clinical and angiographic complexity on outcomes in patients treated with intravascular polymer everolimus-eluting coronary stents as compared to durable-polymer everolimus-eluting Xience stents.

Methods: 2,001 consecutive patients were treated with Synergy (n=400) or Xience (n=1601) stents between May 2013 and May 2015 in two Italian centers. The propensity-score matching was used to assemble a patient cohort with similar baseline characteristics. The study population was stratified into “complex” and “simple”. 1-year outcomes, (major adverse cardiac events (MACE), defined as all-cause death, myocardial infarction, and target lesion revascularization (TLR)) were assessed.

Results: Among the 684 patients identified after matching, 433 (63.2%) were complex and treated with Synergy (n=213) or Xience (n=220). At 1-year follow-up, rates of MI (0.9% vs. 0.5%, p=0.630), and stent thrombosis (0.0% vs. 0.0%) were similar between complex and simple patients. Major adverse cardiac event rates were lower in the complex population (13.1% vs. 2.5%, p<0.001), mainly driven by higher rate of target lesion revascularization (5.6% vs. 0.5%, p=0.009), and death (5.6% vs. 1.5%, p=0.043). Among complex patients major adverse cardiac event rate was 13.0% vs. 13.1% (p=0.929) between Synergy and Xience group. Death, MI, stent thrombosis, and new lesion revascularization rates, stratified for complexity, resulted similar between both stents at 1 year.

Clinical outcomes at 1 year stratified for complexity and type of stent

<table>
<thead>
<tr>
<th>Synergy (n=213)</th>
<th>Complex (n=433)</th>
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</thead>
<tbody>
<tr>
<td>Synergy (n=213 pts)</td>
<td>Xience (n=220 pts)</td>
</tr>
<tr>
<td>MI, % (CI)</td>
<td>0.0</td>
</tr>
<tr>
<td>Death, % (CI)</td>
<td>0.9 (0.1–6.8)</td>
</tr>
<tr>
<td>Stent thrombosis, % (CI)</td>
<td>5.4 (1.4–19.0)</td>
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</table>

Conclusion: The novel Synergy stent appears to be safe and effective, regardless of “complex” baseline and angiographic characteristics.

P4094 | BEDSIDE
Long term clinical results of percutaneous coronary intervention for chronic total occlusions: Latest report from Retrgrade Summit Registry

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Background: Retrgrade Summit Registry has been underway since 2012 to investigate clinical results of percutaneous coronary intervention (PCI) to treat chronic total occlusions (CTO).

Methods: Total 3229 of eligible subjects who received CTO-PCI were enrolled using web based registration system between January 2012 and December 2013 from 56 centres in Japan. Among those cases, 1995 of 1 year follow-up data were collected.

Results: The main results are as follows: mean age was 67±10.4, 274 (8.6%) cases have CABG history and 10.1% were previously failed CTO cases. 2201 (68%) cases were treated by antegrade approach, 569 (18%) cases were treated by retrograde approach and both techniques were used for 459 (14%). The mean success rate of CTO-PCI was 1.5±0.7. The procedure success was achieved in 84.4%, clinical success was 88.1%. Compared with subjects failed CTO-PCI, procedure success group showed lower rates of in-hospital cardiac death (0.07% vs. 0.53%, p=0.017), emergent CABG (0% vs. 0.53%, p=0.0001). Major adverse cardiac and cerebrovascular events (MACCE) free rate at follow-up also lower than failed group (3.31% vs. 8.39%, p=0.002). Independent predictors of MACCE at 1 year follow-up were LVEF≤35% (OR: 0.39; 95% CI: 0.18 to 0.90; p=0.029) and not to use Drug Eluting Stent (OR: 0.26; 95% CI: 0.12 to 0.59; p=0.002).

Conclusion: In our multicentre registry of 3229 CTO cases, high success rate and low MACCE rate were obtained. The result shows the safety and feasibility of both in-hospital and long term of CTO-PCI.

P4095 | BEDSIDE
Application of the DAPT score to the results of the OPTIDUAL trial: is it a useful tool to identify the best candidates for extended DAPT after DES?

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Background: Identifying patients who benefit from extended dual antiplatelet therapy (DAPT) following drug-eluting stents is an important topic. The DAPT score may help clinicians decide who should be treated with extended DAPT.

Methods: The OPTIDUAL randomized trial has tested whether, on a background of aspirin, continuing clopidogrel was superior to stopping clopidogrel at 12 months following DES implantation. Median follow up after stenting was 33.4 months. The DAPT score, composed of eight clinical factors, was applied to 1385 patients randomized in OPTIDUAL.

Results: The primary outcome in OPTIDUAL, i.e net adverse clinical events defined as the composite of death, myocardial infarction, stroke, or major bleeding, was analyzed according the DAPT score. The analysis of the patients divided in quartile showed the best outcome with prolonged DAPT when the DAPT score is 0 to 4.

Conclusion: The results of the OPTIDUAL trial show the potential value of the DAPT score derived from the very large DAPT trial.
P4096 | BEDSIDE
Long-term clinical outcomes after the treatment with two-stent techniques using second generation drug-eluting stents for coronary bifurcation lesions

Background: In the treatment of coronary bifurcation lesions, two-stent techniques using first generation drug-eluting stents (G1-DES) are prone to cardiac vascular events.

Purpose: To assess the long-term outcomes of coronary bifurcation lesions treated with two-stent techniques using second generation drug-eluting stents (G2-DES) in comparison with G1-DES.

Methods: The study sample consisted of 1021 patients treated with two-stent techniques using either G1-DES (502 patients, G1-DES group) or G2-DES (519 patients, G2-DES group) between 2004 and 2014. The primary endpoint was defined as target lesion revascularization (TLR). Cumulative rates were estimated by the Kaplan-Meier method and compared by the log-rank test. Cox proportional hazards models were estimated for predictors of TLR.

Results: The median follow-up duration was 4.7 years (the first and third quartiles, 2.6 and 6.9 years). Between the G1-DES and G2-DES groups, the 5-year cumulative rates were not significantly different in all-cause death (21.9% vs. 21.0%, log-rank p=0.85), cardiac death (6.0% vs. 8.7%, log-rank p=0.20), and definite or probable stent thrombosis (3.1% vs. 1.4%, log-rank p=0.24), except for that of TLR, which was significantly higher in the G1-DES group than in the G2-DES group (23.0% vs. 11.0%, log-rank p<0.001) (Figure). After adjustment for confounders, the excess relative risk of TLR was also significantly higher in the G1-DES group (hazard ratio [HR], 1.90; 95% confidence interval [CI], 1.30 to 2.78; p<0.001). Other independent predictors of TLR were diabetes (HR, 1.73; 95% CI, 1.28 to 2.34; p<0.001), hemodialysis (HR, 3.21; 95% CI, 1.88 to 5.47; p<0.001), and long side branch lesions (HR, 1.94; 95% CI, 1.15 to 3.28; p=0.01).

Conclusion: Two-stent techniques using G2-DES, compared with those using G1-DES, significantly reduced the TLR rate in the long term, showing no significant differences in death and stent thrombosis.

ANTITHROMBOTIC THERAPY IN ATRIAL FIBRILLATION 1

P4097 | BEDSIDE
Atrial fibrillation in haemodialysis patients without a vitamin K antagonist: Insight from the RAKUEN study
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Background: Bridging regimen in stable non-valvular atrial fibrillation (NVAF) patients with non-vitamin K antagonist oral anticoagulants (NO-VKA) is common even in patients with low stroke risk. However, there is a lack of evidence supporting this practice.

Purpose: To compare haemorrhage and ischemic stroke/systemic embolism (IS/SE) risks between bridged (heparin-VKA) and non-bridged (VKA only) patients.

Methods: A retrospective cohort study was conducted on individuals starting oral anticoagulation with vitamin K antagonist (VKA) in both groups. Bridging therapy was defined as the dispensing of a bridging agent (subcutaneous low-molecular weight heparin, fondaparinux, or subcutaneous unfractionated heparin) concomitantly with a VKA at the time of their initiation. Haemorrhage and IS/SE cases were identified using prespecified algorithms from the hospitalisation database linked to the healthcare insurance databases. The difference between the bridged and non-bridged patients in the occurrence of these outcomes was studied during the first and the two following months of anticoagulation using the Cox proportional hazards models adjusted for comorbidities and comedication.

Results: Of 90,826 patients with a mean age of 72 years and composed of 50% women, 30% had a bridging therapy. A total of 318 (0.35%) had haemorrhage and 151 (0.17%) IS/SE cases occurred during the first month of follow-up and 233 (0.25%) and 122 (0.16%) during the two following months. At one month of follow-up, the incidence of haemorrhage was higher in the bridged group (0.47% versus 0.30%; P=0.0001). After adjustment for covariates, a 60% increased haemorrhage risk in the bridged group was observed compared with the non-bridged group (HR=1.60; 95% CI, 1.28–2.01). Differences in both groups disappeared after one-month of follow-up (HR=0.93; 95% CI, 0.70 to 1.23). In addition, during the first month of treatment, the association between bridging and haemorrhage risk was stronger in women (HR=2.04; 95% CI, 1.49–2.80) whereas in men a non-significant trend to increased risk was observed (HR=1.26; 95% CI, 0.91–1.75). No significant difference in the occurrence of IS/SE was found either at one month of follow-up or later.

Conclusion: In stable NVAF patients for whom a VKA treatment is indicated, bridging therapy is not beneficial and is even harmful, and thus unnecessary.

P4099 | BEDSIDE
Atrial ablation is associated with increased risk of ischemic stroke in low risk patients with non-valvular atrial fibrillation
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Background: Patients with non-valvular atrial fibrillation (AF) under the age of 65 and CHA2DS2-VASc risk score of 0 point in men or CHA2DS2-VASc of 1 point in women are considered to be at low risk for future ischemic stroke event, that oral anticoagulation therapy is not indicated.

Objectives: To assess the incidence of ischemic stroke and related mortality among low risk patients with non-valvular atrial fibrillation.

Method: A retrospective study of 25,252 low risk non-valvular AF patients (age 65-84) out of total 343,123 AF patients identified from the Swedish nationwide hospital registries for the period between January 01, 2006 to December 31, 2012.

Results: During a mean follow-up of median (q1–q3), 5 (2.9–6.8) years, ischemic
stroke occurred at an annual rate of 3.4 per 1000 patient-years. The overall mortality was 7.5 per 1000 patient-years in patients without ischemic stroke. 29.8 per 1000 patient-years in patients who had suffered an ischemic stroke during follow-up. Significant predictors of stroke using a multivariable analysis were age, Hazard ratio (HR) 95% confidence interval (95% CI) 1.06 (1.05–1.08) p<0.001 and alcohol abuse HR 1.45 (95% CI 0.42–5.79) p<0.001. Use of oral anticoagulants was associated with lower risk for ischemic stroke, HR 0.78 (95% CI 0.63–0.97) p<0.027.

Conclusion: Lower risk for ischemic stroke was associated with lower risk for ischemic stroke, HR 0.78 (95% CI 0.63–0.97) p<0.027.

P4100 | BEDSIDE
Do baseline characteristics account for geographical variations in event rates in patients with newly diagnosed atrial fibrillation? The GARFIELD-AF registry

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Purpose: To define geographical variations in all-cause mortality, stroke/systemic embolism (SE) and major bleeding in patients with newly diagnosed nonvalvular atrial fibrillation (NVAF) and to determine if this variation is accounted for by baseline risk factors.

Methods: Baseline characteristics and 1-year event rates were analysed for 28,622 patients enrolled in Mar 2010 to Oct 2014 in 32 countries. We fitted a two-level mixed Weibull model on patients’ time-to-event nested for each country.

A random intercept for each country was specified and adjusted for variables defined in the figure. To identify country effects greater or less than the mean global event rate, empirical Bayes means of the posterior distribution of the random coefficients were estimated.

Results: Unadjusted rates of stroke/SE averaged 1.37 per 100 patient-years and crude mortality differed by country by approx. 23-fold (0.5–11.4). There were significant differences in baseline characteristics (Table). However, having adjusted for key variables, the geographic variation in stroke/SE, mortality and major bleeding remained significant (p<0.0001 likelihood ratio test comparing the models with the one-level Weibull regression; Fig). Despite risk adjustment we observed lower mortality in Eastern Asia (Japan and Korea) and higher in countries including India and South Africa. Variations in adjusted rates of stroke/SE and bleeding remained and, unexpectedly, these were not concordant with mortality rates for respective countries (Fig).

Conclusion: Baseline characteristics and 1-year event rates were analysed for 28,622 patients enrolled in Mar 2010 to Oct 2014 in 32 countries. We fitted a two-level mixed Weibull model on patients’ time-to-event nested for each country. A random intercept for each country was specified and adjusted for variables defined in the figure. To identify country effects greater or less than the mean global event rate, empirical Bayes means of the posterior distribution of the random coefficients were estimated.

P4101 | BEDSIDE
Death, stroke and major bleeding risk in patients older than 85 years with atrial fibrillation

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Background: Atrial fibrillation (AF) is a major risk factor for stroke and the prevalence increases with age. Oral anticoagulants (OACs) are effective, but are frequently underused in elderly patients, primarily because of concerns about efficacy and safety issues. We examine the treatment and outcomes in a large contemporary cohort of elderly patients with AF older than 75 years, and in the subgroup of patients older than 85.

Methods: A prospective historical cohort study, conducted using the Clalit Health Services Research Institute database, between 2004 and 2011. All patients older than 75 with non-valvular atrial fibrillation (NVAF) were included. We studied patients aged 75–85 and patients older than 85. Primary end-points were all-cause mortality, ischemic stroke and major hemorrhage.

Results: During the study period we identified 17,574 patients aged 85 and older (average age 89±3±3.8, 41% male) and 31,866 patients between the ages of 75–85 (average age 79±5.2±2.8, 46% male) with NVAF. All patients were classified as high-risk for thrombo-embolic events. Mean follow-up was 48.8 months. Only 16.7% of the elderly patients were treated with Warfarin, compared with 30.8% of the patients aged 75–85. Stroke incidence was 6.7% for ages 75–85 and 5.1% over age of 85. Mortality was 69.8% for age–85 and 45.7% for age–75. In multivariate analysis among elderly population Coumadin was a protective predictor for stroke (HR 0.85) and mortality (HR 0.62). Cerebral bleeding incidence was 1.3% among ages 75–75 and 1% for age–85. Gastrointestinal bleeding rates were 3.3% and 2.7%, respectively. Warfarin treatment was neither protective nor protective of intracranial bleeding.

Conclusion: OAC therapy is associated with a positive benefit-risk balance in elderly patients, reduced stroke and increased survival. Irrespective of age, treatment decisions regarding stroke thromboprophylaxis in all patients with AF should be based on individual potential benefits and risks of treatment and patient preferences.

Acknowledgement/Funding: This study was supported by an unrestricted research grant to Clalit Health Services Research Institute from Pfizer Inc.

P4102 | BEDSIDE
Increased use of oral anticoagulants in patients with atrial fibrillation: Nationwide temporal trends in Denmark from 2005 to 2015

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Introduction: The introduction of non-vitamin K antagonist oral anticoagulants (NOAC) has increased awareness of stroke prophylaxis in patients with non-valvular atrial fibrillation (AF). Yet, it is unknown whether more patients with AF are put on oral anticoagulation (OAC) in contemporary practice.

Purpose: To describe temporal trends from 2005 to 2015 in initiation of OAC treatment (vitamin K antagonists (VKA) and NOAC) among a nationwide cohort of patients with newly diagnosed AF in Denmark.

Methods: From Danish nationwide registries we identified patients with newly
diagnosed AF from January 2005 to June 2015. OAC initiation was assessed from prescription fills +/- 180 days from date of AF diagnosis. Temporal trends in OAC initiation were examined using the Cochran-Armitage trend test.

Results: We identified a total of 116,686 patients with newly diagnosed AF. Of these, 47.7% were not initiated on OAC, 38.3% were initiated on VKA, and 14% were initiated on NOAC (8.7% dabigatran, 2.4% rivaroxaban, and 2.9% apixaban).

The median age (interquartile range) was slightly higher among patients not initiating OAC therapy (72 years [61–82]) compared to OAC initiators (71 years [64–78]). More patients were either <65 or ≥75 years old among non-initiators (33.1% and 43.5%, respectively) compared to the OAC initiators (26.6% and 38.1%, respectively). Non-initiators had more comorbidities but received less concomitant medications. The risk of stroke (mean CHA2DS2-VASc score) was similar in the two groups, but more non-initiators had a CHA2DS2-VASc score = 0 (13.8% and 9.7%, respectively).

From January 2005 to December 2009, OAC initiation rates decreased from 46.3% to 42.4% (p < 0.0001 for trend). From 2010 to study end, OAC initiation rates increased steadily (p < 0.0001 for trend) and by June 2015, 66.6% of the patients with newly diagnosed AF were initiated on OAC (Figure 1). The increased OAC initiation was accompanied by introduction and increased uptake of the NOACs. From mid-2011, NOAC initiation increased rapidly and by June 2015, 48.3% initiated treatment with a NOAC (73% of the OAC initiators used NOAC). The introduction of NOAC was followed by decreasing VKA initiation rates and by June 2015, 18.3% of the newly diagnosed AF patients were initiated on VKA (27% of the OAC initiators).

P4104 | BEDSIDE
Efficacy and safety of non-vitamin K antagonist oral anticoagulants after cardioversion for atrial fibrillation: a meta-analysis
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Conclusion: Since 2010, a higher proportion of patients with incident AF have been initiated on OAC therapy and by June 2015 approximately two thirds were initiated on OAC. The increased OAC initiation rates was likely influenced by the availability of the NOACs but also by the ESC Guidelines for management of stroke prophylaxis in AF, recommending OAC for patients with moderate or high stroke risk.

Acknowledgement/Funding: Recieved funding from Bristol-Myers Squibb

P4105 | BENCH
Myeloid cell specific alpha1-AMPK deletion induces a proinflammatory phenotype and enhances angiotensin II-mediated vascular dysfunction
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Background: Myeloid cells have been proposed as alternatives to vitamin K antagonists (VKAs) for prevention of thromboembolic events in patients undergoing cardioversion. Since the AMP-activated protein kinase (AMPK) is a crucial regulator of intracellular energy homeostasis, its expression and activity may also affect innate and adaptive immunity.

Methods and results: A mouse strain with specific α1-AMPK deletion in myeloid cells was generated by breeding α1AMPKfl/fl mice with LysMCre+ mice. Chronic angiotensin II infusion (1mg/kg/d for 7 days) lead to increased vascular oxidative stress and aggravated endothelial dysfunction in mice lacking the α1AMPK subunit in myeloid cells. This was accompanied by an augmented vascular infiltration of CD11b/F4/80+ macrophages assessed by flow cytometry of aortic tissue.

Conclusions: α1AMPK deletion in myeloid cells may enhance the consequences of α1AMPK deletion in myeloid cells.

P4106 | BENCH
Glycemic control with ipragliflozin, a novel selective SGLT2 inhibitor, did not exacerbate endothelial dysfunction in obese and non-obese diabetic mouse
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Acknowledgement/Funding: Received funding from Bristol-Myers Squibb

Figure 1

VASCULAR BIOLOGY

Figure 1
Conclusions:

animals.

1 in wildtype animals, that was blunted in endothelial specific PGC-1 (TekCre+) with a significant aggravation in endothelial specific PGC-1 deletion. Endothelial specific deletion of PGC-1α was generated by breeding PGC-1α knockout mice as measured by mitoSOX attenuation of phosphorylation of JNK and ameliorated impaired phosphorylation of Akt and eNOSSer1177 in abdominal aorta of a diabetic mouse model. In vitro study, methylyglyoxal (MO), one of the advanced glycation end products, significantly increased the expression of MCP-1, VCAM-1, ICAM-1 (P < 0.05, respectively). Furthermore, pIragliflozin administered attenuation phosphorylation of JNK and ameliorated impaired phosphorylation of Akt and eNOSSer1177 in human umbilical vein endothelial cells (HUVECs).

Conclusion: Iragliflozin decreases blood glucose level and prevents the development of endothelial dysfunction by the attenuation of oxidative stress under hyperglycemic condition at least in part.

P4106 | BENCH

Endothelial PGC-1α preserves endothelial function during chronic diabetes.

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Background: Vascular peroxisome proliferator coactivator 1α (PGC-1α) controls mitochondrial biogenesis and modulates the expression of several antioxidant enzyme systems. In the vasculature, PGC-1α promotes angiogenesis and prevents oxidative stress. However, the role of endothelial expressed PGC-1α is still unclear. Therefore the aim of the current study was to investigate the effects of endothelial PGC-1α deletion in a model of angiotensin II induced vascular dysfunction.

Methods and results: A mouse strain with an endothelial-specific PGC-1α deletion was generated by breeding PGC-1α flox/flox mice with TekCre+ mice. Endothelial specific deletion of PGC-1α resulted in a 70% decrease of PGC-1α mRNA in mouse lung endothelial cells (MLEC). Chronic angiotensin II infusion (0.5mg/kg/d for 7d) caused a mild endothelial dysfunction in wildtype animals (TekCre+) with a significant aggravation in endothelial specific PGC-1α knockout mice (PGC-1αflox/flox x TekCre+). We found a decreased NO-production in aortic tissue as well as in aortic paracrine reaction and significantly lower levels of eNOS mRNA and protein expression in MLEC as well as in aortic tissue. In parallel, vascular oxidative stress from mitochondrial sources was significantly increased in endothelial specific PGC-1α knockout mice as measured by mitoSOX staining. Moreover, angiotensin II induced an upregulation of cytoprotective HO-1 in wildtype animals, that was blunted in endothelial specific PGC-1α knockout animals.

Conclusions: Endothelial PGC-1α maintains eNOS expression, limits mitochondrial ROS production and supports the HO-1 mediated antioxidant defense. All of these processes contribute to the prevention of endothelial dysfunction during chronic angiotensin II treatment.

P4107 | BENCH

Impact of the adiponectin paralog CTRP13 on endothelial cells.

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Background: The C1q/tumor necrosis factor-alpha-related proteins (CTRP), a family of adiponectin paralogs, are secreted regulators of glucose and lipid metabolism as well as whole-body energy balance. One of these paralogs, CTRP13, was described to be preferentially expressed in adipose tissue and mediates insulin sensitizing effects in adipocytes, myotubes and hepatocytes, but the vasoactive properties of most CTRPs remains largely unknown. Here, we investigated the role of CTRP13 in the vasculature.

Methods: CTRP13 expression was analyzed in the aorta of obese ZDF (fa/fa) rats and mice and in the myocardium of young (55-60 g) or old patients (>70 years) undergoing cardiac surgery with a body mass index <25 or >30kg/m². Recombinant mouse CTRP13 was expressed in and isolated from E.coli and used to stimulate HUVECs or rat microvascular endothelial cells (MECs). Signal transduction and gene expression were analyzed by Western Blot, qPCR or immunocytochemistry, cell proliferation by BrDU incorporation, EC migration by wound healing assay, and angiogenesis by 3-D spheroid formation suggesting a angiogenesis modifying and pro-differentiation effect.

Conclusion: The data of present study demonstrate that CTRP13 is a novel adipocytokine that possess significant vaso-modulatory properties.

P4108 | BEDSIDE

Monocyte-platelet aggregates associated with CD14++CD16+ monocytes predict diffuse coronary artery disease: relationship to microvascular function.

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Background: Monocyte-platelet aggregates (MPAs) are pathophysiologically linked to coronary artery disease (CAD). However, which monocyte subsets (Mon1, Mon2, or Mon3) interact more readily with platelets and whether this interaction is affected by CAD severity or microvascular function remains uncertain.

Purpose: To study the relationships between MPAs from different monocyte subsets in patients with stable CAD and investigate the association between subsets of MPAs and microvascular function.

Methods: Peripheral whole blood was drawn from 50 prospectively recruited patients with severe diffuse CAD, 40 patients with severe focal CAD and 50 matched controls with normal coronary arteries and stained with antibodies against CD14, CD16, CD42a and CCR2 and analysed by flow cytometry. Cutaneous blood flow was assessed using laser Doppler flowmetry and iontophoresis of acetycholine and sodium nitroprusside at 100μA for 60 seconds. Patients with CAD had repeat measures at 6 and 12 months.

Results: Baseline counts of MPAs with Mon2 (CD14++CD16+CD14+) were significantly higher in diffuse CAD than in focal CAD or controls without CAD (p<0.001 and p<0.008 respectively) (Table). On multivariate regression MPAs with Mon2 independently predicted diffuse CAD (odds ratio [OR] 1.1, 95% confidence interval [CI] 1.0–1.2, p<0.015) and correlated negatively with endothelium-dependent microvascular vasodilator response to Ach (r=−0.27, p<0.002), an association that persisted after adjustment for age, gender and medication differences. Longitudinal analysis revealed an inverse relationship between MPAs with Mon2 (which declined) and Ach induced microvascular vasodilation (which improved) (repeated measures ANOVA, p<0.001 for MPAs with Mon2 and p<0.01 for maximum percentage flux increase).

Conclusion: MPAs with Mon2 are increased in patients with severe diffuse CAD and therefore could represent an important contributor to coronary atherosclerotic progression by a mechanism involving microvascular endothelial dysfunction.

Acknowledgement/Funding: Rosetrees medical research charity.
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containing recombinant human thrombomodulin in vitro and in a rat model of tissue-factor-induced hypercoagulation in vivo. This paradoxical increase in TG by AT-independent thrombin inhibitors depends on thrombomodulin and protein C (PC). PC is an important factor for negative regulation of the coagulation pathway and activated PC (aPC) suppresses the coagulation response via the degradation of factors Va (FVa) and Va/Va. The precise mechanisms underlying the paradoxical enhancement of TG by AT-independent thrombin inhibitors are unclear, especially the effects on PC and FVas.

Purpose: We determined the effects of AT-independent thrombin inhibitors and a direct factor Xa inhibitor edoxaban on the negative-feedback system of the coagulation cascade, activation of PC and production and degradation of factor Va (FVa).

Methods: TG in human plasma containing 10 nM thrombomodulin was assayed by means of the calibrated automated thrombography. As an index of PC activation, plasma concentration of aPC-PCI inhibitor complex (aPC-PCI) was measured. The amounts of FVas heavy chain and its degradation product (FVa307–506) were examined by western blotting.

Results: AT-independent thrombin inhibitors, melagatran and dabigatran (both at 25–600 nM) and IIai at 3–30 mg/ml, increased peak levels of TG. Melagatran (300 nM) significantly increased FVa heavy chain and decreased FVa307–506. In contrast, edoxaban preferentially inhibited thrombin generation at 25 nM or more, and higher concentrations were required to inhibit PC activation (150 nM or more) and FVas degradation (300 nM).

Conclusion: The present study suggests that the inhibitions of protein C activation were consistent with that for the enhancement of TG. Melagatran (300 nM) and IIai significantly decreased plasma concentration of aPC-PCI complex at 25 nM or more, 75 nM or more, and 10 and 30 mg/ml, respectively. The concentrations of these thrombin inhibitors for the inhibition of PC activation and FVas degradation (300 nM) significantly increased FVas heavy chain and decreased FVa307–506. In contrast, edoxaban preferentially inhibited thrombin generation at 25 nM or more, and higher concentrations were required to inhibit PC activation (150 nM or more) and FVas degradation (300 nM).

Acknowledgement/Funding: Daiichi Sankyo Co., Ltd.

P4110 | BENCH

Pentaerythritol tetranitrate (PETN) in-vivo treatment lowers pulmonary artery pressure, reduces oxidative stress and vascular function in monocrotaline-induced pulmonary hypertension

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Objective: Oxidative stress and endothelial dysfunction induce vascular remodeling and contribute to vessel occlusion and increased pulmonary artery pressure (PAP) in pulmonary arterial hypertension (PAH). The role of the preload-reducing organic nitrate pentaerythritol tetranitrate (PETN) on endothelial function and oxidative stress in PAH has not yet been defined.

Methods: The alkyl monocrotaline (MCT) was injected I.V. to induce PAH in Wistar rats. Animals were treated with low (30mg/kg; MCT30), middle (40mg/kg; MCT40) or high (60mg/kg; MCT60) dose of MCT for two, four and six weeks. Endothelium-dependent relaxation was impaired dependent on MCT dose and treatment duration in pulmonary arteries as well as in aorta. MCT induced pulmonary morphological changes and dose-dependent protein tyrosine nitration. Pulmonary arterial pressure (PAP), heart/body and lung/body weight ratio were increased in MCT40 rats (4 weeks) and decreased by oral PETN (10mg/kg, 3.5 weeks) treatment. PETN therapy improved endothelium-dependent relaxation in pulmonary arteries of rats treated with MCT40. Oxidative stress in the vascular wall (dihydroethidium staining), heart (NADPH oxidase activity and oxidative burst) was increased in MCT40 treated rats and normalized by PETN therapy. Expression (mRNA) of antioxidant protein heme oxygenase-1 (HO-1) was increased in MCT group and further increased by PETN therapy. Endothelin signaling was aggravated in pulmonary hypertensive rats, since mRNA levels of endothelin-converting-enzyme-1 (EC1-1), Endothelin-1 and ET-1 receptor was increased, which was normalized by PETN.

Conclusion: In summary, MCT-induced PAH impairs vascular function (aorta and pulmonary arteries) and increases oxidative stress, which was accompanied by induction of Endothelin-1 signaling, whereas PETN attenuates these adverse effects. Thus, PETN therapy improves pulmonary hypertension beyond its known cardiac preload reducing ability.

P4111 | BEDSIDE

Left atrial function index predicts long term survival in stable heart failure with reduced ejection fraction outpatients

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Background: Left atrial function index (LAFI) is a rhythm independent index that combines left atrial reservoir function (LAEF), adjusted LA volume (LAVi) and the stroke volume. This index reflects both the left ventricle systolic and diastolic function.

Objectives: To evaluate in heart failure with reduced ejection fraction (HF/EF) stable and optimally medicated outpatients, LAFI as a predictor of the long term all cause death.

Population and methods: 203 consecutive outpatients, LVEF <40%, clinically stable in “dry-state”, on optimal HF therapy were followed-up for 3 years in a HF Unit. End-point was all cause death. Clinical stability: no change in NYHA, thera-peutics including diuretics, no decompensation or hospitalization. LAFI calculated according to the validated formula: LAFI = [(LAEF × left ventricular outflow tract velocity time integral) / (LAVi)]. LAFI was categorized according to the quartiles (29.26±16.56±31.92) and the median (16.57). Survival analyses adjusted for 11 significant cofounders including heart rhythm, optimal therapy, and NT-ProBNP.

Results: (1) The 3 year death rate was 30%. Decreased had lower LAFI (25.0±16.8 vs. 14.5±11.8; p<0.001). Greater the quartile, lower the death rate (43.1%±65.1%±25.4%; p<0.001). (2) LAFI correlated significantly with NT-ProBNP (Rs=–0.55 p<0.001). (3) The ROC curve for death was associated with LAFI (AUC=0.695, 95% CI: 0.62–0.77; p<0.001). (4) LAFI per unit increase (HR Cox 0.93, 95% CI: 0.89–0.97; p<0.001) was an independent predictor of survival in relation to LAI and LAFI. (5) LAFI per unit increase (HR Cox 0.97, 95% CI: 0.94–1.0; p=0.049) and LAFI =16.57 (HR Cox 0.35, 95% CI: 0.15–0.79; p=0.013) were associated with improved survival. (6) A subgroup analyses limited to those on sinus rhythm (n=150), LAFI =15.57 remained associated with survival (HR Cox 0.61, 95% CI: 0.44–0.84; p=0.003). All models were adjusted for the significant confounders.

Conclusion: LAFI determination in HF/EF stable outpatients, on optimal therapy, is a strong independent predictor of long term survival.

P4112 | BEDSIDE

Prognostic implication of progression of diastolic dysfunction in patients with coronary artery disease undergoing percutaneous coronary intervention


Background: Diastolic dysfunction is associated with increased mortality regardless of left ventricular (LV) systolic dysfunction. However, there are limited data on whether worsening of diastolic function (DF) after revascularization of coronary artery is associated with worse prognosis in patients undergoing percutaneous coronary intervention (PCI) for coronary artery disease (CAD).

Purpose: The aim of this study was to evaluate impact of the change of diastolic function on adverse clinical outcome in patients who undergoing PCI.

Methods: From June, 2003 to June, 2014, consecutive CAD patients who had baseline echocardiogram and subsequently had a follow-up echocardiogram within 6 months after PCI were evaluated. DF was graded as normal, mild (grade I), moderate (grade II) or severe (grade III) dysfunction. Worsening of LV DF was defined categorically as an aggravation of at least one diastolic functional class. Major adverse clinical events (MACE) including all-cause death, myocardial infarction, stroke and any revascularization were followed. Kaplan-Meier survival analysis and Cox regression analysis with a proportional hazard model were performed to assess outcomes.

Results: A total of 1235 patients were identified (age, 64±11.3 years; 72.1% male). Baseline diastolic dysfunction was present in 1033 patients (83.7%), with mild being the most prevalent (54.1%). After PCI, 750 patients (60.7%) had stable, 219 (17.7%) had worsening, and 266 (21.5%) had improved baseline DF. According to the change of diastolic dysfunction, MACCE rate was significantly different (improved DF group, 19.9%; stable DF group, 30.4%; aggravated DF group, 56.2%; p<0.001). In multivariate analysis, a decrease in LV ejection fraction, old age, male, presence of chronic kidney disease, three-vessel disease and worsening of DF were independently associated with increased risk of MACCE (hazard ratio [95% confidence interval], 0.98 [0.98–0.99], P<0.001; 1.03 [1.02–1.04], P<0.001; 1.38 [1.09–1.74], P=0.008; 1.58 [1.22–2.04], P<0.001; 1.32 [1.06–1.63], P=0.012; and 2.86 [1.95–4.21], P<0.001, respectively). In subgroup analy-
A diabetes associated HNF1B polymorphism increases risk of prevalent diastolic dysfunction in two independent Swedish population cohorts

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Background: Although diabetes, hyperglycemia and insulin resistance increase risk of future cardiovascular disease (CVD), earlier genetic studies have failed to show associations between diabetes-related single-nucleotide polymorphisms (SNPs) and CVD-risk.

Purpose: To examine if 43 SNPs with earlier established genome-wide association with increased risk of type 2 diabetes (T2D), hyperglycemia and insulin resistance were also associated with prevalent early signs of diastolic dysfunction (DD) as measured by echocardiographical examination (UCG) in two independent Swedish population-based cohorts.

Methods: We genotyped 43 SNPs in 43 genes that reported genome-wide significant association with T2D, hyperglycemia and insulin resistance traits, in 1792 subjects from the population-based Malmö Preventive Project (MPP) with full UCG data (mean age 51 years, 52% women, 7% prevalent T2D) (replication cohort). Logistic regression was used to adjust for covariates (age, sex, systolic and diastolic blood pressure, years, ethnicity). For the total cohort (TC) ID was highly prevalent (57%); significantly more so in DD-REF patients (24% vs. 53%, p=0.003). ID was predictive of mortality for the TC (HR 1.49, 95% CI: 1.04–1.21, p=0.03), as well as for DD-REF patients (HR 1.82, 95% CI: 1.18–2.82, p=0.007) but not for DD-PEF patients (HR 0.98, 95% CI: 0.53–1.81, p=0.95).

Results: 770 of the 940 patients enrolled in the PEOPLE study had blood samples available at baseline for iron analyses. 490 patients had DD-REF and 280 DD-PEF. DD-PEF patients were older and more likely to be female than the DD-REF patients (73.7yrs vs 66.7yrs (p<0.001), 45 vs 22% (p=0.001)). Unlike previous published studies our patients with DD-REF did not have a lower mortality rate than patients with DD-REF (HR 0.75, 95% CI: 0.53–1.08, p=0.12).

For the total cohort (TC) ID was highly prevalent (57%); significantly more so in DD-PEF compared to DD-REF patients (64 vs 53%, p=0.003). ID was predictive of mortality for the TC (HR 1.34, 95% CI: 1.04–1.72, p=0.001) and for both the DD-PEF (HR 1.59, 95% CI: 1.13–2.24, p=0.006) and DD-REF (HR 1.31, 95% CI: 1.04–1.69, p=0.02) patients. IDA was strongly predictive of mortality for the TC (HR 2.19, 95% CI: 1.57–3.06, p<0.001) and for both the DD-PEF (HR 2.09, 95% CI: 1.20–3.63, p=0.009) and DD-REF (HR 2.39, 95% CI: 1.56–3.65, p<0.001) cohorts.

Conclusion: ID and IDA are highly prevalent in patients with DD-PEF; two thirds have ID and half are anaemic but unlike patients with DD-REF their presence is not predictive of worse outcomes in our study unless they were concommitantly present. The DD-PEF cohort was smaller in size than the DD-REF cohort and this may explain why statistical significance was not reached.

Acknowledgement/Funding: Greenlane Research and Educational Fund Project Grant
Results: In this cohort (mean age 62.4±10.6 years, 38% males), prehypertension was present in 29% and hypertension in 54% of participants. Subclinical diastolic dysfunction was present in 24%. SBP and DBP were associated with lower E′ (ρ = −0.3; p < 0.001 and ρ = −0.1; p < 0.01, respectively) but only SBP was significantly associated with increased E/E′ ratio (ρ = 0.2; p = 0.001).

Conclusion: In this large community-based cohort, prehypertension (normal and high-normal BP categories of the ESC recommendations) was already associated with impaired diastolic function before the onset of hypertension.

P4116 | BEDSIDE
Gaitec-3 level and the severity of cardiac diastolic dysfunction using cellular and animal models and clinical indices
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Background: Heart failure with preserved ejection fraction (HFPEF) is characterized by myocardial interstitial fibrosis and left ventricular hypertrophy. The aim of this study was to characterize the relationship between Gaitec-3 and the detailed relationship with cardiac diastolic dysfunction in HFPEF patients.

Methods and results: A total of 146 patients with HFPEF were recruited. HFPEF severity was determined using Doppler imaging (E/E′) and also cardiac magnetic resonance imaging (CMR). The association between plasma levels of Gaitec-3 and diastolic function parameters were evaluated. Canine modeling of HFPEF was induced by aortic banding. Hemodynamic and echocardiographic data were obtained before and after pressure loading and myocardial Gaitec-3 was determined. Mechanical stretch of cultured cardiomyocytes served as the cellular model of HFPEF. Patients with severe HFPEF had significantly higher plasma Gaitec-3 levels than controls. Significant correlation between plasma Gaitec-3 and E/Em (r = 0.8, p < 0.001) in advanced HFPEF patients was noted. After 2 weeks of pressure overload in canine models, the protein expression of Gaitec-3 from LV myocardial tissue was significantly increased (p < 0.01) compared to controls. Gaitec-3 expression paralleled the severity of LV diastolic dysfunction by evaluation of CMR (r = −0.58, p = 0.003) and tissue fibrosis (r = 0.59, p = 0.002). After adjusting for confounders for diastolic dysfunction, Gaitec-3 levels were still associated with diastolic parameters both in humans (p < 0.001) and canine model (p = 0.041). Mechanical stretch increased Gaitec-3 secretion in cultured cardiomyocytes.

Conclusions: Both plasma and myocardial Gaitec-3 levels correlated with severity of cardiac diastolic dysfunction. Cardiomyocytes could secrete Gaitec-3 after pressure stimulation and direct influence diastolic function.

IMPROVED RISK PREDICTION AND SUBSEQUENT ACTION

P4117 | BEDSIDE
Personal activity index (PAI) for promotion of physical activity and prevention of CVD
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Background: Low levels of physical activity (PA) has reached pandemic proportions, contributing to >5 million deaths each year worldwide, and making it 1 of the 10 leading causes of death and disability. The major challenge in activity counseling and promotion of PA is to provide clear feedback to individuals with personalized and meaningful information about their activity behaviour. Implicitly, PA behaviors are highly heterogeneous and multi-dimensional in nature, and just one aspect may lead discrepancies in terms of PA status. Although, several methods exist to assess minute-by-minute PA energy expenditure, there is no single outcome measure available that captures all relevant information in a single metric. If such a metric was available, it could potentially be included in wearable devices and provide the user with real-time feedback on whether they are doing enough PA to promote health and reduce the risk of chronic disease.

Methods: Using HUNT Fitness Study (n=4637), we derived an algorithm (Personalized Activity Index: PAI) based on PA questions relating to frequency, duration and intensity of exercise where relative intensities of low, medium and high corresponds to 44%, 73% and 83% of heart rate reserve. The validation cohort consists of general healthy HUNT population (n=39,298; ≥ 20.029; ≥ 19.269), and PAI was divided into 3 groups (< 50, 51–99, and ≥ 100), and inactive (0 PAI) were used as reference.

Results: After a median follow-up of 28.7 years, there were 10,062 deaths, including 3867 deaths (2207 men and 1660 women) from CVD. Men and women with a PAI-level > 100 had 17% (95% CI, 7–27%) and 23% (95% CI, 4–38%) reduced risk of CVD mortality compared to the inactive groups, respectively, after multiple adjustment for confounders. The corresponding risk reduction for all-cause mortality was 13% (95% CI, 6–20%) and 17% (95% CI, 6–28%) for men and women, respectively. The relative risk reductions were dose dependent over groups ranging from inactive, ≥ 50 PAI, 51–99 PAI to the recommended level of ≥ 100 PAI (all p-trends < 0.001). Participants with presence of known risk factors such as smokers, hypertension, overweight/obese, and in different age strata showed similar risk reductions by obtaining > 100 PAI compared to the inactive groups.

P4118 | BEDSIDE
Assessment of coronary artery calcium scoring for statin treatment strategy according to ACC/AHA cholesterol management guidelines in asymptomatic Korean adults
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Background/Introduction: The American College of Cardiology (ACC)/American Heart Association (AHA) cholesterol management guidelines advocate the use of statin treatment for prevention of cardiovascular disease (CVD) based on individual risk assessment. To date, however, the efficacy of statin treatment in primary prevention according to these recent guidelines has not been evaluated beyond Western populations.

Purpose: We aimed to assess the usefulness of coronary artery calcium (CAC) scoring for stratifying risk beyond statin eligibility among asymptomatic Korean adults.

Methods: A total 31,375 subjects who underwent CAC scoring as part of a general health examination were enrolled in the current study. Individuals were categorized according to statin eligibility (e.g., statin recommended [SR, n=13,888], considered [SC, n=6,046], and not recommended [SN, n=13,441]) based on ACC/AHA guidelines. Multivariable Cox regression was employed to estimate the
hazard ratio (HR) with 95% confidential intervals (95% CI) for all-cause mortality after stratiﬁcation by CAC scores 0, 0.1–100, and >100. 

Results: Mean age was 54.4±7.5 years, and 76.3% were male. During a 5-year median follow-up (IQR: 3–7), there were 251 (0.8%) deaths from all-causes. Patients with a CAC score >100 displayed a higher incidence of mortality as compared to the absence of CAC, or CAC scores between 1–100. In each stratum eligibility group (Figure 1). Notably, a CAC score >100 was independently associated with mortality across each stratum eligibility group after adjusting for several cardiovascular risk factors (e.g., SR group: HR, 1.60; 95% CI, 1.07–2.38; SC group: HR, 2.98; 95% CI, 1.29–6.83; and SN group: HR, 3.14; 95% CI, 1.08–9.71).

Conclusion: In a large sample of asymptomatic Korean adults, CAC scoring might prove useful for reclassifying patients’ eligibility for receiving statin therapy based on recently updated 2013 ACC/AHA guidelines.

Analysis/Comment/Funding: Supported by a grant from the Korean Health Technology Research Proﬁt, Ministry of Health & Welfare, Republic of Korea (HI13C0715).

P4119 | BEDSIDE
Fibrates for the primary prevention of cardiovascular disease
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Background: Evidence that ﬁbrates reduces overall or cardiovascular disease (CVD) mortality in primary prevention of CVD is lacking. 

Purpose: This systematic review and meta-analysis aimed at evaluating the clinical beneﬁts and harms of ﬁbrates versus placebo/usual care or ﬁbrates plus lipid-modifying drugs versus other lipid-modifying drugs alone for the primary prevention of a combined outcome of CVD death, non-fatal myocardial infarction, or non-fatal stroke.

Methods: We searched MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials and CINAHL from their inception to May 26th, 2015 with the help of an experienced professional librarian. We used Cochrane sensitive search strategies to include randomised controlled trials evaluating the clinical effects of ﬁbrate therapy in the primary prevention of CVD with a minimal follow-up of 6 months. Two reviewers independently screened titles and abstracts for potential study inclusion and extracted relevant data from included full-text papers. Disagreement was resolved by consensus.

Results: We identiﬁed 8 trials including 27’523 individuals. Mean age of trial participants ranged from 46 to 63 years across trials. Five trials included only individuals with type 2 diabetes. The mean measured treatment duration and follow-up of participants were 5 years. The overall quality of the evidence was moderate. 

Fibrates reduced the risk for the combined primary outcome of CVD death, non-fatal myocardial infarction or non-fatal stroke (RR 0.85, 95% CI 0.77 to 0.94; p=0.002; I2=0%). Fibrates also reduced the risks for coronary heart disease death or non-fatal myocardial infarction (RR 0.80, 95% CI 0.71 to 0.90; p=0.0003; I2=0%) and for the new development or progression of pre-existing diabetic retinopathy (RR 0.71, 95% CI 0.60 to 0.84; p<0.0001; I2=52% in 3 trials including 2901 individuals). Fibrates slightly increased the risks for overall mortality (RR 1.16, 95% CI 1.01 to 1.34; p=0.03; I2=0% in 7 trials) and for non-cardiovascular mortality (RR 2.52, 95% CI 1.51 to 4.25; p=0.0007; I2=32.0% in 7 trials). After excluding 2 clofibrate trials (clofibrate was withdrawn from the market in 2002 due to adverse events), there was no longer evidence for an increased risk for overall or non-cardiovascular mortality in individuals treated with ﬁbrates, while the results for new or progressive diabetic retinopathy, coronary heart disease death and non-fatal myocardial infarction, and for the development or progression of diabetic retinopathy remained robust. Data on quality of life were not available from any trial.

Conclusions: Moderate quality evidence suggests that ﬁbrates lower the risk for cardiovascular events in primary prevention, but the absolute treatment effects are modest (absolute risk reductions <1%). Fibrates are unlikely to reduce mortality, but reduce the risk for the development or progression of diabetic retinopathy.
vs. 0.521, p=0.0058, FRA-CVD: 0.980 vs. 0.563, p<0.0001). In the secondary prevention group, hs-cTnT outperformed all risk scores in the prediction of ACM (DAUC: PRO: 0.319, p<0.0001, FRA-CHD: 0.267, p=0.0147, FRA-HARD: 0.312, p<0.0021, FRA-CVD: 0.259, p=0.0169, Figure 1) and performed superior in the predication of ACM, AMI and stroke as compared to the PRO, the FRA-CHD and the FRA-HARD scores (DAUC: PRO: 0.176, p=0.0476, FRA-CHD: 0.198, p=0.9344, FRA-HARD: 0.178, p=0.0367). In contrast, we observed a comparable diagnostic performance of hs-cTnT risk scores in the non-secondary group.

Conclusions: hs-cTnT provides excellent risk stratification regarding ACM and a composite of ACM, AMI and stroke in a secondary prevention cohort in which risk scores perform poor.

Acknowledgement/Funding: AstraZeneca Germany

P4122 | BEDSIDE

Major in-hospital bleeding events in acute coronary syndrome patients can be predicted by 6 easily obtained variables with results comparable to the CRUSADE-score: Results from the SWEDHEART-registry

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Background: A bleeding event in ACS patients is associated with adverse outcomes. Currently, available risk stratification scores are complex to calculate and may not apply to patients treated according to recent guidelines.

Purpose: Our aim was to create a simple bleeding risk score and to compare the performance of our new score with that of the CRUSADE score.

Methods: From the SWEDHEART registry we included patients with an acute myocardial infarction (MI) enrolled from 2006 to 2014 (n=148 253). Logistic regression models were used to determine the six statistically and clinically most important independent predictors for in-hospital major bleeding from a derivation set (n=118 864). An integer value based on each variables coefficient was assigned to each predictor. In-hospital major bleeding was defined as an intracranial hemorrhage, bleeding requiring transfusion/surgery or resulting in death. The six predictors were then tested and compared with the CRUSADE score in a validation set (n=29654).

Results: In-hospital major bleeding occurred in 1971 patients (1.7%). The six predictors in the final model were anemia (mild if Hb <120 g/L, for women or Hb <130 g/L for men; moderate/severe if Hb <100 g/L), previous bleeding, female sex, renal insufficiency (GFR<60 ml/min), hypotension at arrival (<110 mmHg) and elevated CRP (>10 mg/L). Each of these predictors were assigned 1 point except for anemia and moderate/severe anemia which were assigned 2 and 4 points respectively. Maximum number of points was 9. In-hospital major bleeding events increased with increasing number of points in our score and in the CRUSADE score (figure 1). The performance of our score was better than the CRUSADE score in the whole population (AUC (95% CI): 0.773 (0.750–0.789) vs. 0.721 (0.698–0.744)) and considerably better in non-invasively treated patients (AUC (95% CI): 0.739 (0.703–0.775) vs. 0.618 (0.579–0.657)).

Conclusion: In a contemporary real-world setting, we created a 6-variable easy to use bleeding risk score, with a performance comparable to the CRUSADE score.

P4123 | BEDSIDE

Net Reclassification index of a genetic risk score and standard Framingham risk stratification in a European population

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Cardiovascular risk stratification has included traditional risk factors (TRF) as smoking, metabolic and arterial blood pressure adjusted to age and gender. The utility of genetic risk scores (GRS) as independent risk predictors remains inconclusive.

Objectives: Evaluate the ability of a multiloci GRS to provide additive value to Framingham 10 years risk score (FS) tables subgroups (<5%, 5–20%, >20%) to predict coronary arterial disease (CAD).

Methods: Case-control study of 2703 individuals [1477 coronary patients and 1226 controls, matched in terms of age and gender] divided in three groups according to FS (FS<5, n=391, 64.7% male, FS 5–20, n=1806, 78.6% male and FS>20, n=506, 89.7% male). The multiloci GRS was determined in 33 different genetic variants associated to atherosclerotic disease, in general, and to CAD, particularly according to the multiplicative model and assuming co-dominance. Multivariate analysis and respective ROC curves and area under curve (AUC) were performed using the TRF. The analysis was repeated adding GRS to the evaluation. ROC Curves were compared with DeLong test and Net Reclassification Index (NRI) was determined with R.

The NRI was calculated to assess improvement between the 10-year CHD risk for low (<5%), intermediate (5–20%), and high (>20%) risk categories. Calibration of these models was tested with the Hosmer-Lemeshow goodness-of-fit statistic.

Results: The addition of the GRS to the TRFs significantly improved discrimination, reclassification, and calibration beyond that afforded by TRFs alone. The AUC increased from 0.724 to 0.750 (Δ=0.026, 95% CI, 0.018 to 0.034), and the NRI was 29.2%. By multivariate analysis, GRS was an independent predictor for CAD (OR=2.14; 1.76–2.61, p<0.0001). Diabetes, arterial hypertension, dyslipidemia and smoking (OR=3.05 (2.47–3.77); OR=1.990 (1.67–2.38); OR=2.41 (1.87–3.11); OR=3.20 (2.78–3.96); p<0.0001, respectively) were also independent CAD predictors. GRS also added predictive value to TRF across all risk subgroups. In individuals within low risk (FS<5) the AUC increased from 0.762 to 0.785, in intermediate risk (FS5–10) increased from 0.713 to 0.743 and in the high risk (FS>20) subgroup the traditional risk factors prediction was lower AUC=0.675 increasing to 0.715 after the inclusion of the GRS. NRI showed better increase in the intermediate risk (FS5–10) and <20) with a 30.0%, interpreted as the proportion of patients reclassified to a more appropriate risk category, 28.1% on the lower risk and finally 23.9% in the higher risk.

Conclusion: In our population, addition of a GRS based on direct associations with CHD to TRFs significantly improved discrimination and reclassification increased the predictive value of TRF across all FS risk subgroups. GRS proved a better incremental value in intermediate subgroup.

ADVANCES IN PULMONARY EMBOLISM

P4124 | BEDSIDE

Subgroup analysis of patients with concomitant pulmonary embolism in XALIA, a non-interventional study of rivaroxaban in routine treatment of deep vein thrombosis

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Background: XALIA was a prospective, non-interventional study of rivaroxaban
in the treatment of acute deep vein thrombosis (DVT). After approval of rivaroxaban for pulmonary embolism (PE) treatment, patients with concomitant (but not isolated) PE were included. The overall results in XALIA showed that rivaroxaban was associated with low rates of major bleeding and symptomatic recurrent venous thromboembolism (VTE).

**Purpose:** To compare the management and outcomes of patients with DVT and concomitant PE with patients with DVT alone.

**Methods:** Patients with DVT (later DVT+PE) aged ≤18 years and planned to receive ≥3 months of anticoagulation with rivaroxaban or standard therapy were eligible. Therapy type, dose and duration were at the physician's discretion. The rivaroxaban cohort consisted of patients receiving heparin/fondaparinux for ≤48 hours; if heparin/fondaparinux was administered for >48 hours–14 days and/or a VKA for 1–14 days before changing to rivaroxaban, patients were termed 'early switchers'. The primary outcomes were major bleeding, recurrent VTE and all-cause mortality.

**Results:** 5136 patients were enrolled; 4584 (89.3%) had DVT alone and 552 (10.7%) had DVT+PE. Of the patients with DVT alone, 2399 (52.3%) received rivaroxaban, 1894 (41.3%) standard therapy, and 291 (6.3%) were early switchers. Of the patients with DVT+PE, 220 (39.9%) received rivaroxaban, 255 (46.2%) standard therapy, and 77 (13.9%) were early switchers. Incidence rates for the primary outcomes are reported (Figure). The median lengths of hospital stay for rivaroxaban-treated patients with DVT+PE vs DVT only were 6.0 vs 4.0 days, respectively; for patients receiving standard therapy these were 8.0 vs 7.0 days, respectively. Early switchers had a median hospital stay of 7.0 days for both DVT+PE or DVT alone.

**Conclusions:** Patients treated with rivaroxaban in XALIA for DVT+PE were more likely to receive longer treatment with heparin than patients with DVT alone, suggesting that physicians exercised greater caution with a newly approved drug for PE treatment. Patients with DVT+PE had a longer median duration of hospital stay than patients with DVT alone; patients with DVT+PE receiving rivaroxaban had shorter hospital stays than those in the standard therapy and early switch groups, respectively, for differences of 2.0 and 4.0 days, respectively. Major bleeding and recurrent VTE rates in patients with DVT+PE were low in all three treatment groups; mortality was highest in the standard therapy group, likely owing to the allocation of more patients with active cancer. The data indicate that rivaroxaban is a safe and effective treatment for patients with DVT+PE.

**Acknowledgement/Funding:** Bayer Pharma AG and Janssen Pharmaceuticals

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**P4125 | BENCH**

Prothrombotic fibrin clot phenotype is associated with recurrent pulmonary embolism following discontinuation of anticoagulant therapy


**Background:** Pulmonary embolism (PE) is a life-threatening manifestation of venous thromboembolism (VTE). Formation of denser fibrin clots displaying impaired lysability has been reported in previous idiopathic VTE. It is unknown whether such fibrin clot phenotype has a predictive value in VTE.

**Purpose:** We tested the hypothesis that abnormal prothrombotic fibrin clot properties are predictive of recurrent PE.

**Methods:** We investigated 156 consecutive white patients (men 82, 53%) aged 18 to 65 years following the first episode of PE, including 103 (66%) subjects who experienced VTE recurrence. We then performed a follow-up study of 4 ± 1 years after the index PE, looking for recurrent VTE. Recurrence was defined as a new PE event confirmed by imaging or, for recurrent death, documented by a death certificate or an autopsy report. The incidence of recurrent VTE was compared between patients with and without fibrin clot phenotypes using univariate and multivariate logistic regression analysis. The model was adjusted for baseline characteristics, and the presence of recurrent VTE was assessed using Kaplan-Meier survival analysis, log-rank test, and competing risks regression analysis. The main outcome measure was the incidence of recurrent VTE.

**Results:** During a median follow-up of 4 ± 1 years, recurrent VTE episodes were confirmed in 15 of 156 patients (9.6%). The risk of recurrent VTE was significantly higher in patients with a prothrombotic fibrin clot phenotype compared to those with a normal fibrin clot phenotype (11.8 vs. 3.9%, p = 0.036). The risk of recurrent VTE was also significantly higher in patients with a prothrombotic fibrin clot phenotype compared to those with a normal fibrin clot phenotype (11.8 vs. 3.9%, p = 0.036). The risk of recurrent VTE was also significantly higher in patients with a prothrombotic fibrin clot phenotype compared to those with a normal fibrin clot phenotype (11.8 vs. 3.9%, p = 0.036). The risk of recurrent VTE was also significantly higher in patients with a prothrombotic fibrin clot phenotype compared to those with a normal fibrin clot phenotype (11.8 vs. 3.9%, p = 0.036). The risk of recurrent VTE was also significantly higher in patients with a prothrombotic fibrin clot phenotype compared to those with a normal fibrin clot phenotype (11.8 vs. 3.9%, p = 0.036). The risk of recurrent VTE was also significantly higher in patients with a prothrombotic fibrin clot phenotype compared to those with a normal fibrin clot phenotype (11.8 vs. 3.9%, p = 0.036). The risk of recurrent VTE was also significantly higher in patients with a prothrombotic fibrin clot phenotype compared to those with a normal fibrin clot phenotype (11.8 vs. 3.9%, p = 0.036). The risk of recurrent VTE was also significantly higher in patients with a prothrombotic fibrin clot phenotype compared to those with a normal fibrin clot phenotype (11.8 vs. 3.9%, p = 0.036). The risk of recurrent VTE was also significantly higher in patients with a prothrombotic fibrin clot phenotype compared to those with a normal fibrin clot phenotype (11.8 vs. 3.9%, p = 0.036). The risk of recurrent VTE was also significantly higher in patients with a prothrombotic fibrin clot phenotype compared to those with a normal fibrin clot phenotype (11.8 vs. 3.9%, p = 0.036). The risk of recurrent VTE was also significantly higher in patients with a prothrombotic fibrin clot phenotype compared to those with a normal fibrin clot phenotype (11.8 vs. 3.9%, p = 0.036). The risk of recurrent VTE was also significantly higher in patients with a prothrombotic fibrin clot phenotype compared to those with a normal fibrin clot phenotype (11.8 vs. 3.9%, p = 0.036). The risk of recurrent VTE was also significantly higher in patients with a prothrombotic fibrin clot phenotype compared to those with a normal fibrin clot phenotype (11.8 vs. 3.9%, p = 0.036).

**Conclusions:** The findings suggest that a prothrombotic fibrin clot phenotype is a predictive factor for recurrent VTE. Further studies are needed to confirm these findings and to determine the clinical relevance of this observation.

**Acknowledgement/Funding:** Bayer Pharma AG and Janssen Pharmaceuticals

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**P4127 | BEDSIDE**

Home treatment of patients with pulmonary embolism: the experience of a referral centre in Italy

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**Introduction:** The last european guidelines on management of pulmonary embolism (PE) suggest early discharge and outpatient treatment for patients with Pulmonary Severity Index (PSI) class I or II or with simplified PESI (sPESI) zero. The present study aimed at investigating the feasibility and safety of home treatment of patients with PE in daily clinical practice.

**Methods:** We included consecutive adult patients with objectively confirmed PE, presenting to a single tertiary referral hospital. In our center we considered for discharge patients with primary diagnosis of right ventricular (RV) dysfunction/injury and important comorbidities needing hospitalization. The social background was also taken into account. A short stay in hospital (less than 48 hours) was allowed in the home treatment group. Home treated patients were instructed to immediately contact the emergency department in case of signs or symptoms of recurrent venous thromboembolism (VTE) (dyspnea, chest pain, syncope, leg pain or swelling) or haemorrhage. A follow-up visit at one month was arranged in a dedicated service.

**Results:** From January 2014 to November 2015, we screened 798 patients for PE and 234 (29%) were objectively diagnosed. Of 101 (43%) were judged low risk according to local policy and were discharged from the emergency department on anticoagulant treatment within 48 hours. At a month follow-up, only one outpatient experienced VTE recurrence and 2 (2%) were readmitted because of major haemorrhage. Among early discharged patients, 67 (76%) showed a PSI class ≤ II and 75 (75%) a sPESI ≥ 0. Conversely, among 133 hospitalized patients, 24 (18%) showed a PSI class I or II and 18 (13%) a sPESI ≥ 0; among these “low-risk” patients 8 (33%) were admitted because of signs of RV dysfunction/injury.

**Conclusions:** In an Italian referral centre 43% of patients with pulmonary embolism were actually treated without hospitalization with a low incidence of recurrent VTE and of major haemorrhages. The addition of clinical decision rules does not seem to improve the selection of patients for home treatment.
diagnosed with recurrent VTE. The cut of points E-selectin > 39 ng/ml and sICAM-1 > 655 ng/ml indicated the group with no recurrent VTE.

Kaplan-Meier analysis of VTE recurrence

Conclusions: Patients after episode of APE have impaired endothelial function assessed by FMD and biomarker levels. The low concentrations of E-selectin and high of sICAM-1, biomarkers of endothelial dysfunction, are associated with the extremely high risk of recurrent thromboembolism, especially in patients with history of unprovoked APE.

P4128 | BEDSIDE
Costs of major adverse outcomes in patients with incident venous thromboembolism in clinical practice in the United Kingdom
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Methods: Costs for each adverse outcome in the first 2 years following the initial VTE.

Results: All adverse outcomes in the VTE cohort of 16,623 incident VTE patients cation of HCRU rate differences with related costs per HCRU event over the one year period. Costs for each adverse outcome were calculated by multiplying HCRU attributable to adverse outcomes was estimated from the rate differences of hospitalization days, referrals, GP visits, investigations and prescriptions in patients with and in patients without a respective adverse outcome in the first 2 years following the initial VTE.

Conclusion: Venous thromboembolism (VTE) represents a substantial personal and economic burden. The standard of care for acute VTE is initiation of anti-coagulation for ≥3 months. VTE treatment objectives include the prevention of recurrences, post-thrombotic syndrome (PTS), and chronic thromboembolic pulmonary hypertension (CTEPH) and minimize bledding complications. This study aimed to investigate the costs of these adverse outcomes in a large cohort of patients with first VTE.

P4129 | BEDSIDE
Echocardiographic in the post-acute, pre-discharge assessment of pulmonary embolism: prevalence and prognostic impact of right ventricular dysfunction and residual pulmonary hypertension
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Background: Echocardiographic assessment is pivotal for risk-stratification of acute pulmonary embolism (PE); however, its impact in the post-acute, pre-discharge assessment of PE on long-term prognosis remains uncertain.

Purpose: To assess the prognostic impact of post-acute, pre-discharge echocardiographic determination of right ventricular (RV) dysfunction in patients with low- and moderate-risk PE.

Methods: In this non-concurrent prospective cohort study, consecutive patients hospitalised because of low- and intermediate-risk PE were included. All patients underwent post-acute, pre-discharge comprehensive 2D echocardiography to assess RV dysfunction by (PEITHO criteria): i) parasternal RV end-diastolic diameter > 30 mm, ii) apical right-to-left ventricular end-diastolic diameter > 0.9, iii) apical tricuspid anular plane systolic excursion < 1.8 cm, and/or iv) tricuspid regurgitation (TR) systolic velocity > 2.6 m/s. Multivariable Cox proportional hazards were developed to predict all-cause mortality.

Results: A total of 632 patients were included: mean age was 64±18, 53% were female, 23% had idiopathic PE and 17% had associated malignancies. 37% patients had echocardiographic signs of RV dysfunction at discharge. During a median follow up of 1103 (interquartile range 619–1621) days, 89 (14.1%) patients died. Among echocardiographic indices of RV dysfunction, only TR systolic velocity emerged as an independent predictor of all-cause mortality after adjusting for age, gender, malignant aetiology of PE, and blood pressure and heart rate (Figure): A 1.75-fold increase in all-cause mortality was associated with every 0.1 m/s increase in TR systolic velocity (95% confidence interval 1.02–3.01, p=0.044). However, when B-natriuretic peptide (BNP) levels were added to the model, statistical significance for prediction was not retained.

Conclusion: Echocardiographic signs of RV dysfunction are highly prevalent in the post-acute, pre-discharge phase of low- and moderate-risk PE. However, only TR systolic velocity independently predicts long-term all-cause mortality. Additionally, when BNP levels are taken into account, predictive power is not retained. Our findings suggest that post-acute, pre-discharge echocardiographic assessment provides only moderate long-term prognostic information in patients with low- and moderate-risk PE.
in the emergency department before final diagnosis. Emergency physicians or cardiologists expert in basic echocardiography and CUS performed the tests. PCI was established by multi-detector CT pulmonary angiography (CTPA), pulmonary angiography or by autopsy.

**Results:** We included 94 patients, with a mean age of 74±12 years. Forty (43%) patients showed RVD and 30 (21%) a proximal deep vein thrombosis; 35 (37%) patients had a final diagnosis of PE. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of CUS were 86% (CI 95% 73–94), 83% (CI 95% 76–98), 75% (CI 95% 64–82) and 91% (CI 95% 82–96), respectively. CUS showed lower sensitivity (51%, CI 95% 40–66) and higher specificity (97%, CI 95% 90–99%) and PPV (90%, CI 95% 70–98%) than CUS (p<0.05 for all). When both CUS and CUS were positive (16 out of 94 patients, 17%) the PPV raised to 100%, whereas when both CUS and CUS were negative (50 out of 94 patients, 53%) the NPV only slightly increased to 94% (95% CI 85–98%).

**Conclusion:** Emergency echocardiography showed high but not optimal sensitiveness specificity and specificity for PE in patients presenting with shock. The addition of CUS significantly increased specificity so that when both tests are positive PE diagnosis is almost certain.

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**CORONARY REVASCULARISATION: HOW AND HOW MUCH**

**P4131 | BEDSIDE**

**Routine invasive versus selective invasive strategies for non-ST-elevation acute coronary syndrome: an updated meta-analysis of randomised trials**

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**Background:** Initial studies documented significant benefits from treating patients with non-ST-elevation acute coronary syndromes (NSTE-ACS) with a routine invasive strategy compared with a selective invasive strategy. An updated systematic approach comparing these 2 strategies is lacking.

**Purpose:** To systematically determine if a routine invasive strategy in patients with NSTE-ACS is associated with improved outcomes compared with a selective invasive strategy in the era of stents and potent antiplatelet therapy.

**Methods:** Electronic databases and major conference proceedings were searched for randomised trials that compared a routine invasive strategy versus a selective invasive strategy in patients with NSTE-ACS. The outcomes assessed in this study were the composite of all-cause mortality or myocardial infarction (MI), and each outcome individually. Summary odds ratios (OR) were primarily constructed using a Peto’s model.

**Results:** Twelve trials with 9,650 patients were included. Compared with a selective invasive strategy, a routine invasive strategy was associated with a reduction in the composite of all-cause mortality or MI (16.4% vs 19.0%; OR 0.84, 95% confidence interval (CI) 0.75–0.93, p=0.001) at a mean follow up of 38 months, primarily due to a reduction in the risk of MI (11.8% vs. 12.5%, OR 0.85, CI 95% 0.80–0.89, p<0.0001). The risk of all-cause mortality was non-significantly reduced with a routine invasive strategy (8.9% vs 10.2%; OR 0.88, 95% CI 0.77–1.01, p=0.07). Among the subgroup that experienced a lower frequency of major adverse cardiovascular events (MACE), the invasive strategy was associated with a significant reduction in all-cause mortality at intermediate follow-up (OR 0.85, 95% CI 0.58–0.98, p=0.04). The risk of recurrent angina was reduced with a routine invasive strategy (15.4% vs 23.6%; OR 0.55, 95% CI 0.49–0.62, p<0.0001).

**Conclusions:** In patients with NSTE-ACS, a routine invasive strategy reduces the risk of ischemic events. Survival benefit from a routine invasive strategy might be enhanced if major bleeding rates are low.

**Acknowledgement/Funding:** This work was supported by Gatorade Trust through funds distributed by the University of Florida, Department of Medicine.

**P4132 | BEDSIDE**

**Differential impact of incomplete revascularization as assessed by reduced SYNTAX score on long-term mortality in patients with STEMI versus NSTEMI: a propensity-matched analysis**

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**Background:** Although incomplete revascularization has been associated with improved outcomes after percutaneous coronary interventions (PCI), limited evidence is available regarding its potentially different effects in patients with ST-segment elevation vs. non-ST-elevation myocardial infarction (STEMI vs. NSTEMI).

**Purpose:** The aim of this study was to compare the impact of incomplete revascularization on 3-year mortality in patients with STEMI vs. NSTEMI.

**Methods:** We propensity-matched 212 patients with NSTEMI from the randomized RIDDLE-NSTEMI study, who were invasively managed within 72 hours of admission, with 212 STEMI patients undergoing primary PCI, from an electronic, prospective, all-comer primary PCI registry. Both groups were treated in our center during 2009–2013. Propensity score matching was carried out by psmatch2 command in STATA. Incomplete revascularization was defined as residual SYNTAX score (SScore) >8.

**Results:** After propensity-matching, baseline characteristics were similar, including Killip class on admission (9% in STEMI vs. 8.5% in NSTEMI; p=0.86) and the presence of multivessel coronary artery disease (CAD) (61.3% in STEMI vs. 63.7% in NSTEMI, p=0.62). Despite the similar rate of multivessel disease, angiographic findings were more complex in patients with NSTEMI (median baseline SScore was 18 in NSTEMI vs. 14 in STEMI, p<0.01). The rate of residual SScore >8 was similar, 63.6% in STEMI and 57.4% in NSTEMI patients (p=0.20). Mortality rates did not differ in patients with STEMI vs. NSTEMI at both 30 days (1.9% vs. 2.8%, respectively; p=0.52) and 3 years (7.1% vs. 8.0%, respectively; p=0.71). In the STEMI group, patients with residual SScore >8 had similar 3-year mortality as patients with SScore >8 (6.1% vs. 8%, respectively; HR 1.32, 95% CI 0.46–3.81, p=0.60). On the contrary, in patients with NSTEMI, residual SScore >8 was associated with significantly lower risk of 3-year mortality compared to residual SScore >8 (4.3% vs. 12.6%; HR 3.19, 95% CI 1.11–9.19, p=0.03).

**Conclusions:** Incomplete revascularization is associated with increased risk of 3-year mortality in patients with NSTEMI, but not in their propensity-matched STEMI counterparts. This finding may suggest a comparatively greater impact of non-coronary factors, such as the extent of irreversible myocardial damage, on the long-term mortality after STEMI.

**P4133 | BEDSIDE**

**Complete or incomplete coronary revascularization in ACS patients with multivessel coronary disease. One year outcomes according to clinical presentation from the real life Bleemacs registry**

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**Background:** The benefit of incomplete (“culprit only”) or complete (“culprit” and “non- culprit lesions”) percutaneous coronary intervention (PCI) in patients with acute coronary syndrome (ACS) and multivessel disease remains debated.

**Methods:** We conducted a multicenter study including all multivessel ACS patients included in the Bleemacs (International Multicenter Acute Coronary Syndrome) registry. Patients were considered according to admission diagnosis (STEMI, NSTEMI and Unstable angina) and divided in two groups before and after comparison with propensity score with matching: Complete revascularization (CR), Incomplete Revascularization (IR). Primary endpoint was death rate at one-year follow-up. Secondary endpoints were in-hospital repeated myocardial infarction (re-AMI), in-hospital heart failure (HF), major cardiovascular events (MACE) and myocardial infarction at one year.

**Results:** Out of 15401 patients, 3995 (26%) were admitted with a diagnosis of ACS and multivessel disease. The majority of them presented with a diagnosis of STEMI (3061; 60.3%), followed by NSTEMI (1458; 28.7%) and Unstable angina (UA) (561; 11.0%) and CR was performed in 833 (27.2%), 619 (42.4%) and 58 (3.7%) respectively. Recanalisation was associated with a lower one-year death rate (4.5% vs 8.5%; p=0.002), re-AMI rate (3.7% vs 6.6%;
All-cause mortality, new myocardial infarction (MI), major bleeding, target vessel revascularization (TVR), vascular complications, stent thrombosis (ST) and stroke. The Mantel-Haenszel (MH) method for odds ratios (OR) and 95% confidence intervals (CI) were computed. A fixed-effect model was used; if heterogeneity (I²) > 40%, effects were obtained using a random model.

Results: Four RCTs (n=389 patients) and six cohort studies (n=1174 patients) were included in the analysis. No difference was found between both strategies for MACE (OR, 0.78; 95% CI 0.53–1.15). We found a significant reduction in all-cause mortality (OR, 2.52; 95% CI 1.72–3.68) and ST (OR, 2.75; 95% CI 1.23–6.12) favoring staged MV PCI. No differences were observed between index and staged MV PCI outcomes for subsequent MI (OR, 1.04; 95% CI 0.62–1.75), major bleeding (OR, 1.31; 95% CI 0.77–2.25), TVR (OR, 0.89; 95% CI 0.60–1.32), vascular complications (OR, 0.92; 95% CI 0.33–2.61) and stroke (OR, 1.48; 95% CI 0.84–2.58). Exclusion of single study from the analysis did not alter the overall result. No evidence of bias was observed.

Conclusions: Staged MV PCI is associated with a lower rate of all-cause mortality and stent thrombosis that index “one time” PCI in STEMI patients. A deferred angioplasty strategy of nonculprit lesions should remain the standard approach to patients with STEMI and MV CAD pending the results of a properly designed randomized trial answering this questions.

P4134 | BEDSIDE

Transradial coronary percutaneous coronary intervention could reduce adverse site complications in STEMI patients requiring intra-aortic balloon pumping support

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Background: Several reports have showed that transradial approach (TRA) decreased access site complications with STEMI patients undergoing acute myocardial infarction (STEMI), compared with transfemoral approach (TFA). Although intra-aortic balloon pumping (IABP) stabilizes patients with impaired hemodynamics, its use may require specific management to prevent cardiovascular bleedings. Published studies show the aim of this study is to investigate which TRA could reduce access site complications in STEMI patients requiring IABP compared with TFA.

Methods: We retrospectively analyzed 196 patients undergoing IABP insertion (17.0%) of 1152 consecutive STEMI patients who received primary percutaneous coronary intervention (PCI) within 12 hours of onset in our hospital between December 2007 and June 2014. TRA was initially performed as possible. The primary end point was in-hospital access site bleeding defined by Bleeding Aca-

Conclusions: In this observational study, TRA might prevent serious access site complications and blood transfusion in high-risk STEMI patients requiring IABP support. In order to reduce access site complications, bifemoral approach should be avoided whenever possible.

P4137 | BENCH

Transradial vs. transfemoral access in patients with ACS: bleeding complications and outcome

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Background: The use of transradial access for PCI is growing and the newly published ESTABLISH guidelines on treatment of NSTEMI/ACS take account of this, providing the necessary experience exists. We studied ways of access in treatment of ACS patients under real world conditions in a big city.

Results: Our Registry collects data on hospital treatment of patients with ACS since 1999. Since 1.4.11 data on different ways of PCI access are collected. We included all 10,146 patients treated with PCI from 20 hospitals (1.4.11–31.12.14). We studied bleeding complications (GUSTO) and the influence of access on hos-

Conclusions: In this observational study, TRA might prevent serious access site complications and blood transfusion in high-risk STEMI patients requiring IABP support. In order to reduce access site complications, bifemoral approach should be avoided whenever possible.
Results: 4165 patients were treated with transradial (41.1%), 5981 with transfemoral (58.9%) PCI access. Transfemoral vs. transradial access influences hospital mortality (OR=1.53; 95% CI: 1.18–1.98) and also influences chances of moderate to severe bleeding (OR=1.69; 95% CI: 1.17–2.45) even after adjustment for differences in patient characteristics and antiplatelet and antithrombotic therapy. Differences between patients with tran...

Conclusion: Our conditioning protocols.

Introduction: The opening of mitochondrial permeability transition pore (mPTP) and myocardial infarction may cooperatively progress myocardial ischemia-reperfusion (IR) injury, which hampers therapeutic effects of primary reperfusion therapy for acute myocardial infarction. Hypothesis: Novel nanoparticle-mediated medicine that simultaneously targets mPTP and myocardial infarfection may settle the unmet needs to suppress severe IR injury. Methods and results: We employed mice lacking cyclophilin D (CypD, a key molecule for mPTP opening) and CCR2 (a receptor for monocyte chemoattrac-
tant protein-1) and found that CypD contributed to progression of myocardial IR injury with shorter duration (30–45 min) of ischemia, whereas CCR2 contributed to IR injury with longer duration (60–90 min) of ischemia (Fig. A). Double deficiency of CypD and CCR2 showed superior cardioprotection over single defi-
ciency regardless of the duration of ischemia (Fig. A). CCR2 deficiency markedly reduced IL-1βeta protein levels and the number of Ly6Chigh activated monocytes in IR-injured myocardium, whereas CypD deficiency reduced infarct size without affecting infarction in the IR heart. Then we engineered poly (lactic-co-glycolic acid) nanoparticle containing cy-
closporine A (CsA-NP) that inhibits mPTP opening and pilavastatin (Pit-NP) that reduces monocyte-mediated inflammation. In CypD-KO mice, Pit-NP reduced the recruitment of Ly6Chigh inflammatory monocytes and infarct size, whereas CsA-NP reduced infarct size in CCR2-KO mice. Simultaneous treatment with CsA-NP and Pit-NP at the time of reperfusion presented a remarkable reduction in infarct size after IR injury with 30 or 60 min of ischemia (Fig. B).

Discussion: Remote ischemic conditioning results in oxidative stress reduction and nitrate-nitrite-nitric oxide pathway activation in acute myocardial infarction patients. Remote ischemic conditioning attenuates ischemia-reperfusion injury in patients with STEMI. However, its effects on vascular function and bio-
chemical mechanisms are not fully defined.

Methods: We examined 110 patients with STEMI and 30 healthy controls. Pa-
tients were randomized in 2 remote ischemic conditioning protocols after a base-
line assessment of vascular function (T0), a) one with two ischemic conditioning
sessions in FITC-dextran labelling (our surrogate for blood flow blockages) tended

Results: Compared to the double cuff inflation, the single cuff inflation proto-
col resulted in a more uniform aortic elasticity improvement (PWV T0: 12.94±0.9m/s, T1:11.7±4m/s, T2:11.5±9m/s, T3:11.8±2m/s) with the greatest difference measured
at T3 compared to baseline in STEMI (2.1±0.15 at T3 vs 2.59±0.15 at T0, >0.001). Conversely, in healthy controls, PWV and PBR
remained unchanged throughout the study (p=0.05). MDA was significantly re-
duced at T3 compared to baseline in STEMI (12.0±15 at T3 vs 2.59±0.15 at T0, p=0.001) in both protocols while it remained unchanged in healthy controls.

Conclusion: Remote ischemic conditioning by a single 5 min cuff inflation, con-
fers acute short-term improvement of vascular function, likely through oxidative stress reduction and nitrate-nitrite-N0 pathway activation.

Results: In % Transradial access Transfemoral access p
Age ≥75 J 25.4 29.3 0.001
Women 26.0 31.2 0.001
STEMI 50.9 50.6 0.794
Diabetes mellitus 27.1 30.3 0.001
Renal failure 12.4 17.0 0.001
CHF 9.4 16.1 0.001
Previous MI 15.5 20.0 0.001
Previous PCI 19.3 23.4 0.001
Cardiogenic shock on admission 2.8 10.4 0.001
IABP 0.7 3.5 0.001
Bleeding (Gusto)
mild 1.4 3.3
moderate 0.8 1.5 >0.001
severe 0.3 0.8
Hospital mortality 2.8 7.8 >0.001

Patient characteristics and in antiplatelet and antithrombotic therapy.

Results: Patients treated with transradial access are older, more often women, suffer from more co-
morbidities and are acute more severely ill. They bleed and die more often in the hospital.

Conclusion: • Transradial access is being used in 41.1% of cases in our registry for treatment of ACS patients.
• Mild, moderate and severe bleeding occurred significantly less often after trans-
radial access.
• Chances of moderate to severe bleeding are increased with transfemoral ac-
cess even after adjustment.
• Hospital mortality is higher for patients with transradial access even after adjust-
ment.
known to relax retinal pericytes (Matsugi et al., 1997) and to reduce the incidence of adverse ventricular remodelling when given during primary percutaneous coronary intervention (Niccoli et al., 2014), reduced the number of capillaries showing no-reflow from 42% to 34% (p<0.042 comparing microvascular perfusion in the infarct core).

Conclusion: These findings suggest an unexpected role for ischaemia-evoked constriction of cardiac pericytes in generating coronary no-reflow. Pericytes are an attractive therapeutic target for limiting infarct size and the associated long term morbidity and mortality of MI, particularly left ventricular remodelling and heart failure.

Acknowledgement/Funding: Supported by the European Research Council, MRC, Rosetrees Trust and Welcome Trust.

NON-CODING RNAS AND THE CONTROL OF NEOINTIMA FORMATION

4199 | BENCH Interstitial transfer of miR-126-3p by endothelial microparticles reduces VSMC proliferation and limits neointima formation by inhibiting LRP6

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Background: Vascular smooth muscle cell (VSMC) proliferation is of importance in the pathogenesis of vascular diseases such as restenosis or atherosclerosis. Endothelial microparticles (EMP) regulate function and phenotype of target endothelial cells (ECs), but their influence on VSMC biology is unknown. We aim to investigate the role of EMPs in the regulation of vascular smooth muscle cell (VSMC) proliferation and vascular remodelling.

Methods and results: Systemic treatment of mice with EMPs after vascular injury reduced neointima formation in vivo. In vitro, EMP uptake in VSMCs diminished VSMC proliferation and migration, both pivotal steps in neointima formation. To explore the underlying mechanisms, Taqman microRNA-array was performed and miR-126-3p was identified as the predominantly expressed miR in EMPs. To explore the underlying mechanisms, Tagman microRNA-array was performed and miR-126-3p was identified as the predominantly expressed miR in EMPs. Next, we analyzed whether miR-100 also modulates contractile marker genes in human vascular aortic smooth muscle cells (hVSMCs) by transfecting precursor (pre-miR-100) or antisense (anti-miR-100) oligonucleotides specific for miR-100 and the corresponding control compounds (pre-miR-cont./anti-miR-cont.). We found an enhanced expression of contractile marker genes following miR-100 overexpression and a decreased expression if miR-100 was inhibited. Accordingly, these in vivo and in vitro findings indicated a crucial role of miR-126-3p in the process of neointima formation.

Conclusion: Although further experiments have to be performed, our first data induce a protective function of miR-100 in the process of neointima formation by upregulating the expression of contractile marker genes in VSMCs.

4201 | BENCH Local inhibition of microRNA 146a using a clinically applicable approach attenuates neointima formation

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Background: Drug-eluting stents and -balloons allow a defined local application of anti-proliferative agents to reduce neointima formation. However, the currently used unsel ective substances also impair endothelial healing and increase the risk for stent thrombosis. MicroRNAs (miRs) are promising therapeutic targets since they exert cell specific functions and can be effectively targeted in vivo.

Methods/Results: Microarray analysis revealed that miR146a is highly upregulated in neointimal lesions of C57BL/6J mice following wire-induced injury of the femoral artery (2.84-fold, p<0.01). In vitro, the knock down of miR146a led to an opposing effect on SMC and endothelial cells (EC). Proliferation and migration were significantly reduced in SMC (62.59%, p<0.05 and 70.38% p<0.001) whereas enhanced in EC (141.90% p<0.05 and 152.96% p<0.05) respectively. Mechanistically relevant for the cell specific effect, vonin, a transmembrane protein specifically expressed in SMC, was shown to be a direct target of miR146a as assessed by qRT-PCR, Western Blot analysis and luciferase activity assays. Consistently, vonin mRNA and protein expression was reduced in neointimal lesions but remained high in LNA-146a treated vessels. Moreover, overexpression of vonin prevented SMC proliferation in vitro. In vivo, local application of a miR146a inhibitor (LNA-146a) in a self-degrading pruronic gel after wire-induced injury of the femoral artery in C57BL/6J mice led to a significant reduction of neointima formation 21 days after injury (Neointima/Media Ratio 61% of control in treated animals n=8; p<0.01). Proliferation of SMC was reduced as assessed by Ki67 immunostaining (22.72% vs 10.26% of neointimal cells, p<0.05). In contrast, re-endothelialization was significantly improved, as determined by en face microscopy of 4 drug ath following Everol’s Blue staining of arterial injury (37.64% vs 62.88% covered area p<0.01). In a further translational approach towards a clinical application, we utilized a rat carotid artery injury model and applied LNA-146a locally using a clinically approved drug application balloon catheter (Sting, 2-4Atm.). Consistently, re-endothelialization was improved and proliferation of neointima SMC (Ki67 positive cells, 8.95% vs 1.92% p<0.01) as well as neointima formation (Neointima/Media Ratio 1.41 vs 0.22, n=8, p<0.001) were significantly reduced 14 days after injury.

Conclusion: This study reports an essential role of miR-146a during acute vascular remodeling in different species. A local and single administration of a miR-146a inhibitor using a clinically approved delivery catheter offers a significantly improved outcome after balloon injury. Thus, local inhibition of miR-146a might
Results of genotype guided antiplatelet therapy in patients undergone percutaneous coronary intervention with stent

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Background: Clopidogrel has provided beneficial effects in acute coronary syndromes and percutaneous coronary intervention. Different polymorphisms have been associated in differences in clopidogrel response. The aim of this study was to check if CYP2C19/ABCB1-genotype-guided strategy reduces the rates of cardiovascular events in patients treated with clopidogrel versus patients treated with other antiplatelet therapies used in genotyping conditions.

Methods: Experimental study included patients undergoing percutaneous coronary intervention with stent. The prospective genotype-guided strategy (intervention group) was compared against a retrospective non-tailored strategy (control group). Primary efficacy endpoint was the composite of cardiovascular death, acute coronary syndrome or stroke during 12 months after intervention. Secondary end-point was to compare the efficacy of the different antiplatelet therapies used in genotyping conditions.

Results: The study included a total of 719 patients undergone stent, more than 86% with acute coronary syndrome. The primary end-point occurred in 32 patients (10.1%) in the genotyping group and in 59 patients (14.1%) in the control group (HR 0.63, 95% CI 0.41 - 0.97, p=0.037). There was no difference in TIMI major and minor bleeding between the two groups (4.1% vs. 4.7%, HR 0.80, 95% CI 0.39–1.63, p=0.55). In intervention group, there was no difference in the rate of restenosis.

Conclusion: Our results demonstrate that genotype-guided strategy reduces the rates of composite cardiovascular death, acute coronary syndrome or stroke during 12 months after percutaneous coronary intervention compared to a non-genotype-guide strategy.

Acknowledgement/Funding: This work was supported by the Ministry of Health of Government of Andalusia, Grant number: PI-057/2012
THE CHANGING FACE OF CARDIOPULMONARY RESUSCITATION

4232 | BEDSIDE
Distance to invasive heart centre, performance of acute coronary angiography and angioplasty and associated outcome in out-of-hospital cardiac arrest: a nationwide study
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Introduction: Field-triage directly to heart centres for acute coronary angiography (CAG) and percutaneous coronary intervention (PCI) regardless of longer transportation distance, may be associated with improved survival in patients with out-of-hospital cardiac arrest (OHCA).

Purpose: To evaluate whether distance from site of event to an invasive heart centre, acute CAG/PCI and hospital-level of care (invasive heart centre versus local hospital) are associated with survival in patients with OHCA.

Methods: Nationwide, historical follow-up of 41,186 patients with OHCA, in whom resuscitation was attempted between 2001 and 2013, identified in the Danish Cardiac Arrest Registry.

Main outcome measures: Crude and adjusted hazard ratios (HR) of 30-day survival and temporal changes in 30-day survival, admission to invasive heart centre, acute CAG/PCI.

Results: During the study period, we observed an increase in the proportion of patients receiving bystander CPR (18% in 2001 to 60% in 2013, p < 0.001), achieving return of spontaneous circulation (ROSC) (10% in 2001 to 29% in 2013, p < 0.001), and being admitted directly to an invasive centre (26% in 2001 to 45% in 2013, p < 0.001). Simultaneously, 30-day survival increased from 5% in 2001 to 12% in 2013, p < 0.001. Among patients achieving ROSC, an increasing proportion underwent acute CAG/PCI (5% in 2001 to 27% in 2013, p < 0.001). Introducing a CAG/PCI index, defined as the proportion of patients undergoing acute CAG/PCI each year in each region, the following variables were associated with survival in multivariable analyses: direct admission to invasive heart centre (HR 0.96, 95% CI 0.93–0.99), CAG/PCI index (adjusted HR 0.27, 95% CI 0.25–0.29), population density (HR 0.92, 95% CI 0.88–0.92), age per 10 year increase (HR 1.04, 95% CI: 1.03–1.05), bystander CPR (HR 0.95, 95% CI: 0.93–0.97), non-shockable heart rhythm (HR 1.33, 95% CI: 1.29–1.37), witnessed OHCA (HR 0.89, 95% CI: 0.87–0.91) whereas distance to the nearest invasive centre was not. These findings support a centralized strategy for immediate post-resuscitation care in patients with OHCA.

Conclusion: Among patients with OHCA, admission to an invasive heart centre and acute CAG/PCI were associated with improved survival, whereas distance to the invasive centre was not. These findings support a centralized strategy for immediate post-resuscitation care in patients with OHCA.

4233 | BEDSIDE
A systematic review and meta-analysis on extracorporeal membrane oxygenation in patients with acute myocardial infarction complicated by cardiogenic shock or with cardiac arrest
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Background: The current European guidelines recommend to consider short-term mechanical circulatory support in ACS patients with cardiogenic shock. Veno-arterial extracorporeal membrane oxygenation (ECMO) is increasingly used in patients during cardiac arrest and in cardiogenic shock due to acute myocardial infarction. Although ECMO usage has improved, increased lack of evidence on the effectiveness of ECMO exists in this setting. In the absence of data from randomised controlled trials, we performed a systematic review and meta-analysis to study the effectiveness of ECMO in patients during cardiac arrest and in cardiogenic shock due to acute myocardial infarction or cardiac arrest.

Method: Publications on the use of ECMO in patients after myocardial infarction complicated by cardiogenic shock or during cardiac arrest were identified by searching medical literature databases using a wide variety of search terms for ECMO combined with myocardial infarction or cardiac arrest. Studies that did not report on survival to discharge, 30-day mortality or long term mortality were excluded.

Results: A total of 1035 publications were identified and title and abstracts were screened by 2 independent reviewers. After detailed full-text evaluation and exclusion of duplicate cohorts, 14 studies were selected for analysis. All studies were case-control studies. Four studies included patients with cardiogenic shock and 9 studies included cardiac arrest patients. A total of 217 patients were included in the cardiogenic shock analysis (151 ECMO versus 66 control patients) and 3098 patients were included in the cardiac arrest analysis (708 ECMO versus 2390 control patients). Five of the cardiac arrest studies provided a propensity matched analysis including a total of 438 patients. In patients with cardiac shock, ECMO showed a decrease in 30-day mortality compared with IABP (risk difference -33%, 95% CI, -52 to -14%; p < 0.001). When compared to TandemHeart or Impella 5.0, there was no difference in mortality (risk difference 3%, 95% CI -14 to 21%; p > 0.70). In the setting of cardiac arrest, the use of ECMO was associated with an decreased mortality at 30-day (risk difference -13%, 95% CI, -20 to -6%; p < 0.001) as well as long term (risk difference -15%; 95% CI, -20 to -11%; p < 0.0001). Also, there was a higher rate of favourable neurological outcome (CP 1 or 2) on both 30-day (risk difference 14%; 95% CI, -6 to -18%; p < 0.0001) and long term (risk difference 11%; 95% CI, 6 to 16%; p < 0.0001).

Conclusions: In the setting of cardiogenic shock, the use of ECMO decreased the mortality compared with IABP. In the setting of cardiac arrest, the use of ECMO was associated with a decrease in mortality as well as an increase in favourable neurological outcome. The use of ECMO should be considered when patients in cardiogenic shock and cardiac arrest.

4234 | BEDSIDE
Prognostic impact of no-flow time, time from cardiac arrest to beginning of basic life support, on 30-day neurological outcomes in patients received extracorporeal cardiopulmonary resuscitation
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Background: Immediate extracorporeal cardiopulmonary resuscitation (ECPR) reportedly improves neurological outcome in patients with out-of-hospital cardiac arrest (OHCA) who do not respond to conventional CPR. However, how time-courses of cardiac resuscitation after OHCA influence neurological outcomes in patients treated with ECPR is unclear. Here we examined this issue by data from consecutive patients with OHCA.

Methods: Of consecutive 1,796 patients with OHCA of endogenous origin admitted to the emergency room in our institute from January 2010 to October 2015, 191 patients were treated in the coronary care unit (CCU) following advanced cardiac life support. Eighty-five of them received ECPR according to the institutional criteria: (1) age under 75 years old, (2) presumed cardiac origin of OHCA and witnessed by bystander, and (3) incessant ventricular fibrillation that was not terminated by conventional CPR. We defined "total collapse-duration" as a time interval from OHCA onset to obtaining stable hemodynamic state with cardiopulmonary bypass or recovery of spontaneous cardiac circulation and "no-flow time" as a time interval from OHCA onset to beginning of basic life support. Mild hypothermia was performed in unconscious patients with stable hemodynamic parameters after OHCA; target core temperature was 34°C and it was maintained for 24–48 hours using extracorporeal cooling system, followed by gradual rewarming over at least 24 hours. Thirty-day neurological outcome was classified into CPC performance category (CPC), and patients were divided into a favorable recovery group (CPC1–2) and an unfavorable recovery group (CPC3–5).

Results: Of 85 patients received ECPR, 33 patients (38.8%) were survived and these favorable recovery group consisted of 14 patients (16.5%). No-flow time was shorter in the favorable recovery group than that in the unfavorable recovery group (1.4±3.0 vs. 5.4±5.9 min, p < 0.001). However, there was no significant difference in total collapse-duration between the two groups (50.1±13.2 vs. 54.9±14.9 min, p = 0.27). Multivariable logistic regression analysis using Glasgow coma scale score on ER arrival, no-flow time, and max creatine kinase-MB during CCU as explanatory variables showed no-flow time (OR 0.85, 95% CI 0.68–0.99, p < 0.05) and max creatine kinase-MB (OR 0.99, 95% CI 0.99–0.99, p < 0.05) were independently associated with the favorable recovery. In receiver operating characteristic curve analysis, optimal cut-off value of no-flow time to predict the favorable outcome was 5 min, of which sensitivity and specificity were 85.7% and 52.1%, respectively (area under curve 0.70, p < 0.05).

Conclusions: The results of no-flow time” is a better predictor of neurological outcomes in OHCA patients received ECPR than “total collapse-duration”. Clinical benefit of ECPR for OHCA patients might be improved by shortening a time interval between cardiac arrest to basic life support.

MOBILE HEALTH FOR CARDIAC MONITORING

4237 | BEDSIDE
Detecting atrial fibrillation via existing smartphones without any add-ons
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Introduction: Atrial fibrillation (AF) is a very common cardiac rhythm abnormality,
present in approximately two percent of all people, i.e. in approximately 140 million people globally. Due to failure of the atrium to contract effectively, a blood clot may form within, which may enter blood flow at a later time and in some cases block a blood vessel in the brain, resulting in a stroke. Up to 25 percent of all strokes are caused by AF. AF sometimes begins as asymptomatic (“silent” AF), in which case an otherwise healthy patient remains unaware of the condition. However, the risk of suffering a stroke due to periodical silent AF is similar to recurrent or persistent AF; hence, when silent AF is detected, similar anticoagulant medication is prescribed as in the case of symptomatic continuous AF. We propose detecting AF with IMU (Inertial Measurement Unit) sensors available in modern smartphones and wearable devices.

**Purpose:** Our objective is to provide simple and cost-effective means for detecting AF (including the “silent” AF). Since many existing mobile devices, such as smartphones, are today equipped with accelerometers and gyroscopes (IMU), they can be used for monitoring the operation of the heart. The purpose is to prevent the consequences of undetected AF with early prevention.

**Methods:** In order to detect AF, a mobile/wearable device is placed on the chest of the patient, and an accelerometer and gyroscope measurement recording is taken from the subject. The patient is advised to lie in a prone/supine position when the measurement is taken. The procedure is non-invasive and can be taken without support from medical staff (or other persons). An automated algorithm extracts features such as autocorrelation and spectral entropy from the pre-processed (FFT filtering and potential noise exclusion) IMU data. A machine learning algorithm, which operates based on the extracted features, is used for classification. We used state-of-the-art machine learning methods such as SVM (Support Vector Machine), Kernel SVM (K SVM) and Random Forest (RF) classifier. The used data was captured in controlled conditions from total of 16 AF patients and additional 20 recordings from healthy volunteers. The data from each person was divided into 10 second non-overlapping segments for feature extraction and classification. The learning part was implemented in desktop environment and the critical data acquisition was implemented on a smartphone.

**Results:** We used 10-fold cross validation to verify classifier performance. The best performing classifier was K SVM with sensitivity of 98.5% and specificity of 95.2%. Out-of-bag classification error for RF was 4.95% (200 grown trees).

**Conclusions:** We proposed a method for detecting AF using smartphone only solution without any add-on hardware. It can be implemented as a software solution for the existing smartphones globally available.

**Acknowledgement/Funding:** Finnish funding agency for innovation (Tekes), Academy of Finland.

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**4238 | BEDSIDE**

**Comparative analysis of a 4-lead portable smartphone-based versus standard 12-lead electrocardiograph for cardiovascular screening in low-income settings**


**Background:** Mobile health technologies are revolutionizing cardiovascular medicine. However, a low-cost, user-friendly smartphone-based electrocardiograph that enables the acquisition of multiple lead Electrocardiograms (ECG), with high similarity to real world standard electrocardiograph, is still lacking. The D-Heart Electrocardiograph has been developed for iOS and Android, enabling the acquisition of the ECG through 5 electrodes (4 peripheral and 1 precordial (V5)) connected to a portable hardware that streams via Bluetooth the trace to the smartphone. Because of the potential impact of this technology as a screening strategy in low-income countries, we performed the present study in a regional hospital in Africa.

**Purpose:** To determine the accuracy of D-Heart Electrocardiograph in the stratification of ECG morphological abnormalities compared to a standard 12 lead ECG, assumed as the gold standard.

**Methods:** Consecutive patients referred for routine medical evaluation to the Regional Hospital of Ziguinchor (Senegal) were enrolled. D-Heart recordings were obtained followed by 12 lead ECGs. The severity of ECG abnormalities was defined by a semi-quantitative score based on the sum of 9 criteria (Del Cre, Int J Cardiol. 2013): abnormal cardiac rhythm, QRS duration <100 ms, Romhilt–Estes (R-E) score <5, fascicular block and/or bundle-branch block, ST-T abnormalities, ST-T segment elevation >0.2 mV, prolonged QTc interval, pathological Q waves and absence of normal Q wave. Four ECG groups were identified: normal (0 criteria); mildly abnormal (1–3 criteria); moderately abnormal (4–6 criteria); markedly abnormal (7–9 criteria). ECGs were analyzed blindly by two independent observers. Discordant adjudications were resolved by a third observer.

**Results:** We evaluated 117 patients (69 males, mean age 39±11 years) of African origin with a mean blood pressure of 119/78 mmHg. Eight (7%) patients had a diagnosis of hypertension, whereas 5 (4%) had history of coronary artery disease. Adjudication according to 12-lead ECG and D-Heart – respectively - was as follows: normal ECG: 69 (59%) vs 72 (61%); mildly abnormal ECG: 45 (38%) vs 42 (36%); moderately abnormal ECG: 3 (3%) vs 3 (3%). Cohen’s kappa ( test showed a concordance of 0.949 (p=0.029) between the two techniques. Thus, while the 12-lead ECG was expectedly more sensitive for mild abnormalities, there was 100% concordance for the moderately abnormal tracings. Of note, concordance was also high regarding to the R-E score (κ=0.868, p=0.038). Comparison of PR and QRS intervals (Bland-Altman method, non-parametric approach) showed excellent accuracy for D-Heart measurements (95% limit of agreement -20 to +20 ms for PR and -10 to +10 ms for QRS).

**Conclusion:** D-Heart ECGs provided accurate, allowing a stratification of ECG abnormalities comparable to the standard 12-lead ECG. This new technique opens promising perspectives for low-cost community cardiovascular screening programs in low-income settings.

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**4239 | BEDSIDE**

**Translation of home-based m-health cardiovascular rehabilitation in real practice**

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**Background and purpose:** Cardiac Rehabilitation (CR) is pivotal to the recovery of individuals surviving a cardiac event. Despite the large benefits, such as improved functional capacity and quality of life, and reduced cardiovascular mortality and hospitalisations, uptake and completion of these programmes remain low (<20%). Barriers to uptake and completion are due to geographical distance/inaccessibility and facilitating factors (transport, conflicting demands with lifestyle and occupational responsibilities), respectively. Recently, a randomized controlled trial (RCT) of an innovative home-based CR programme (m-Health CR) using smartphone and Internet technologies demonstrated the viability of better uptake and completion than, and equal clinical outcomes as that of traditional centre-based CR programmes. The m-Health CR was subsequently employed in a healthcare setting. The objective of this study is to demonstrate its translation to real world practice.

**Methods:** This m-Health CR was implemented within a 6-week CR programme in a health service setting in May 2015. The delivery involved offering eligible patients the option of m-Health CR, using a smartphone CR app on their android mobile handset with set individualized goals to attend the CR programme from their home and/or workplace. As shown in the Figure below, measurements and progress of their CR goals were updated daily via an Internet portal, and discussed and mentored by a clinician on weekly schedules.

A preliminary performance of the m-Health CR programme in real practice over 9 months (May 2015-Jan 2016) was measured via data collected for uptake and completion of the CR programme, functional capacity (6-minute walk test), weight, waist circumference, and blood pressure.
Results: By February 2016, 31 eligible patients were offered the m-Health CR programme. Uptake was 68% (21 patients aged 34 to 67 (mean±SD=55±9 years), 13 male and 8 female). Aside from 4 patients that are still active in CR, and excluded in the analysis, completion rate was 94% with only 1 withdrawal. Patients completing the m-Health CR programme demonstrated an average improvement in the 6-minute walk test (427±36 to 486±63m) with significant reduction in weight (104.7±28 to 102.8±26kg) and waist circumference (115.7±19 to 113.1±20cm) over the 6 weeks. No significant change was observed in blood pressure.

Conclusion: Similar to the RCT study, the m-Health CR programme in real practice shows potential as an optional offering to improve CR service utilization overall. The m-Health CR, unlike the traditional centre-based CR programme, facilitates a more personalized and person-centred CR provision, overcoming patient and geographical barriers. A 12-month evaluation of the m-Health CR programme will be presented.

CORONARY CTA BEYOND THE LUMEN

4242 | BEDSIDE
CT-derived coronary plaque burden and morphological features are associated with impaired myocardial perfusion using [15O]H2O PET independent of conventional risk factors.
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Background: Next to coronary lesion severity, atherosclerotic plaque characteristics may influence downstream myocardial perfusion.

Purpose: The purpose of the current study was to evaluate the association between quantitative plaque burden and plaque morphology using coronary computed tomography angiography (CCTA) and absolute quantitative myocardial perfusion using [15O]H2O positron emission tomography (PET).

Methods: 203 Patients (64% men, age 58±8.7 years) with suspected coronary artery disease were prospectively included. All patients underwent 256-slice CCTA and [15O]H2O PET. Quantitative plaque burden and morphology were assessed using commercially available software.

Results: Atherosclerotic plaques were present in 178 patients and 411 of 607 evaluable coronary arteries. On a per-vessel basis, traditional coronary stenosis indices, such as plaque length and volume, minimal lumen area, plaque burden, and stenosis percentage were significantly associated with impaired haemodynamic myocardial blood flow (MBF). In addition, morphological features such as positive remodelling (PR) and low attenuation plaque (LAP) were other predictors. After adjusting for conventional risk factors, CTA-stenosis severity and plaque type; LAP <60HU and NR-sign remained significant (p<0.001), with an enhancing effect for the NR-sign.

Conclusions: LAP <60HU and NR-sign by CTA are powerful MACE predictors. Prognosis is excellent over a long-term FU period if CTA is negative for CAD, and worsening with an increasing non-calculating plaque component.

4243 | BEDSIDE
Coronary CT angiography characteristics of OCT-defined thin-cap fibroatheroma: section-to-section comparison study

Objectives: This study evaluated whether plaque characteristics and burden assessed by coronary computed tomography angiography (CCTA) were associated with the presence of thin-cap fibroatheroma (TCFA) defined by optical coherence tomography (OCT) in a section-to-section comparison.

Background: CCTA characteristics of OCT-defined TCFA is not well described in per-section level.

Methods: 727 pairs of cross-sections of co-registered CCTA and OCT from 31 coronary lesions in 28 consecutive patients were enrolled retrospectively. By CCTA, plaque characteristics including low attenuation plaque (LAP, <300HU), napkin ring sign (NRS), positive remodeling (PR, remodeling index ≥1.10), and spotty calcification were assessed. Plaque area and plaque burden (plaque area divided by vessel area) were measured using CCTA. By OCT, presence of TCFA, lumen area, arc of lipid, and fibrous cap thickness were determined.

Results: OCT revealed the TCFA in 69 (9.4%) sections from 19 (61.2%) lesions. In per-section analysis, sections with OCT-TCFA showed higher frequency of LAP (58.0% vs. 18.5%), NRS (31.9% vs. 8.8%), PR (68.1% vs. 48.0%), and greater plaque burden (70.6% vs. 61.9%) as compared to the sections without OCT-TCFA (all p<0.05). In multivariable analysis, LAP (odds ratio [OR] 4.05, 95% confidence interval [CI] 2.30–7.20, p<0.001), NRS (OR 2.47, 95% CI 1.29–4.63, p=0.005), and plaque burden (OR 1.03 [per %], 95% CI 1.00–1.06, p=0.042) were associated with the presence of OCT-TCFA. CCTA-measured lumen area correlated well with OCT-measured lumen area (R=0.859, limits of agreement -0.5±3.7 mm²). Non-calculating plaque area by OCT showed significant correlation with OCT-measured arc of lipid (R=0.42, p<0.001).

CVD: FROM PARADOX TO PARADIGM?

4251 | BEDSIDE
Influence of body-mass index and fat distribution on risk of mortality and cardiovascular events in patients with cerebrovascular disease
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Background: A higher body mass index (BMI, kg/m²) has counter-intuitively been shown to relate to a survival advantage in patients with chronic or symptomatic disease, including cerebrovascular disease. This so-called obesity paradox, can lead to uncertainty about weight-loss advice in a select group of patients. The inability of BMI to differentiate between lean body mass and fat may contribute to the unexpected findings.
Purpose: To investigate the relation between different adipose tissue measurements, including those with the ability to estimate body-fat distribution, and risk of cardiovascular events, vascular mortality, and all-cause mortality in patients with cerebrovascular disease.

Methods: In 2124 patients with cerebrovascular disease enrolled in the SMART-cohort, the relation between BMI and risk of cardiovascular events, vascular mortality, and all-cause mortality was estimated using Cox proportional hazards analyses with multivariable adjustment for confounders. BMI was analysed both according to World Health Organization BMI-classifications with normal weight (BMI 18.5–24.9) as reference, and as a continuous variable. Additionally, the relation between risk of outcomes and abdominal visceral adipose tissue thickness (VAT), subcutaneous adipose tissue thickness (SAT), both measured with ultrasound, and VAT expressed as a percentage of total abdominal fat was investigated in a subset of 1703 patients. Restricted cubic splines were made if the relations of interest were non-linear.

Results: The risk of all-cause mortality was lower for overweight (BMI 25–29.9) compared to normal weight patients (HR 0.78; 95% CI 0.64–0.96); a similar but non-significant pattern was observed for vascular mortality (HR 0.82; 95% CI 0.63–1.08). There was no relation between BMI and cardiovascular events. BMI analysed as a continuous variable conferred a U-shaped risk (p-value for non-linearity <0.05) for both all-cause and vascular mortality, with a BMI of approximately 27 related to the lowest risk. A 1SD (1.26 cm) higher SAT was not related to a significant risk of any outcome. However, the relation between SAT and all-cause mortality formed a U-shaped curve (p-value for non-linearity <0.05) with the lowest risk observed for a SAT of approximately 3.5cm, well above the population median of 2.3cm (IQR 1.6–3.1cm). A 1SD (2.6cm) higher VAT (HR 1.17; 95% CI 1.03–1.33) and a 1SD (10%) higher VAT% (HR 1.23; 95% CI 1.03–1.43) was related to an increased risk for all-cause mortality. VAT was best modeled linearly.

Conclusion: A BMI of approximately 27 is related to the lowest risk for all-cause and vascular mortality in patients with a history of cerebrovascular disease. High and low BMI are both related to increased mortality risk. Higher VAT and VAT% were related to a higher risk of all-cause and vascular mortality in patients with cerebrovascular disease, demonstrating the importance of body fat distribution on survival.

828 Cardiobesity: from paradox to paradigm? / Heart failure with preserved ejection fraction

4252 | BEDSIDE
Impact of body mass index and nutritional status on cardiovascular outcomes in patients with stable coronary artery disease

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Background: An inverse association between obesity defined by body mass index (BMI) and prognosis has been frequently reported in patients with coronary artery disease. However, the ability to use this algorithm effectively in daily clinical practice is limited due to the absence of validated and reproducible tools. A simple, fast and reproducible echocardiographic approach to grade left ventricular diastolic function. However, the ability to use this algorithm effectively in daily clinical practice is limited due to the absence of validated and reproducible tools.

Cox regression analysis

Conclusion: BMI in combination with CONUT score is a useful predictor of cardiovascular events in patients after elective PCI.

4253 | BEDSIDE
The Obesity Paradox in patients with non-valvular atrial fibrillation: observations from the SPORTIF trials

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Background: Obesity is a major cardiovascular (CV) risk factor and confers a higher risk for developing atrial fibrillation (AF), however the relationship between obesity and non-valvular AF (NVAF) and outcomes is still unclear.

Purpose: To ascertain the prevalence of overweight and obesity in NVAF patients, and their influence on adverse events and the relationship with anticoagulation control.

Methods: Post-hoc analysis of SPORTIF III and V trials. All patients assigned to the warfarin arm with data on body mass index (BMI), categorised according to WHO. Time in therapeutic range (TTR) was used as an index of the quality of anticoagulation control.

Results: Among 3,630 patients (median [IQR] age 72 [66–77] years; 69.7% males) based on BMI, 909 (24.1%) were of normal weight, 1,446 (39.8%) overweight, and 1,310 (36.1%) obese. Survival analysis showed that patients with normal weight had a higher risk for the composite outcome of stroke and death (Log-Rank:24.860, p<0.001), stroke (Log-Rank:9.204, p=0.010) and all-cause death (Log-Rank:16.801, p<0.001) occurrence. Both overweight (p=0.015) and obese (p<0.001) categories were inversely associated with the composite outcome, as well as for the endpoint of stroke (p=0.047 and p=0.007,respectively). All-cause death was only inversely associated with obesity (p=0.008). Cox regression analysis using TTR as a continuous variable showed attenuation of the association between overweight and stroke risk (hazard ratio:0.64,95% confidence interval:0.39–1.04, p=0.073). In patients with TTR>70%, BMI category was not associated with both composite outcome and stroke.

Cox regression analysis

HEART FAILURE WITH PRESERVED EJECTION FRACTION

4260 | BEDSIDE
A simple, fast and reproducible echocardiographic approach to grade left ventricular diastolic function

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Background: The American Society of Echocardiography and European Association of Echocardiography (ASE/EAE) have published an algorithm for the grading of diastolic function. However, the ability to use this algorithm effectively in daily...
Due to inconsistencies between diastolic myocardial wall velocities and results:

**Purpose:** To test the feasibility of the ASE/AE algorithm for grading of diastolic function and to compare this with a new Thoraxcenter (TXC) algorithm.

**Methods:** The ASE/AE and TXC algorithms were applied to 200 patients. The ASE/AE algorithm starts with assessment of diastolic myocardial wall velocities and left atrial (LA) volumes with subsequent assessment of E/A ratio, E-wave deceleration time and pulmonary venous flow. The TXC algorithm reverses these steps, uses LA dimension instead of volume and does not include a Valsalva manoeuvre and pulmonary venous flow.

**Results:** Due to inconsistencies between diastolic myocardial wall velocities and LA volumes and a not covered E/A ratio in the range of 1.5–2 it was not possible to classify 48% of patients with the ASE/AE algorithm, as opposed to only 10% by the TXC algorithm. LA volume was always needed in the ASE/AE algorithm. In only 64% of patients LA size was necessary by the TXC algorithm. When LA volume would have been used instead of LA dimension, grading of LV diastolic function would have been different in only 2% of patients without apparent improvement. Assessment of LA dimension was considerably faster than LA volume.

**Conclusions:** In daily practice it is not possible to feasibly use the algorithm endorsed by the ASE/AE for grading LV diastolic function. On the other hand, the proposed TXC algorithm did allow assessment of LV diastolic function in 90% of consecutive patients in sinus rhythm in an efficient manner. The TXC algorithm to grade LV diastolic dysfunction was compared to the ASE/AE algorithm simpler, faster, better reproducible and yielded a higher diagnostic outcome.

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**4261 | BEDSIDE**

**Peak left atrial strain is determined by left ventricular systolic function and filling pressure**

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**Introduction:** Peak left atrial (LA) strain during left ventricular (LV) systole has been proposed as an index of LV filling pressure. Since LA filling is determined mainly by the suction effect that results from systolic descent of the atrioventricular (AV) valve, we hypothesized that LV longitudinal shortening is a determinant of LA strain. Potentially, LA volume may also influence LA strain, as a large cavity is associated with relatively reduced deformation.

**Purpose:** To explore determinants of LA strain.

**Method:** In 45 patients we performed simultaneous echocardiography and measurement of pulmonary capillary wedge pressure, which is an indirect measure of LV filling pressure. LA strain and LV global longitudinal strain (GLS) were assessed by speckle tracking echocardiography. We used GLS as a measure of LV longitudinal shortening. LA volume was measured by echocardiography. We analyzed the relationship between LA strain and each of the three putative predictors: LV GLS, LV filling pressure and LA volume.

**Results:** Using single regression analysis, we found that LA strain correlated significantly with each of the three predictor variables (Fig. 1 a–c), but the strongest correlation was with LV GLS. Using multiple regression analysis, only the correlations to LV GLS and LV filling pressure remained significant (Fig. 1 a–c).

**Conclusion:** LV GLS and LV filling pressure were strong determinants of LA strain. This implies that LA strain is determined by LV systolic as well as diastolic function. Therefore, the ability of the LA strain to predict LV filling pressure is confounded by interaction with LV systolic function.

**Acknowledgement/Funding:** South-Eastern Norway Regional Health Authority

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**4262 | BENCH**

**Finerenone improves diastolic function in a preclinical model of type-2 diabetes mellitus**

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**Background:** Obesity and diabetes are independent risk factors for cardiovascular and chronic kidney disease (CKD) development, while heart and kidney injury induced by diabetes is associated with increased inflammation and fibrotic remodeling. Although mineralocorticoid receptor (MR) antagonism has shown beneficial effects against CKD and cardiovascular injury induced in animal models of diabetes, the benefit of novel non-steroidal MR antagonists (MRAs), such as finerenone (Fin), in this context is unknown.

**Purpose:** To test the efficacy of Fin, a non-steroidal MRA, against kidney injury and left ventricular (LV) remodeling in Zucker fa/fa rats.

**Methods:** We assessed in Zucker fa/fa rats the effects of short- (8 days; DB) and long-term (90 days; D90) Fin (1 mg/kg/day as food additive) on LV remodeling (echography), LV hemodynamic (catheterization) and renal function.

**Results:** After 3 months untreated Zucker rats presented a slight raise in plasma urea, an increase in renal vascular resistance, an extensive renal interstitial fibrosis and increased TGF-beta, Collagen I and CTGF mRNA levels in the renal cortex. Fin did not significantly prevent these alterations. Zucker rats developed proteinuria and elevation of NGAL, a renal injury marker; Fin decreased proteinuria after 1 month (Zucker: 185±21 mg/24 h, Zucker+Fin: 127±14 mg/24 h, p < 0.05) and 3 months (Zucker: 362±27, Zucker+Fin: 289±18 mg/24 h, p < 0.05). Three months treatment with Fin also decreased the renal NGAL mRNA levels by 50%. Fin prevented LV diastolic dysfunction observed in Zucker rats (Table) and reduced LV hypertrophy (Lean: 0.92±0.20 g; Zucker: 0.99±0.20 g, p < 0.05 vs lean; Zucker+Fin: 0.92±0.30 g, p < 0.05 vs Zucker) as well as LV collagen density (Lean: 1.9±0.3%; Zucker: 3.4±0.5%; p < 0.05 vs lean; Zucker+Fin: 1.9±0.2%, p < 0.05 vs Zucker).

**Conclusions:** We show that the non-steroidal MRA Fin prevents proteinuria and LV diastolic dysfunction in a preclinical model of type-2 Diabetes Mellitus.

**Acknowledgement/Funding:** Financial support from Bayer Pharma AG

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**AORTIC VALVE INTERVENTIONS: A REVOLUTION?**

**4269 | BEDSIDE**

**In-hospital outcome of surgical low risk patients after TAVI compared to surgical cardio surgery - a case control analysis of all patients in Germany 2014**

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**Background:** The in-hospital mortality of patients after isolated elective or urgent aortic valve replacement (AVR) and logistic EuroScore (ESC) > 10 and comparable ES values is significantly lower after transfemoral catheter based procedure (TAVI-TF) compared to surgical valve replacement (SAVR). This does not apply for patients with ESC < 10 [1].

**Objective:** Can the difference of in-hospital mortality after TAVI-TF compared to SAVR (2.3% vs. 1.5%, p < 0.009) be explained by the different risk profile of TAVI-TF patients?

**Methods:** Case control analysis of all patients in Germany in 2014 with elective or urgent AVR based on the dataset of the AQUA institute according to German law (§137 SGB V). Due to the fact that no patient with ESC < 10 was treated by TAVI-TF, only cases with ESC ≥ 1.505 and < 10 were included. The adjusted mortality risk was determined by AXL score, which is - based on multiple logistical regression analysis - the official (authorized and published) risk adjustment for isolated AVR
in Germany. For each patient with TAVI-TF (n=2751) one case out of the SAVR cohort (n=8844) with identical mortality risk was selected.

Results: 1223 pairs (1 SAVR and 1 TAVI-TF) with identical AKL risk score were identified. Basic characteristics of these patients (age, sex, ASA classification, co-morbidities like diabetes) were identical or without statistically significant differences except parameters shown in Table 1.

In-hospital mortality was 2.1% after SAVR and 2.2% after TAVI-TF (ns). Compared to the SAVR-group the TAVI-TF-group showed either the same or a higher risk-level for procedural risk-factors.

Table 1. Significant differences between patients with SAVR and TAVI-TF

<table>
<thead>
<tr>
<th>Parameter</th>
<th>SAVR (%)</th>
<th>TAVI-TF (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ES (%)</td>
<td>4.6±1.6</td>
<td>6.0±1.7</td>
<td>0.007</td>
</tr>
<tr>
<td>NYHA III (%)</td>
<td>61.8</td>
<td>74.0</td>
<td>0.001</td>
</tr>
<tr>
<td>Prior PCI (%)</td>
<td>9.2</td>
<td>14.2</td>
<td>0.001</td>
</tr>
<tr>
<td>Neurological disease (%)</td>
<td>6.5</td>
<td>15.0</td>
<td>0.001</td>
</tr>
<tr>
<td>Cerebrovascular disease (%)</td>
<td>4.7</td>
<td>9.0</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Conclusion: There is no difference in in-hospital mortality after SAVR and TAVI-TF of low surgical risk patients with ES ≥1.505 and ≤10 and identical risk according to AKL score.


Acknowledgement/Funding: German Cardiac Society

4270 | BEDSIDE
Mortality trends in low-, intermediate- and high-risk patients undergoing transcatheter aortic valve implantation: real-world experiences except parameters shown in Table 1

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Aims: This study aims to describe 30-day and 1-year mortality trends in patients undergoing TAVI. Patients were subdivided and compared by risk category as determined by their STS score.

Methods and results: Between October 2006 and November 2015, 1354 patients underwent TAVI in our center. All patients were considered inoperable or at high surgical risk by a multidisciplinary team. The transfemoral approach was used in 63.0% of cases. Society of Thoracic Surgeons Predicted Risk of Mortality (STS PROM) score was used to subdivide patients into low-risk (STS < 4%: n=423; 31.1%), intermediate-risk (STS 4 - 8%: n=608; 44.9%) and high-risk subgroups (STS > 8%: n=325; 24.0%). Mean STS score in the low-, intermediate- and high-risk subgroups was 2.9%, 5.7%, and 13.0%, respectively. Mean age was 79.1, 85.0 and 86.1 years, respectively (p < 0.0001). Mean EuroScore 2 was 3.8%, 6.4% and 10.0% in the three subgroups, respectively (p < 0.0001). Patients were also subdivided into tertiles according to procedure date (T1: 2006 to 2012; n=435; T2: 2012 to 2014; n=348; T3: 2014 onwards: n=571). Low-risk patients represented 20.2%, 28.4% and 41.0% of T1, T2 and T3, respectively (p < 0.0001). Intermediate-risk patients were present in the following proportions of T1, T2 and T3, respectively: 43.9%, 51.1%, and 40.9% (p < 0.0001). High-risk patients were present in the following proportions of T1, T2 and T3, respectively: 35.9%, 20.4%, and 17.2% (p < 0.0001).

Thirty-day mortality was 14.3%, 9.6%, 4.3% in the high-, intermediate- and low-risk groups, respectively (log-rank p < 0.05 for all pairwise comparisons). In T3, 30-day mortality was 2.3% in the low-risk group. Overall 1-year mortality (median follow-up: 267 days) was 23.2% by Kaplan-Meier estimate. Mortality at 1 year was 34.2% in the high-risk, 22.1% in the intermediate-risk and 15.5% in the low-risk subgroup (log-rank p < 0.01 for all pairwise comparisons; Figure 1).

Conclusion: There is no difference of in-hospital mortality after SAVR and TAVI-TF of low surgical risk patients with ES ≥1.505 and <10 and identical risk according to AKL score.

4271 | BEDSIDE
Single center long-term results after aortic valve-sparing operation (David procedure) in over 500 patients


Background: Composite replacement with a prosthetic-valved conduit (Bentall procedure) has been seen as the “Gold standard” for the treatment of a combined pathologic of the ascending aorta and the aortic valve. However, disadvantages are the need for life-long anti-coagulation (mechanical valve) or degeneration (tissue valve). Valve sparing aortic root operations such the re-implantation (David) procedure preserve the native valve.

Purpose: Few long-term results of aortic valve sparing David procedure have been published. We present our results in over 500 patients that underwent the David procedure in our institution in over 10 years.

Methods: Between 7/1993 and 10/2015 622 patients underwent David Procedure at our center. 582 patients (mean age 53±15 years, 69% male) were operated according to the original technique proposed by Titone David (David I). The rest underwent David Procedure with Valsalva Prosthesis. One-sortic aortic valve-sparing operations such the re-implantation (David) procedure preserve the native valve.

Results: 410 patients (70%) received concomitant procedures (e.g. CABG, mitral valve repair, aortic arch surgery). 51 patients (9%) underwent additional aortic valve cuspid plastic; 35 patients (6%) were operated through minimally invasive access. Perioperative mortality was 3.8% (2.3% elective; 10% acute dissections; 0.6% isolated David Procedure). Stroke rate was 2.6% (15/582). Discharge echocardiography showed no aortic insufficiency (AI 0°) in 53% (312/582) or trivial AI in 37% (215/582). Follow-up (mean follow up 6.8±4.0, maximum 23 years) was 95% complete. 116 patients (20%) died during follow up (4.2±3.5 years post surgery); 9 deaths (7.6%) were valve related. 5, 10, 15 and 20 year survival was 88%, 77%, 74% and 73%, respectively. 57 patients (9.8%) underwent aortic valve re-operations during follow up (3.5±3.4 years post surgery). Cause of reoperation was AI >2 in 68% (39/57) and endocarditis in 14% (8/57). 5, 10, 15 and 20 year freedom from aortic valve related reoperation was 92%, 87%, 86% and 85%, respectively. Follow-up echocardiography of 525 (90.2%) event-free patients showed AI 0° in 46 (8.8%) and AI 1+ in 3 (0.6%) patients after 6.6±4.0 years.leaflet degeneration due to proposed leaflet contact with the straight Dacron graft was not observed.

Conclusions: Valve-sparing David I procedure has excellent long-term results. Freedom from valve related complications such as stroke or major bleeding are exceedingly low. Erosion due to supposed leaflet contact with the straight Dacron graft in “David I” procedure was not observed in a single patient. The “squared valve” – being native living tissue – seems to be more resistant to infection than prosthetic valves.

ENDOTHELIAL CELLS

4277 | BENCH
Dysfunctional endothelial primary cilia promote cardiac fibrosis by enhancing endothelial to mesenchymal transition

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Background: Cardiac fibrosis represents the final common pathway through which various risk factors lead to irreversible cardiac failure. Endothelial to mesenchymal transition (EndMT) has been postulated to represent an important source of fibroblasts that contribute to cardiac fibrosis. The primary cilium has emerged as a vital sensory organelle that responds to mechanical and biochemical stimuli and transduces intravascular signals to regulate nuclear expression patterns and guide fate and lineage decisions.

Purpose: We sought to determine if the primary cilium limits aberrant EndMT and accordingly limit cardiac fibrosis.

Methods: To conclusively evaluate the role of endothelial primary cilia towards cardiac fibrosis we used the Cre-loxP technology to generate mice with endothelial
Biology and Neurobiology - IBCN, Rome, Italy; 5 Dermopatic Institute of the
Conclusions:
miR-200c disrupts SIRT1/FOXO1/eNOS regulatory loop. This event
These results were validated in two in vivo models of oxidative stress i.e. skin
Results:
endothelial nitric oxide synthase (eNOS) and forkhead box O1 (FOXO1). SIRT1
previously demonstrated that hydrogen peroxide (H2O2) induced miR-200c ex-
Results:
endothelial COX2-mediated pro-inflammatory and pro-fibrotic genes collagen-I and CTGF, and Wnt/β-catelin signaling. In vivo, lung
endothelial cells isolated from IFT88endo mice demonstrated a mesenchymal phenotype with concomitant reductions in endothelial markers and elevations in mesenchymal markers. IFT88endo mice exhibited 30% higher mortality following TAC, with evidence of increased cellular fibrosis, and cardiac dysfunction.

Conclusions: Endothelial primary cell cultures as a completely novel and previ-

Acknowledgement/Funding: Canadian Institutes of Health Research

4287 | BENCH
Oxidative stress-induced miR-200c disrupts the regulatory loop
among SIRT1, FOXO1 and eNOS, causing endothelial dysfunction
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Background: Oxidative stress plays a causal role in different pathophysiological conditions including aging, diabetic vascular disease and reperfusion injury. We previously demonstrated that hydrogen peroxide (H2O2) induced miR-200c expression in endothelial cells (EC) by provoking apocynin and nazarosine. As a glut
Salutare (IRCCS), Unità di Biologia Vascolare e Medicina Rigenerativa, Milan, Italy

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Methods: Human Umbilical Endothelial Cells (HUVECs) were treated with 200 mM H2O2 for 8h, 16h, 24h. miR-200c over-exression in HUVECs was induced by lentiviral infection with pre-miR-200c encoding vectors compared to miR-scramble control virus. MiR-200c inhibition in HUVEC was achieved by transient transfec-
tion of antimiR-200c or anti-scramble sequences. 3'UTR luciferase constructs, control virus. MiR-200c inhibition in HUVEC was achieved by transient transfec-
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Results:

Purpose: We aimed to dissect the role of miR-200c on SIRT1/eNOS/FOXO1 auto-regulatory loop.

Methods: Human Umbilical Endothelial Cells (HUVECs) were treated with 200 mM H2O2 for 8h, 16h, 24h. miR-200c over-expression in HUVECs was induced by lentiviral infection with pre-miR-200c encoding vectors compared to miR-scramble control virus. MiR-200c inhibition in HUVECs was induced by transient transfection of anti-miR-200c or anti-scramble sequences. 3'UTR luciferase constructs, wild type or sequence deleted, were transfected with miR-200c or scramble sequences in HEK-293 cells. Luciferase assay was performed to determine miR-200c targeting. Hindlimb ischemia was induced in 2–3-month-old C57BL/6N mice by dissection of the left femoral artery. Human skin fibroblasts were

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Background: We previously demonstrated that transglutaminase-2 (TG2) may contribute to the angiogenes- 

Purpose: Here we hypothesized that TG2 may contribute to the impaired functional properties of resistance arteries from angiogenes- 

Methods: TG2-knockout mice (TG2-K/O, 12 weeks old, n=6) and age-matched wild type (WT) mice were treated or not with angiogenes- 

Results:

Conclusion: miR-200c targeting. Hindlimb ischemia was induced in 2–3-month-old C57BL/6N mice by dissection of the left femoral artery. Human skin fibroblasts were

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2481 | BENCH  
**The microRNA mir-483-3p affects vascular response to injury by promoting endothelial cell apoptosis**

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**Background:** We have observed a significant upregulation of miR-483-3p in mouse early outgrowth cells (EOCs) from patients with coronary artery disease (CAD) and concomitant type 2 diabetes (T2D) associated with a reduced capacity to support endothelial repair. This led us to investigate the functional relevance of miR-483-3p for endothelial homeostasis and the response to acute vascular injury.

**Methods:** Expression of the miR-483-3p was assessed by RT-qPCR in human aortic endothelial cells (HAEC) and in EOCs obtained from CAD patients with or without T2D and from healthy controls. HAEC or EOC were transfected with a precursor (miR-483-3p-P) or Power Inhibitor of miR-483-3p (antimiR), as compared to scrambled control (scr). After 24h, survival, proliferation and migration of the transfected cells to in vitro and in vivo re-endothelialization were assessed. In HAEC, apoptosis was assessed by flow cytometry. Regulation of the predicted target Vascular Endothelial Zinc Finger-1 (VEZF-1), an anti-apoptotic and pro-angiogenic transcription factor, by miR-483-3p was assessed by lucerase assay. The in vivo expression and regulation of mmu-miR483* and VEZF-1 was studied in aortae Leptin-receptor deficient (db/db) mice or wildtype (WT) mice after i.v. injection with anti483 or scr.

**Results:** Transfection of HAEC with mmu-miR483 reduced VEZF1 mRNA expression (mir-483: 3.83±0.32 vs scr: 4.81±0.24; P=0.03), induced apoptosis (mir483: 13.6±1.1% vs. scr: 4.21±1.7%; P<0.04) and impaired HAEC in vitro re-endothelialization (mir483: 19.48±4.4% vs. scr: 44.5±3.1%; P<0.0001). Co-transfection of HAEC with mmu-miR483 significantly reduced luciferase activity from the VEZF-1 3’UTR vector. Mmu-483* is low expressed in the vascular wall of WT B6 mice but significantly increased in db/db mice. LNA-anti483 injection reduced vascular mmu-483* levels in db/db mice. VEZF1 is basally expressed in aortae of WT but not detectable in db/db mice. I.v. injection of anti483 partially restored VEZF1 expression in db/db mice. Transection of EOC from H volunteers with mmu483 reduced their capacity to support re-endothelialization in vitro and in a mouse model of acute vascular injury (mir483: 33.5±3.2% vs. scr: 24.8±2.3%; P<0.05). Vice versa, transection of EOC from CAD-T2D patients with anti483 enhanced their capacity to support in vivo re-endothelialization (anti483: 31.2±3.1% vs. scr: 21.6±2.6%; P=0.03).

**Conclusion:** Upregulation of miR-483-3p may jeopardize re-endothelialization after vascular injury in patients with T2D. Within vascular endothelial cells, the downregulation of the proangiogenic transcription factor VEZF-1 via miR-483-3p appears to permit increased endothelial cell apoptosis. Additionally, elevated miR-483 levels in EOC may affect their paracrine support for the re-establishment of a homogenous endothelium. The repression of miR-483-3p levels in patients with T2D potentially offers a therapeutic strategy to improve their vascular response to injury.

_Acknowledgement/Funding:_ Deutsches Zentrum für Herz-Kreislauf-Forschung (DZHK), Berlin Institute of Health (BiH), Bank Vantobel

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2482 | BENCH  
**Absence of endothelial tumor suppressor p53 in mice prevents the enhanced venous thrombus formation and delayed thrombolysis resolution observed with age**

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**Background:** Venous thromboembolism (VTE) is a leading cause of morbidity and mortality, especially in elderly people. Endothelial cell dysfunction constitutes a major risk factor for thrombosis. Increased expression of p53 has been implicated in the development of vascular senescence, i.e. age-associated changes in the arterial and venous vasculature system.

**Purpose:** To determine the importance of endothelial p53 expression for venous thrombosis and to examine whether vascular senescence and increased levels of endothelial p53 may be causally involved in the exponential increase of VTE with age.

**Methods:** Male mice with conditional, endothelial cell-specific deletion of p53 (End-p53-KO) and their age- and sex-matched wildtype littermates (End-p53-WT) were subjected to subtotal ligation of the inferior Vena cava (IVC) to induce venous thrombosis followed by non-invasive ultrasound measurements over three weeks.

**Results:** IVC ligation in aged (i.e. 12 month-old) End-p53-WT mice was associated with a non-significant increase in the rate of thrombus formation compared to adult (i.e. 2 week-old) End-p53-WT mice (11 of 18 vs. 9 of 21 mice; P=0.65). In male and larger median thoracic area in aged compared to adult End-p53- WT mice (3.7 [0.7–4.7] vs. 0.0 [0.0–5.2] mm²; P=0.226). On the other hand, aged End-p53-KO mice were protected from the development of venous thrombosis following IVC ligation (0 out of 14 mice; P<0.01 vs. aged End-p53-WT mice). Sevral in vivo measurements were performed that indicated reduced thrombus formation more slowly in aged End-p53-WT mice (99 vs. 77% thrombotic lumen occlusion after 14 days). Histological analysis of veins obtained at tissue harvest 21 days after injury confirmed significantly larger residual thrombi in aged vs. adult End-p53-WT mice only (P<0.05). In line with more advanced thrombus organisation, higher amounts of interstitial collagen were observed in thrombi of aged vs. adult End-p53-WT mice (P<0.05). Immunohistochemistry revealed a greater CD31-immunopositive area in adult vs. aged End-p53-WT mice (P<0.05), suggesting that reduced thrombus revascularisation may have contributed to the delayed thrombus resolution in aged animals. On the other hand, similar numbers of Mac2-immunopositive macrophages were observed in adult and aged End-p53-WT mice (16.4±1.3 vs. 13.2±1.6%; P=0.196). Analysis of human vein endothelial cells with replicative cellular senescence (as confirmed by increased expression of senescence markers phospho-histone H2AX and p16INK4a) revealed a marked increase of p53 as well as the anti-fibroinhibitory factor plasminogen activator inhibitor-1 in senescent HUVEC.

**Conclusion:** Our findings suggest that endothelial senescence and increased p53 expression contribute to venous thrombosis by altering thrombus revascularisation and the expression of endothelial factors regulating fibrinolysis.

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2483 | BENCH  
**Deficiency of protease-activated receptor 1 and 2 reduce the progression of experimental pulmonary hypertension in mice**

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**Background:** Pulmonary arterial hypertension (PAH) is a fatal disease, harbouring a high mortality. PAH is characterized by pulmonary vasoconstriction and increased migration and proliferation of vascular smooth muscle cells (SMC) contributing to vascular remodeling. Progressive vascular obstruction elevates pulmonary vascular resistance leading to right ventricular (RV) hypertrophy and dysfunction. Recent data indicate that protease-activated receptors (PARs) 1 and 2 may induce SMC migration and proliferation and thus promote vascular remodeling. Notably, PARs can be activated via the coagulation proteases Factor Xa (FXa) and thrombin.

**Objective:** Here, we tested the hypothesis that activation of PAR-1 and 2 critically contributes to experimental pulmonary hypertension (PH) and that thrombin and FXa induce proliferation and migration of pulmonary arterial SMC (PASMC) via activation of PAR-1 and PAR-2. Hence, PAR-1 and PAR-2 deficiency was analyzed in the model of hypoxia-induced PH in mice. Finally, thrombin and FXa-elicited migration and proliferation were tested in both human and murine PASMC isolated from wildtype (WT), PAR-1 (−/−) and PAR-2 deficient (PAR-2−/−) mice.

**Methods:** To induce PH, 8 week-old, male WT, PAR-1−/− and PAR-2−/− mice were exposed to hypoxia (10% O2) for 21 days. RV systolic pressure (RVS) was measured via heart catheter and the RV hypertrophy was determined as ratio of RV weight to body weight (RV/BW). WT, PAR-1−/− and PAR-2−/− mice kept under normoxia served as healthy controls. Cellular proliferation was determined via BrdU incorporation and chemotaxis was studied in a modified Boyden chamber. Underlying signaling events were characterized by Western Blot and the use of specific inhibitors.

**Results:** PAR-1 deficiency significantly decreased hypoxia-induced RVSP- el...
Novel nanosystems to combat atherosclerosis: Functional effects on human endothelial and monocytic cells


Background: The potential clinical impact of nanotechnology in terms of detection and treatment of cardiovascular diseases is enormous, but no specific nanoparticle-based system has been approved for diagnosis or therapy of atherosclerosis. To ensure clinical safety, the diagnostic and drug-carrying nanoparticles need to be subject to a close toxicologic scrutiny in vitro. Thus, the purpose of this work was to investigate the effects of different types of nanoparticles on endothelial (EC) and monocytic cell functions.

Methods: Long-term effects of nanoparticles on EC viability were assessed by real-time cell analysis and live cell imaging. ECs grown in bifurcating slides were treated with nanoparticles, polymeric and iron oxide nanoparticles. Some of the nanosystems contained P-selectin targeting agent (fucoidan), contrast agent (gadolinium). The majority of the formulations (lauric acid and albumin-coated) inhibited monocytic cell chemotaxis, by affecting Rac1-mediated MR signaling and oxidative stress, by inducing oxidative stress, by affecting Rac1-mediated MR signaling and oxidative stress, by affecting Rac1-mediated MR signaling and oxidative stress, by affecting Rac1-mediated MR signaling and oxidative stress.

Conclusions: These results demonstrate a crucial role for PAR-1 and PAR-2 in the modulation of the molecular mechanisms underlying the benefit of MR antagonists in atherosclerosis.

Benefit of finerenone in renal ischemia/reperfusion injury: mandatory role of MR in aortic smooth muscle cells

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Aortic dissection (AD) is a common and fatal disease for which pathogenesis is largely unknown. Although AD is known to be associated with inflammatory response, the significance of inflammatory response in AD remains to be clarified. Recently we and others reported that Jak/STAT3-activating cytokines are increased in the serum of AD patients. In this study we aimed to determine the specific contribution of the MR expressed in endothelial and smooth muscle cells.

Results: Benefin of finerenone in renal ischemia/reperfusion injury (IR) was assessed using a mouse model of renal IR injury. Mice were studied 24 h after reperfusion. Primary rat SMC cultures were used to signal pathways modulated by MR.

Conclusion: Finerenone limits renal injury induced by IR. Moreover, genetic deletion of MR in SMC only has similar effects. This benefit was associated with reduced oxidative stress, by affecting Rac-mediated MR signaling and oxidative stress.

Lipid nanoparticles also dose-dependently reduced monocyte cell adhesion to ECs under non-uniform shear stress. Lipid nanoparticles may be used in the treatment of atherosclerosis.
4287 | BENCH
Susceptibility to induced ventricular tachycardias increases with time after transplantation of induced pluripotent stem cell-derived cardiomyocytes into infarcted mouse hearts

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Introduction: One major concern regarding cardiac cell replacement therapy is the potential arrhythmic risk after transplantation of stem cell-derived cardiomyocytes (CM). Previous studies provided conflicting results on pro- or antiarrhythmic effects of embryonic stem cell-derived CM after transplantation, but did not include induced pluripotent stem cell derived cardiomyocytes (iPSCM). Thus, we investigated the arrhythmic potential of iPSCM after transplantation in infarcted mouse hearts.

Methods: Murine iPSCM expressing eGFP and a puromycin resistance under control of the alpha-3HMC promoter were purified by bacterial挑选. iPSCM (500,000 cells/10 μl) or PBS (10 μl) were injected into adult mouse hearts after LAD ligation. At different time points (6 days, 6 weeks and 3 months) after transplantation, programmed stimulation was applied by a right ventricular electrophysiological catheter. External ECG recordings revealed number and duration of induced fibrillation episodes. Afterwards, hearts were resected and viable ventricular tissue sections were harvested for electrograms of iPSCM in transplanted iPSCM and host CM. Slices were stimulated by a unipolar electrode placed in healthy host tissue.

Results: Microscopic evaluation revealed no eGFP positive iPSCM within the infarct area, but persistence and electrical integration of iPSCM could be demonstrated in the perifarct zone. The maximal stimulation frequency without induction of ventricular fibrillation was 9±1.5Hz. Transplanted iPSCM were able to follow this frequency, indicating a high quality of electrical integration. Action potential recordings 6 weeks after transplantation revealed significant differences between iPSCM and host CM (P=0.05 for all parameters). iPSCM had a lower maximum diastolic potential (64.0±2.8mV vs. 70.2±6.1mV), amplitude (70.0±7.8mV vs. 84.2±2.2mV) and maximum upstroke velocity (51.1±24.4 vs. 12.8±21.9 ms). Action potential duration at 50% repolarization (APD50) was longer (18.2±3.3 ms vs. 10.7±0.9 ms). APD90 was shorter (65.1±2.0 ms vs. 10.7±0.9 ms).

Discussion: After transplantation, induced pluripotent stem cell-derived cardiomyocytes increased with time after transplantation in iPSCM treated mice. This proarrhythmic effect may be explained by substantial differences in action potential properties compared to host cardiomyocytes.

Conclusions: iPSCM treated mice are able to integrate into surrounding viable host tissue. The quality of electrical integration and action potential properties of iPSCM and host CM are significantly different. Further studies are necessary to understand the underlying electrophysiological mechanisms and drug screening.

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Atrial & ventricular progenitor cells from the same heart show differential characteristics for cardiac regeneration but are superior to the endothelial progenitor cells from the same patient

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Introduction: Deciding the best cell type for cardiac regeneration still remains a challenge, however, no studies have directly compared the functional efficacy of cardiac progenitor cells (CPCs) with extra-cardiac progenitors isolated from the same patient.

Objective: To compare the functional characteristics of endothelial progenitor cells (EPCs), right atrial (RAA) CPCs and left ventricular (LV) CPCs isolated from the same patient.

Methods and results: Flow-cytometry on CPCs (>12 patients) revealed RAA CPCs had significantly lower cell death (0.9±0.7%) vs. EPCs (2.5±1.1%) after 72h (P<0.05). The expansion potential was superior for RAA CPCs (500,000 cells/10 μl) vs EPCs (500,000 cells/10 μl) or PBS (10 μl) at 500,000 cells/10 μl) were injected into adult mouse hearts after LAD ligation. At different time points (6 days, 6 weeks and 3 months) after transplantation, programmed stimulation was applied by a right ventricular electrophysiological catheter. External ECG recordings revealed number and duration of induced fibrillation episodes. Afterwards, hearts were resected and viable ventricular tissue sections were harvested for electrograms of iPSCM in transplanted iPSCM and host CM. Slices were stimulated by a unipolar electrode placed in healthy host tissue.

Results: Microscopic evaluation revealed no eGFP positive iPSCM within the infarct area, but persistence and electrical integration of iPSCM could be demonstrated in the perifarct zone. The maximal stimulation frequency without induction of ventricular fibrillation was 9±1.5Hz. Transplanted iPSCM were able to follow this frequency, indicating a high quality of electrical integration. Action potential recordings 6 weeks after transplantation revealed significant differences between iPSCM and host CM (P=0.05 for all parameters). iPSCM had a lower maximum diastolic potential (64.0±2.8mV vs. 70.2±6.1mV), amplitude (70.0±7.8mV vs. 84.2±2.2mV) and maximum upstroke velocity (51.1±24.4 vs. 12.8±21.9 ms). Action potential duration at 50% repolarization (APD50) was longer (18.2±3.3 ms vs. 10.7±0.9 ms). APD90 was shorter (65.1±2.0 ms vs. 10.7±0.9 ms).

Discussion: After transplantation, induced pluripotent stem cell-derived cardiomyocytes increased with time after transplantation in iPSCM treated mice. This proarrhythmic effect may be explained by substantial differences in action potential properties compared to host cardiomyocytes.

Conclusions: iPSCM treated mice are able to integrate into surrounding viable host tissue. The quality of electrical integration and action potential properties of iPSCM and host CM are significantly different. Further studies are necessary to understand the underlying electrophysiological mechanisms and drug screening.

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Flecainide suppresses an arrhythmogenic substrate in Anderson-Tawil syndrome-induced pluripotent stem cell-derived cardiomyocytes

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Background: Anderson-Tawil syndrome (ATS) is a rare inherited channelopathy characterized by periodic paralysis, dysmorphic features, and ventricular arrhythmia. The cardiac phenotype in ATS is typified by a prominent U wave and ventricular arrhythmia. An effective treatment for this disease remains to be established. This study aimed to establish a patient-specific induced pluripotent stem cell (iPSC) model for ATS and to investigate the poorly understood cardiac pathogenesis.

Methods and results: We reprogrammed somatic cells from three ATS patients, each carrying a KCNJ2 mutation (R218W, R67W, R218Q, respectively) to generate iPSCs. Multi-electrode arrays (MEAs) were used to record extracellular recordings of iPSC-derived cardiomyocytes, revealing strong arrhythmic events in the ATS-iPSC-derived cardiomyocytes. Ca2+ imaging of cells loaded with the Ca2+ indicator Fluo-4 enabled us to examine intracellular Ca2+ handling properties, and we found a significantly higher incidence of irregular Ca2+ release in the ATS-iPSC-derived cardiomyocytes than in control-iPSC-derived cardiomyocytes. Drug testing using ATS-iPSC-derived cardiomyocytes further revealed that antrilin, an agent, feclainide, a potassium channel blocker, and pilsicainide, significantly suppressed these irregular Ca2+ release and arrhythmic events, suggesting that flecainide’s effect in these cardiac cells was not via sodium channels blocking. A reverse-mode Na+ /Ca2+ exchanger (NCX) inhibitor, SEA0400, was also found to suppress the irregular Ca2+ release. To elucidate the effects of flecainide on INCX, the whole-cell voltage-clamp experiment was conducted in isolated guinea-pig ventricular cardiomyocytes. In the result, it was confirmed that flecainide could directly affect the NCX current (ICN).

Conclusions: ATS-iPSC-derived cardiomyocytes utilize abnormal electrophysiological phenotypes and serve as a useful model for exploring disease mechanisms and drug screening.
adult mesenchymal cells by inducing the overexpression of myocardin (MYOCD), a promyogenic transcription factor with anti-apoptotic activity, and telomerase reverse transcriptase (TERT), an anti senescence protein.

Objectives: We used a murine model of AMI to assess the efficacy of transplanted adipose tissue-derived mesenchymal stromal cells (AT-MSCs) engineered to overexpress MYOCD and TERT.

Methods: Twelve-month-old C57BL/6 mice underwent coronary artery ligation to induce AMI and were randomized into 3 treatment groups: phosphate-buffered saline (PBS) (20±L; n=7), mock-transduced AT-MSCs (2.5x10^5 cells in 20±L; n=5), or AT-MSCs overexpressing TERT and MYOCD (2.5x10^5 cells in 20±L; n=7). Sham-operated mice (n=7) were used as controls. The AT-MSCs were obtained from 12-month-old male green fluorescent protein-transgenic C57BL/6 mice and transduced with lentiviral vectors encoding TERT and MYOCD.

Results: When transplanted into the infarcted hearts of C57BL/6 mice, AT-MSCs overexpressing TERT and MYOCD preserved myocardial fractional shortening (Figure A), increased arteriogenesis and cell entrainment and decreased fibrosis formation (Figure B), compared with PBS alone or mock-transduced AT-MSCs. These effects were accompanied by increased numbers of Ki-67+ cells and c-Kit+/low cardiac cells (Figure B) and enhanced expression of cardiac actin, GATA4, Nkx2.5, and myocardin (Figure C).

Conclusions: Delivering TERT and MYOCD genes into AT-MSCs before transplantation promotes activation of the cardiomyogenic pathway, vasculogenesis, and stem cell survival in a murine model of AMI.

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The heart has a constant and significant cardiomyocyte replacement rate by endogenous cardiac stem cells in the adult life
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Introduction: The mammalian heart contains a pool of resident tissue-specific cardiac stem/progenitor cells (CSCs). CSCs were initially identified, isolated and studied to determine their differentiation potential in vitro and in vivo. Nevertheless, all the cells which possess clonogenic, self-renewing and cardiac tri-lineage multipotent differentiation potential in vitro and in vivo reside within the myocyte-depleted CD45-negative CD31-negative c-kit+/low cardiac cell fraction. In the adult mouse heart approach to quantitatively assess the progeny of CSCs in vivo. Furthermore, these data show that even if low expressed, c-kit physiologic transcription from the two alleles is necessary for the main regenerative properties of adult CSCs.

Methods: c-kit/CreERT2 knock-in allele does not efficiently fate-track c-kit positive resident cardiac stem cells and impairs their regenerative potential
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Introduction: c-kit-expressing adult resident cardiac stem cells (c-kit+/low) have been shown to be clonogenic, self-renewing and multipotent in vitro and in vivo. Despite the latter, it has been assumed that the location identification of c-kit expression in any cardiac cell equates to the identification of a CSC. On this basis, considerable controversy has arisen about the nature, physiological role and regenerative capacity of "c-kit+ cardiac cells". Indeed, a mouse model for c-kit genetic fate mapping using a Cre kit-CreERT2/+ mice with the adult double-fluorescent Cre reporter mice (R26RmT/mG) to permanently switch from Tomato to GFP expression the c-kit+/CreERT2 expressing cells and map the fate and that of their progeny in the adult life.

Methods: We cross-bred the heterozygous TAM-inducible c-kit-CreERT2/+ mice with the global double-fluorescent Cre reporter mice (R26RmT/mG) to permanently switch from Tomato to GFP expression the c-kit+/CreERT2 expressing cells and map their fate and that of their progeny in the adult life.

Results: Cre knock-in of the exon 1 of c-kit gene creates a null allele that is incompatible with life in homozygosis and that in heterozygosis creates a c-kit gene expression defect. TAM efficiently recombined tissues with known domains of c-kit protein expression like testis and bone marrow in double mutant c-kit-CreERT2/+R26Emt-mG mice. However, when the whole c-kit positive cardiac cell fraction and establishing a net dichotomy of CD45 positive (lineage positive) and CD45 negative (lineage negative) fractions, 80% of the c-kit-CreERT2+c-kit+ cardiac cells (mast cells and endothelial cells) were recombined to express GFP while less than 8% of CD45neg-c-kit+ cardiac cells (enriched for true CSCs) were recombined to express GFP. Furthermore, when compared to WT c-kit+/+ CSCs, c-kit-CreERT2+/+ CSCs show a significant reduced self-renewal and treatment of the myocardial c-kit-CreERT2/+ CSC pool of mice with ISO+5-FU induced cardiomyopathy and replenished their myocardium with new CSC-derived myocytes restoring LV function, engrafted CSCs and their myocyte-progeny were practically negligible in the myocardium of the respective animals injected with a Cre kit-CreERT2/+ mice. Conversely, c-kit gene defect correction in c-kit-CreERT2/+ CSCs by the transfection of a BAC spanning the entire WT c-kit gene locus rescued their cell expansion and differentiation defect in vitro and in vivo.

Conclusions: c-kit/CreERT2 knock-in allele cannot be used as a genetic fate map approach to quantitatively assess the progeny of CSCs in vivo. Furthermore, these data show that even if low expressed, c-kit physiologic transcription from the two alleles is necessary for the main regenerative properties of adult CSCs.

4292 Selective loss of adult cardiomyocytes is replenished by new endogenous cardiomyocyte formation in the presence of a patent coronary circulation
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Introduction: The degree of cardiomyocyte (CM) turnover in the adult my- ocardium remains more passively argued for in the absence of the phenom- enon itself. Some reports have calculated an annual average rate of CM turnover of ~0.5%/year in adult healthy humans. Yet, some other studies have extrapolated a rate up to 20%/year in humans. In small mammals, the results obtained have been ranged from ~0.0005% to 4%, which implies that the methods used so far are not reliable.

Methods: We employed a genetic mouse model to determine an acute and selective loss of CMs in presence of a normal coronary circulation. Transgenic mice were generated using a Tamoxifen (TAM) inducible membrane-estrogen-receptor linked Cre recombinase (mER-Cre-emer) under the alpha myosin heavy chain (myh6) promoter were crossed with transgenic mice mutated in the Rosa 26 (R26R) locus to express a floxed "cre erasable" Stop sequence in front of the Diphtheria toxin A gene (R26R-stop-DTA). Thus, TAM treatment in these double transgenic mice (hereafter Tg cmyo-Cre-mer2/DTA) activates the expression of Diphtheria toxin A (Ly6A/E) gene has only 4-exons in less than 15Kbs, which makes it easy to use as a transgene for fate mapping studies. Thus, we have characterized the cardiac gene defect correction in c-kit-CreERT2/+ CSCs by the transfection of a BAC spanning the entire WT c-kit gene locus rescued their cell expansion and differentiation defect in vitro and in vivo.

Conclusions: These results indicate that the adult heart robustly replenishes the cardiomyocytes lost by wear and tear and after injury. This adult cardiomyocyte formation is mainly dependent on activation of the resident CSCs and their commitment to the myogenic lineage. The actual myocyte replacement rate is likely to be higher than shown here because Sca-1 is expressed in only a little over half of the multipotent c-kit+/low CSCs.
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A patient-specific iPSC model for Heart-Oram Syndrome reveals TBX5-dependent dysregulation of down-stream targets

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Background: The Heart-Oram syndrome (HOS) is an autosomal dominantly inherited disorder affecting 1 in 100,000 live births. It is defined by upper limb malformations and congenital heart defects. In 70% of the cases TBX5 mutations are responsible for the development of the syndrome with varying phenotype most likely due to the location of the TBX5 mutation.

Purpose: At present no patient-specific induced pluripotent stem (iPS) cell model for HOS has been established. This model enables the investigation of early cardiac developmental processes and potential molecular dysfunctions in a human disease stem within the context of the disease.

Methods: We selected a male 16 months old patient suffering from severe HOS carrying a yet undescribed TBX5 de novo mutation. Primary fibroblasts of the HOS-patient were reprogrammed using the integration-free Sendai virus to generate a patient-specific iPS line. The preserved TBX5 mutation in the iPS line was set in the context of congenital heart defects. In silico analysis of the HOS patient showed a highly conserved DNA-binding domain at position 920 (C→A). The mutation leads to an amino acid change at position 85 (proline→threonine). Control and iPS lines showed the absence of Sendai virus at p7 after reprogramming. The de novo TBX5 mutation was conserved in the HOS iPS line. Furthermore, HOS and control iPS lines expressed endogenous pluripotency markers and stained positive for NANOG, SOX2 and TRA-81. HOS and control iPS lines were differentiated using a spontaneous as well as a chemically defined differentiation protocol for enhanced cardiac differentiation. Gene expression of all three germ layers and the kinetics of cardiac differentiation were performed.

Results: The novel TBX5 mutation is located in the highly conserved DNA-binding domain at position 920 (C→A). The mutation leads to an amino acid change at position 85 (proline→threonine). Control and iPS lines showed the absence of Sendai virus at p7 after reprogramming. The de novo TBX5 mutation was conserved in the HOS iPS line. Furthermore, HOS and control iPS lines expressed endogenous pluripotency markers and stained positive for NANOG, SOX2 and TRA-81. HOS and control iPS lines were differentiated using a spontaneous as well as a chemically defined differentiation protocol for enhanced cardiac differentiation. Gene expression of all three germ layers and the kinetics of cardiac differentiation were performed.

Conclusion: We have identified a yet undescribed de novo occurring mutation in a highly conserved area of the TBX5 gene. Patient-specific iPSC model validated no changes in the expression of cardiac TFs suggesting a regular induction of early cardiac development. Regular expression of mutated TBX5 combined with a down-regulation of NPPA indicated an induction of a loss-of-function of mutated TBX5 compared to wildtype.

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Mesenchymal stem cells grow under chronic hypoxia traffic to regions of myocardial infarction, suppress splenic natural killer cells, and attenuate adverse remodeling in mice with large acute MI

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Background: Mesenchymal stem cells (MSC) for acute myocardial infarction (MI). While most studies were performed with intracoronary injection, IV allogeneic MSC infusion would be clinically easier and may suppress inflammation and attenuate adverse remodeling following MI through paracrine effects.

Methods: CD1 male mice underwent 45 minutes of left anterior descending artery occlusion. Tail-vein injection of human MSCs grown chronically at 5% O2 was performed 24 hours following MI. MSCs were labeled with iodine-111 oxine, and the animal was injected with 1.1x106 cells, and ex vivo autoradiography of the heart was performed 24 hours following MSC injection. In a separate study, mice underwent baseline echocardiography followed by MI surgery. 24 hours following MI surgery, mice were randomized to either injection with 2x106 MSCs (n=16) or saline control (n=16). Echocardiography was repeated 7 days later. Bone, blood, spleen, and hearts were then harvested; we performed TCT staining of the hearts (below the level of coronary ligation) and flow cytometry of the spleen.

Results: Radiolabeled MSCs preferentially trafficked to regions of myocardial injury while there was minimal trafficking to control mice (MI 1). We found no difference in percent LV infarction by TCT staining (28.3% for MSC group vs 25.3% for control group). As seen in Figure 1B, control saline treated...
mice with large infarcts (>25% LV) demonstrated an increase in adverse LV remodeling vs. mice with small infarcts: end systolic volume in large vs. small infarcts was 77±20 vs. 33±3 ul (p<0.04) and end diastolic volume was 112±17 vs. 68±5.5 ul (p<0.03). However, with MSC treatment mice with large infarcts did not demonstrate an increase in adverse remodeling vs. mice with small infarcts: end systolic volume in large vs. small infarcts was 41±8 vs. 35±4 ul (p=0.53) and end diastolic volume was 79±8 vs. 70±6 ul (p=0.47), thus demonstrating that MSCs prevented the adverse LV remodeling occurring in mice with large infarcts. In addition, both systolic and diastolic posterior wall thickness were greater in the MSC group, and anterior wall thickening was greater during systole (p=0.01) compared with the control group. Importantly, MSC injection resulted in a significant decrease in splenic natural killer (NK) cells compared with control injection (2.6±0.13 vs 3.4±0.36, p<0.04). In vitro transwell experiments demonstrated MSCs significantly suppress NK cell proliferation through paracrine effects.

Conclusions: MSCs grown under chronic hypoxic conditions home to regions of MI, engraft into NK cells, which are key mediators of inflammation, and prevent adverse remodeling in mice with large MI.

Acknowledgement/Funding: Research Grant from CardioCell, Inc

BEST POSTERS SESSION 5
BEST POSTERS IN CMR

P4298 | BEDSIDE
Beneficial myocardial remodelling after TAVI as assessed by T2 mapping CMR
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Background: Severe aortic stenosis (AS) leads to increased morbidity and mortality besides hypertrophic cardiomyopathy (HCM). It has been shown, that transcatheter aortic valve implantation (TAVI) results in beneficial left-ventricular cardiac remodelling. Recently, parametric cardiovascular magnetic resonance (CMR) for analysis of fluid imbalance and myocardial fibrosis revealed increased myocardial T2 relaxation time in patients with HCM. If this parameter responds to TAVI procedure or procedures with prognostic implications in terms of beneficial remodelling is currently unknown.

Hypothesis: T2 relaxation time decreases after TAVI alongside beneficial myocardial remodelling. Additional, baseline T2 values identify patients who benefit the most from TAVI.

Methods: CMR was conducted with a 1.5 Tesla MRI-System using a 32-channel coil. T2 mapping was performed using a respiratory navigator gated Gradient-And Spin-Echo sequence (GRASE, 15 T2 echoes separated by 10 ms, res. 1x1x10mm³, 3 short axis slices). Images were post-processed using software based on the LabView environment for local T2 value generation (T2 mapping). A cohort of age and gender matched volunteers served as controls. CMR was performed at baseline and 6 months after TAVI. Ejection fraction (EF), left ventricular mass by body surface area (LV/BMA) and interventricular septum thickness (IVS) were measured as well.

Results: 56 patients with severe AS (25 males, 80.9±10.3 years) received baseline CMR, 33 patients pursued 6-months follow-up. Baseline EF was 58.2±14.2%. Compared to baseline, 6 months after TAVI, LV/BMA and IVS significantly improved (EF: 70.8±7.3 to 63.3±4.3%, p<0.005, 10.6% improvement). Myocardial function was improved after TAVI as assessed by baseline IVS=15mm, T2 time=70ms and EF<55%.

Conclusion: Patients with severe AS were characterized by myocardial hypertrophy especially in the basal septum alongside increased T2 time. 6 months after TAVI, average T2 time significantly declined coincident with reduction of mass and improvement of myocardial function. At baseline, T2 time predicts functional outcome after TAVI.
PH. Receiver-operating characteristics curve demonstrated sepal inversion ratio to be useful marker of recovering from PH (cut-off value 0.53, Odds ratio 21.5)

Conclusions: PTPA can improve not only hemodynamics but also right ventricular function. Magnetic resonance imaging can non-invasively evaluate the pulmonary circulation by measuring right ventricular function precisely.

P4301 | BEDSIDE
Long-term prognostic value of left ventricular dyssynchrony as assessed by cardiac magnetic resonance feature-tracking imaging after a first ST-segment elevation myocardial infarction

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Aim: The omen impact of left ventricular (LV) dyssynchrony on prognosis among patients with heart failure is well known; conversely, scarce data are available regarding its prognostic impact among patients with recent ST-segment elevation myocardial infarction (STEMI). Aim of the present study was to investigate the long-term prognostic value of LV dyssynchrony as assessed by feature-tracking cardiac magnetic resonance (FT-CMR) in patients with a first ST-segment elevation myocardial infarction (STEMI).

Methods: 107 patients with STEMI (mean age 59±12 years, 82% male) were included. All patients underwent primary percutaneous coronary intervention (PCI). After a median of 8 days (IQ range 4–18) following admission, CMR with LGE imaging was performed to assess left ventricular (LV) function, infarct size (IS) and microvascular obstruction. In addition, feature-tracking analysis was applied to cine CMR basal, mid and apical short-axis images to assess LV dyssynchrony, defined as the standard deviation of the time-to-peak radial strain of the LV segments expressed as percent cardiac cycle (systolic dyssynchrony index [SDI]). Patients were followed-up for a median of 97 months (IQ range 32–101); the primary endpoint was defined as a composite of death, myocardial infarction and hospitalization due to heart failure.

Results: Median IS was 14% of the LV mass (IQ range 5–30) and microvascular obstruction was observed in 32% patients; median SDI was 16.7% (IQ range 9.6–21.2%). The outcome event occurred in 22% of patients. At multivariate Cox proportional-hazards analysis, after correction for the traditional clinical prognostic parameters, age (HR=1.05, IC=1.00–1.09; p=0.041), infarct size (HR=1.06, IC=1.02–1.09; p=0.001) and SDI (HR=1.08, IC=1.00–1.16; p=0.047) were the only variables significantly and independently related to the primary endpoint. Adding SDI to the multivariate model slightly but significantly increased the global $R^2$ of the model ($R^2$ change 4.17; p=0.041). Kaplan–Meier survival curves for the outcome event comparing patients according to IS and SDI are shown in Figure 1. Patients with IS > median and IS > median at baseline CMR had a significant worse prognosis (log-rank p < 0.001).

Conclusions: LV dyssynchrony assessed by feature-tracking CMR represents a significant and independent marker for the prediction of adverse outcomes among patients with a recent first STEMI; in addition, the prognostic value of LV dyssynchrony is also incremental over infarct size.

BEST POSTERS IN DIAGNOSTICS IN HYPERTENSION
P4303 | BEDSIDE
Ten-year prognostic significance of QTc dispersion, dispersion of QTc-peak interval and T-peak to T-end interval in patients with arterial hypertension and left ventricular hypertrophy

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Background/Introduction: It is well known and well documented that occurrence of left ventricular hypertrophy in patients with arterial hypertension is a bad prognostic marker. However, it is important to know if there are other non-invasive parameters which are of diagnostic significance for such patients.

Purpose: The aim was to examine the correlation between left ventricular mass index (LVMI) and different parameters of QTc dispersion (dispersion of QTc-peak interval and corrected T-peak to T-end interval). Additional aim was to examine the outcome and prognostic significance of QTc dispersion in patients with essential arterial hypertension (AH) and left ventricular hypertrophy (LVH) during a ten-year follow-up.

Methods: All 124 patients with AH and LVH (age 57±5; 80 male and 44 female) were examined by means of echocardiography (two independent examiners - Acuson-Sequence), exercise testing, 24-h Holter monitoring, 24-h ambulatory blood pressure monitoring. QTc interval dispersion, dispersion of QTc-peak interval and corrected T-peak to T-end interval was calculated as the difference between QTc interval and QTc-peak interval. The QTc dispersion was calculated as the difference between the maximum QTc interval and minimum QTc interval in each subject. Patients used regular medication therapy during the follow-up.

Results: During a ten-year period of follow-up, 40 (32.3%) patients experienced cardiovascular and cerebrovascular adverse events (AE). At the beginning of the study, patients with AH had larger LVMI (178.9±29.5 g/m² vs. 165.5±29.5 g/m²; p < 0.05). In patients with AE QTc dispersion was greater than in patients without AE (54.8±19.4 ms vs. 84.1±24.7 ms; p < 0.05). There were hypertensions between LVMI and QRS duration, QTc interval (r = 0.429 and r = 0.235; p < 0.01), QTc-peak interval and corrected T-peak to T-end dispersion (r = 0.190 and r = 0.214; p < 0.05). Using multiple linear regression analysis, the best predictor of bad prognosis in QTc-peak interval dispersion (beta = 0.200; p < 0.05; for model R² = 0.040, adjusted R² = 0.032 standard error of the estimate = 0.46171; p < 0.05). The best correlation was between QTc dispersion and corrected T-peak to T-end dispersion (r = 0.492; p < 0.01).

Conclusions: Only QTc dispersion was of prognostic significance for new cardiovascular events in patients with left ventricular hypertrophy. Although we found the correlation between left ventricular mass index and QTc-peak interval and corrected T-peak to T-end dispersion, they did not have prognostic significance. QTc dispersion was mostly determined by corrected T-peak to T-end interval dispersion.

P4304 | BEDSIDE
Patterns of renal and cardiac haemodynamics in symptomatic essential hypertensives

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Background/Introduction: It is noteworthy that asymptomatic organ damage (OD) of the kidney and heart in patients with essential hypertension occurs more frequently than previously thought. Importantly, renal pathologies are associated with a more advanced atherosclerotic burden, increasing the risk of cardiovascular events. Hypertension is associated with left ventricular hypertrophy (LVH) and increased left ventricular filling pressure. As a result, there is a need for the development of non-invasive and easily accessible diagnostic markers for the detection of left ventricular filling pressure.

Methods: We studied 360 patients with essential hypertension [183 males, aged 55 years, office blood pressure (BP) = 144/86 mmHg] that underwent transthoracic echocardiographic study for determination of mitral annular early diastolic velocity (E' velocity) and blood sampling for assessment of metabolic profile. Moreover, intrarenal Doppler ultrasound data on renal resistive index (RI), obtained by Doppler ultrasound sampling of the intrarenal arteries, were retrospectively analyzed. The distributions of RRI and E/e' were split by the median (0.623 and 7.8, respectively).

Results: Age, systolic and diastolic office BP, body mass index (BMI) and E/e' were the independent predictors of RRI (R² = 0.478, p < 0.001). Age, systolic office BP and RRI were the independent predictors of E/e' (R² = 0.400, p < 0.001). Patients with high RRI and high E/e' (n=122), compared to those with low RRI and low E/e' (n=78) were characterized by increased LVMIheight (by 6.2 g/m²; p < 0.05), office PP (by 16.4, p < 0.001), ACR (by 25.1 mg/g, p < 0.01), PWV (by 1.6 m/s, p < 0.05), and prevalence of LVH (45 vs. 12%, p < 0.001).

Conclusions: Increased RRI in conjunction with pronounced left ventricular filling pressure is accompanied by augmented LV mass, PP, ACR, PWV, and higher LVH rates. Furthermore, the coexistence of impaired renal and cardiac haemodynamics suggests the occurrence of multiple target OD progression.

P4305 | BEDSIDE
Arterial compliance is associated with target organ damage in hypertensives

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Background/Introduction: Total arterial compliance (TAC) has been recognized as an independent risk factor for cardiovascular events. Hypertension is associated with higher cardiovascular risk as well as several markers of subclinical target organ damage (TOD).

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Purpose: We sought to investigate relationship between TAC and markers of TOD in never-treated hypertensives.

Methods: We enrolled 990 consecutive essential hypertensives (mean age 53±12 years, 526 males) without known cardiovascular disease (CVD). Markers of subclinical TOD (ankle-brachial index (ABI), estimated glomerular filtration rate (eGFR), left ventricular mass index (LVMi) and pulse wave velocity (PWV)) were evaluated in all patients. ABI was calculated by dividing the highest ankle systolic blood pressure by the highest brachial systolic blood pressure. LVMi was assessed echocardiographically using the Devereux formula. Carotid-femoral PWV was estimated with the Complior device. eGFR was calculated by the Cockcroft-Gault formula. Augmentation index (Alx@75) was also assessed as an index of wave reflections. The ratio of stroke volume to pulse pressure was measured echocardiographically as a surrogate of TAC.

Results: In multivariable regression analysis, TAC exhibited significant association with LVMi (p=0.004, adjusted R² of model=0.318), PWV (p=0.001, adjusted R² of model=0.335) ABI (p=0.001, adjusted R² of model=0.325), decreased ABI (0.9) and decreased renal function (eGFR<60ml/min). Specifically, TAC exhibited significant association with left ventricular hypertrophy (p=0.003, adjusted R² of model=0.318), increased aortic stiffness (p<0.001, adjusted R² of model=0.320) and renal dysfunction (p=0.003, adjusted R² of model=0.318). These associations were independent of age, gender, mean blood pressure, body-mass index, smoking habits, glucose, low-density lipoprotein and C-reactive protein.

Conclusions: Our findings support the close relationship between TAC and TOD in hypertension, as well as, the predictive ability of TAC for TOD.

P4306 | BEDSIDE Dynamic contrast enhanced ultrasound quantification of renal microcirculation in hypertension

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Background: The hypertension induced renal damage is common and the degree of renal impairment is considered a major predictive factor of future cardiovascular events and mortality. The modalities by which changes in renal microvasculature can be early identified are useful diagnostic methods in different stages of hypertension.

Purpose: To identify the value of dynamic contrast enhanced ultrasound (D-CEUS) quantification for renal microcirculation damage in patients with primary hypertension (HT).

Method: 108 patients with HT grade I-III from which 34 with diabetes and 11 with chronic kidney disease as associated comorbidities, age=61.95±10.96, Males=40.7% and 21 healthy adults were investigated by D-CEUS with sulfur hexafluoride. After intravenous administration of 1.2 ml contrast agent, the images were recorded continuously for 3 minutes. Renal microcirculation was evaluated in different vascular phases: early cortical phase (N=10–14s), late cortical phase (N=15–20–40s) and medullar phase (N=45–120s). The quantitative evaluation - Time-intensity curves (TIC) – was obtained using Contrast Dynamics software analyzes. Arrival Time (AT), Time to Peak (TP), Peak Intensity (PI), Area Under The Curve (AUC) and Mean Transit Time (MTT).

Results: The enhancement times were progressively prolonged in the study group according to the grade of the hypertension and more in patients with associated comorbidities. TIC analyze were similar: AT in HT group was 16.79±4.47s, in diabetes 21.44±14.10s and in CKD 17.27±3.72s vs. healthy 9.95±1.56s. TP, PI, AUC were also well correlated with the grade of the hypertension and associated comorbidities. No adverse effect was noted during the study. No changes in biological status were noted in the study group after D-CEUS.

Conclusions: D-CEUS is a reliable, non-invasive, simple and safe method to evaluate in real-time the renal microcirculation damage in all grades of hypertension and associated comorbidities. TIC parameters (AT, PI and AUC) accurately assess the renal micro-vascular impairment in different stages.

Acknowledgement/Funding: This work received financial support through the project entitled "CERO-Career profile: Romanian Researcher", grant number POSDRU/159/1/S/5/135760, co
P4300 | BEDSIDE

Relationship between increasing age, platelet reactivity, and future events after drug-eluting stent percutaneous coronary intervention: the ADAPT-DES study

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Background: Previous studies suggest that elderly patients exhibit an impaired response to clopidogrel; however, these studies had small sample sizes and provided no correlation to future thrombotic or bleeding events.

Purpose: We sought to investigate the correlation between increasing age, platelet reactivity, and subsequent ischemic and bleeding outcomes.

Methods: ADAPT-DES was a prospective, multicenter, non-randomized, “all-comers” study of 8533 consecutive patients at 11 international centers designed to determine the frequency, timing, and correlates of stent thrombosis and adverse clinical events at 2 years after drug-eluting stent implantation. Platelet reactivity was assessed following percutaneous coronary intervention with the VerifyNow assay. In order to assess age-related correlations, we stratified the study cohort into age tertiles.

Results: Demographic characteristics varied significantly among tertiles with an increased frequency of comorbidities with advancing age. Platelet count exhibited an opposite trend. Platelet reactivity and resistance to clopidogrel progressively increased in advancing age tertiles irrespective of cutoff value used. Major adverse cardiac events, death, and bleeding demonstrated increasing trends, similar to platelet reactivity; however, myocardial infarction and stent thrombosis did not appear to correlate with age or platelet reactivity.

Table 1

<table>
<thead>
<tr>
<th>Age (mean)</th>
<th>Low tertile (N=2762)</th>
<th>Intermediate tertile (N=2820)</th>
<th>High tertile (N=3000)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>51.1±5.8</td>
<td>63.6±2.9</td>
<td>75.1±4.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PRU (mean)</td>
<td>177.3±96.3</td>
<td>187.3±94.8</td>
<td>198.3±97.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>&gt;208 PRU</td>
<td>38.3%</td>
<td>42.4%</td>
<td>47.2%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>&gt;230 PRU</td>
<td>31.4%</td>
<td>34.5%</td>
<td>38.9%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>MACG</td>
<td>10.25%</td>
<td>9.90%</td>
<td>12.14%</td>
<td>0.02</td>
</tr>
<tr>
<td>Death</td>
<td>2.15%</td>
<td>2.95%</td>
<td>6.22%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>1.56%</td>
<td>1.81%</td>
<td>1.90%</td>
<td>0.33</td>
</tr>
<tr>
<td>Stent thrombosis</td>
<td>1.36%</td>
<td>1.02%</td>
<td>0.96%</td>
<td>0.16</td>
</tr>
<tr>
<td>All major bleeding</td>
<td>6.0%</td>
<td>7.4%</td>
<td>12.1%</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Conclusions: In this unadjusted analysis, increasing age appeared to correlate with increasing platelet reactivity but did not show any correlation with future ischemic events. Adjustments for baseline differences are required to further define independent correlations among age, platelet resistance, and future ischemic outcomes.

P4310 | BEDSIDE

Trends in percutaneous coronary angioplasty (PTCA) in the United States, 2003-2013


Objectives: To describe the trends in rate, cost and demographics of patients undergoing percutaneous coronary angioplasty from 2003 to 2013.

Background: The number of percutaneous coronary angioplasties performed over the past decade has steadily decreased. Beyond the decrease, little is known about the impact on the cost of healthcare. Longitudinal analysis of percutaneous coronary angioplasty provides insight in the changes in cost, morbidity, mortality over a decade of care delivery.

Methods: We retrospectively analyzed admissions for patients undergoing principle percutaneous angioplasty between January 1, 2003, and November 30, 2013 in the National Inpatient Sample. The NIS is the largest publicly available all-payer inpatient database of the United States, with discharge data from 1,045 hospitals. Direct comparison of discharge rate, in-hospital mortality, and median cost of service was made between 2003 and 2013 cohorts.

Results: The rate of primary percutaneous coronary angioplasty has decreased significantly since 2003 from 654.270 to 403.550 cases in 2013 (p <0.001). The mean hospital charge per admission, however, more than doubled, from $39,174 to $75,391 (p <0.001). Length of hospital stay also increased approximately 25% from 4.6 to 3.3 days (p <0.001). Demographic characteristics, including gender, age distribution, and insurance type did not significantly change over time.

Conclusions: Using the largest publicly available all-payer inpatient database in the United States from 2003–2013, we have shown that the volume of admissions for PTCA has decreased by 38% and length of stay has decreased by 25%, that the cost of an admission for a percutaneous coronary angioplasty has more than doubled, with an average annual increase of 7.2%. This is three fold the average historical US inflation rate of 2.38% over the same time period. The increase in cost of PTCA has far outpaced inflation rates from 2003–2013, and further investigation into possible causes is warranted.

P4311 | BEDSIDE

Gender difference in chest pain after stenting in patients with coronary artery disease: a patient-level pooled analysis from two large randomized trials

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Background: Gender-based data on chest pain after percutaneous coronary interventions with newer generation drug-eluting stents are scarce.

Purpose: We aimed to assess the impact of gender differences in chest pain following interventions with newer generation drug-eluting stents.

Methods: A patient-level pooled analysis was performed of the TWENTE and DUTCH PEERS trials– two large randomized studies that enrolled a broad patient population, treated with newer generation permanent polymer-coated drug-eluting stents. Patient-oriented composite endpoint (POCE), a composite endpoint of all-cause death, any MI, or any coronary revascularization was assessed over 2-years. Patient-reported chest pain was classified into scores: 0= no chest pain at all; 1= chest pain only during severe physical exertion; 2= chest pain at moderate physical effort (during normal daily activities); 3= chest pain at mild physical effort or at rest.

Results: At 1 and 2-years, clinical follow-up was available in 99.9% and patient-reported chest pain data in 94.1% and 93.6%. Among all 3,202 patients, the 871 (27.2%) women were significantly older than men (67.5±10.2 years vs. 62.8±10.6 years, p=0.001) and they had more cardiovascular risk factors, such as diabetes (24.2% vs. 17.8%, p<0.001), hypertension (63.6% vs. 51.6%, p<0.001), and positive family history for coronary disease (54.5% vs. 51.0%, p=0.03). At 1 and 2-year follow-up, women had more clinically relevant chest pain (16.3% vs. 10.5%, p<0.001, and 17.2% vs. 11.1%, p<0.001, respectively) (Figure 1). Multivariate analysis demonstrated that female gender independently predicted clinically relevant chest pain at 1 and 2-year follow-up both during daily activities and at minimum physical exertion at rest (1-year: adjusted OR 1.7, 95%-CI:1.2–2.4, p<0.002; and adjusted OR 1.8, 95%-CI:1.3–2.5, p<0.001; 2-year: adjusted OR 1.8, 95%-CI:1.3–2.6, p<0.001; and adjusted OR 1.7, 95%-CI:1.3–2.3, p<0.001). Nevertheless, for both genders the 2-year rates of POCE (9.4% vs. 9.5%, p=0.93) and the rates of its individual components were almost identical.

Figure 1. Chest pain at 2 years follow-up

Conclusion: While the incidence of adverse cardiovascular events was low and similar for both genders, women showed a significantly higher prevalence of clinically relevant chest pain, which might be largely related to mechanisms other than epicardial coronary obstruction.
Acknowledgement/Funding: The TWENT and DUTCH PEERS trials were supported by grants from Abbott Vascular and Medtronic, and Boston Scientific and Medtronic, respectively.

BEST POSTERS IN MECHANISMS OF ARRHYTHMIAS

P4313 | BENCH
Meta-analyses in ~44,000 individuals identify fifteen genetic loci associated with the electrocardiographic P-wave
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Background: The P-wave on an electrocardiogram is a measure of atrial electrical function and its characteristics may serve as predictors for atrial arrhythmias. Increased mean P-wave duration and P-wave terminal force traditionally have been used as markers for left atrial enlargement and both have been associated with increased risk of atrial fibrillation.

Purpose: First, to identify new genetic regions associated with P-wave morphology. Second, to integrate these findings with known genetic associations and identify genetic regions associated with multiple vs. specific atrial electrophysiological traits.

Methods: We meta-analyzed genome-wide association study (GWAS) results for P-wave duration and P-wave terminal force from twelve studies. A total of 44,456 individuals were included, of which 6,778 (16%) were of African ancestry. Genotyping, imputation, and GWAS were performed at each study site. Summary level results were meta-analyzed centrally using inverse-variance weighting.

Results: In meta-analyses of P-wave duration, we identified six novel loci (SSBP3, EPAS1, CAND2, CAMK2D, HCN1, MYH6) that reached genome-wide significance (P<5×10⁻⁸), and replicated a prior association with SCN10A. CAND2 was only significant in combined ancestry analysis, whereas CAMK2D was only significant in Europeans. We identified three loci at SCN5A/SCN10A, TBX5, and CAV1/CNAV2 that were jointly associated with the PR-interval, PR-segment, and P-wave duration. We also identified seven novel loci in meta-analyses of P-wave terminal force (KCND3, PCDH18, C6orf195, SPON1, MYH6, ALPK3/NMB, PPP5D1), PCDH18 was only significant in combined ancestry analysis, whereas SPON1 was only significant in African-Americans. Four of the identified genetic loci were significantly associated with gene expression (SSBP3, TBX5, CAV1/CNAV2, ALPK3/NMB) in 329 human left atrial tissue samples. Finally, we observed that some of the loci associated with the P-wave were linked to multiple phases of atrial conduction, whereas others identified distinct phases.

Conclusion: We identified fifteen genetic loci associated with atrial conduction. Future studies of these loci may aid identification of new targets for drugs that may modify atrial conduction and treat atrial arrhythmias.

P4314 | BEDSIDE
Clinical characteristics and long-term prognosis of patients with genotype-unknown long-QT syndrome
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Background: Long-QT syndrome (LQTS) is caused by mutations in several ion channel genes, and approximately 70% of LQTS patients has three major LQTS-genes such as KCNQ1, KCNH2 and SCN5A, whereas 30% of LQTS cases remains clinically and genetically elusive. We hypothesized that those without carrying the specific familial LQTS mutations still had a comparable risk of cardiac events.

Methods: From 1100 LQTS probands who underwent gene testing between 2008 and 2014 in our institute, we excluded patients with known LQTS genes (genotype-positive) or secondary LQTS due to structural heart diseases, thus registered 235 phenotype-positive/genotype-negative LQTS probands (55% female, 18±13 years-old, QTc=460±41 ms). We investigated clinical characteristics and long-term prognosis of the genotype-unknown LQTS patients.

Results: One hundred patients had cardiac events including syncope (n=73), ventricular fibrillation or cardio-pulmonary arrest (VF/CPA) (n=39) and both (n=13), syncope occurred more likely in younger (18±14 years old) than older and cardiac events highly occurred in female than male (68 vs. 32; p=0.001). Compared with the genotype-positive probands in LQT1 (n=231), LQT2 (n=270) and LQT3 (n=67), genotype-unknown probands had a lower but comparable cardiac events rate (Figure). Furthermore, VF/CPA occurred during exercise (n=9), rest (n=18), emotional stress (n=3) or others including no special triggers for the events (n=10). Finally, multivariate Logistic analysis revealed that female gender was the significant risk (HR=2.44, 95% CI: 1.38–4.3: p=0.002) but age at first events, QTc interval and family history of LQTS or sudden cardiac death under 50 years old were not associated with cardiac events.

Conclusion: Genotype-unknown LQTS patients may have heterogenic backgrounds, and even though a genetic screening could not identify the known LQTS-genes, the risk of cardiac events cannot completely be excluded in LQTS patients.

Acknowledgement/Funding: Research Grant for Cardiovascular Diseases from the Ministry of Health, Labour, and Welfare, Japan

P4315 | BEDSIDE
Copy number variations in SCN5A associated with Brugada syndrome
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Background: Loss-of-function mutations in SCN5A encoding the major sodium channel (Nav1.5) in the heart are associated with Brugada syndrome (BrS) and approximately 20% of BrS cases had mutations in SCN5A. More than 200 point mutations in SCN5A associated with Brugada syndrome (BrS) have been identified until now. On the other hands, several cases of Brugada syndrome associated with large DNA deletions/duplications were reported in recent years, for example long QT syndrome, arrhythmogenic right ventricular cardiomyopathy and catecholaminergic polymorphic ventricular tachycardia. However, there have been only one case of BrS carrying CNVs in SCN5A, and the frequency of CNVs in SCN5A remains unknown in BrS patients.

Objective: The aim of this study was to search for BrS patients caused by CNVs in SCN5A and investigate the clinical characteristics of them.

Methods: The study cohort consisted of 121 BrS probands who were symptomatic or who had family history of sudden death, syncope, BrS or arrhythmic diseases. We excluded 22 patients with point mutations in SCN5A, which were considered as pathogenic. We applied Multiplex Ligation-dependent Probe Am-
The purpose of this study was to assess the dynamics of neuro-cardiac coupling, and determine the mechanisms of communication between sympathetic nerves and cardiomyocytes occurs, in vitro and in vivo.

Methods: In vitro: Cocultures of sympathetic ganglia neurons and neonatal cardiomyocytes, were used to assess the β-AR dependent response to neurolymphatic release of norepinephrine. In all anesthetized, neonatal cardiomyocytes, responses to neurolymphatic stimulation need to be potent and operate rapidly and with minimal neurotransmitter expenditure. The existence of direct neuro-cardiac junctions, which would fulfill such requirements has been hypothesized, but never demonstrated directly thus far.

**BEST POSTERS IN INTEGRATIVE BIOLOGY**

P4318 | BENCH

Zoledronic acid inhibits calcification of aortic valve in an experimental model of aortic valve stenosis

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Background: Local delivery of bisphosphonates has been recently proven to inhibit calcification of the arterial wall in an experimental model of atherosclerosis.

**Purpose:** The aim of the present study was to evaluate the anticalcific action of Zoledronic Acid, in an experimental model of aortic valve calcification.

**Methods:** Twenty four New Zealand rabbits were placed on vitamin D enriched atherogenic diet for 3 weeks. At that time a cardiac ultrasound was performed to assess the aortic stenosis and aortic calcification of the aortic valve by measuring the transvalvular gradient (mmHg), the valve area (cm²) and the ratio of the valve area to the left ventricular outflow tract size. In vivo: Rabbits were divided into four equal groups: 1) Placebo: received saline on the cusps; 2) Zoledronic Acid: received zoledronic acid on the cusps; 3) Zoledronic Acid + Adrenergic stimulation: received zoledronic acid and an adrenergic stimulation on the cusps; 4) No treatment: received saline on the cusps. In addition, 2 rabbits were killed at each stage and the aortic valve, by a dedicated balloon catheter. A placebo mixture was administered with the same technique on another eight animals, while eight animals were left without intervention and were used as controls. At 28 days all animals were sacrificed. All aortic valves were fixed in 10% neutralized buffered formalin solution for 24 hours. The cusps (left, posterior and right) were separated in a radial direction and then embedded in paraffin waxes. Serial sections 4 μm thick were obtained and routinely stained with eosin–hematoxylin and von Cossa stain for calcium deposits. The stained slides were digitized using a light microscope (Nikon Eclipse 80i, Nikon Corp., Tokyo, Japan) with an attached digital camera. The files processed in a computer with the appropriate software (Image Pro Plus, version 1.1, MD, USA), and the calcified areas were expressed as the percentage to the total area. Statistical analyses were carried out with the Statistical Package for the Social Sciences (SPSS, Chicago, IL) release 13.0.

Results: At baseline, all animals developed aortic valve stenosis with severe calcification. No differences regarding AVA were recorded between both groups. (P=0.18). In all animals the local delivery of zoledronic acid and placebo mixtures was successful and uncomplicated. A total of 72 cusps were histologically examined. The cusps treated with zoledronate had significantly lower expression of calcium content compared to the cusps of the placebo group (16.6±0.99 vs 28.4±1.10% of the area, p<0.0001). Similarly the cusps treated with zoledronate had significantly lower expression of calcium content compared to the cusps of the placebo group (16.6±0.99 vs 27.0±6.12% of the area, p<0.0001). No differences were observed between the cusps of the placebo group and the controls in any of the analyzed areas (P>0.05).

Conclusion: Local delivery of zoledronic acid on the aortic valve can inhibit calcification in an experimental model of aortic stenosis.
Targeting miR-218 and miR-34a protects against maladaptive chromatin remodelling and oxidative stress in the diabetic heart

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Background: In patients with diabetes risk of heart failure is not eradicated by intensive glycemic control (IGC). The mechanisms underlying persistent myocardial damage despite glucose normalization remain to be deciphered. Small non-coding RNAs such as miRNAs are key epigenetic marks implicated in maladaptive transcriptional programs and cardiovascular damage.

Purpose: To investigate whether epigenetic modifications contribute to long-lasting oxidative stress and myocardial dysfunction in the diabetic heart.

Methods: Diabetes was induced in 4–6 months mice by streptozotocin. IGC was achieved by slow-release insulin implants placed subcutaneously 3 weeks after the induction of diabetes and maintained for the following 3 weeks. Mouse miRNAome profiling was investigated by real-time PCR array. DNA methylation was performed by bisulfite analysis of transcriptionally active CpG regions whereas chromatin immunoprecipitation (ChIP) was employed to study histone modifications. Mitochondrial superoxide anion (O2-) was detected by ESR spectroscopy. Left ventricular function was assessed by high resolution Micro-Ultrasound System in vivo.

Results: Mitochondrial O2- was significantly increased in the diabetic heart and IGC did not revert this phenomenon. Consistently, glucose control did not rescue left ventricular systolic dysfunction, assessed by ejection fraction and fractional shortening. miRNAome analysis revealed that miR-218 and miR-34a were significantly upregulated in the diabetic heart, and IGC did not affect their expression. We found that miR-218 and miR-34a respectively caused persistent downregulation of methyltransferase DNMT3b and deacetylase SIRT1 in the diabetic heart. Disturbed DNMT3b/SIRT1 caused DNA demethylation and histone 3 acetylation, leading to enhanced transcription of the mitochondrial adaptor p66Shc, a key pro-oxidant gene. Of note, inhibition of miR-218 and miR-34a in human cardiomyocytes suppressed glucose-induced p66Shc upregulation and ROS generation.

Conclusion: Here we show that miR-218 and miR-34a orchestrate chromatin modifiers DNMT3b and SIRT1 thus leading to adverse epigenetic remodelling of p66Shc promoter. This cascade causes persistent cardiac p66Shc upregulation and ROS generation despite glycometric control. Our results may contribute to explain why normoglycemia restoration fails to rescue phenotypic abnormalities in the diabetic heart.

Acknowledgement/Funding: European Foundation for the Study of Diabetes, Swedish Heart and Lung Foundation

P4321 | BEDSIDE
Effects of selective carotid body stimulation in humans
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Background: Carotid arterial bodies (CB) play an important role in the pathophysiology of sympathetically-mediated diseases such as hypertension or heart failure. However, the effects of selective, direct stimulation of CB in conscious, spontaneously breathing humans remain unknown.

Aims: We tested hemodynamic and ventilatory responses to direct, unilateral stimulation of CB with -adrenochrome, which does not cross blood-brain barrier and administered locally, due to its ultra-short plasma half-life time of less than 10s, does not exert systemic action.

Methods: We performed single-blinded, placebo-controlled study on 11 patients (9 men), 66±5 years. All underwent diagnostic carotid angiography due to unilaterally carotid artery stenosis. During the procedure at the non-stenosed side (9 men), 66±5 years. All underwent diagnostic carotid angiography due to unilaterally carotid artery stenosis. During the procedure at the non-stenosed side

Conclusions: Selective carotid body stimulation with low-dose adenosine increases MV. Nonetheless, hemodynamic responses remain dissociated. While SBP is augmented by direct CB stimulation, HR is simultaneously reduced. Establishing the link between SBP and CB activity further supports therapies targeting overactive CB for the treatment of arterial hypertension.

Acknowledgement/Funding: Authors received a scientific grant from Cibiem Inc.
P4234 | BEDSIDE
Prognostic value of simple frailty screening tools in patients with acute heart failure
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Background: Frailty is common in older adults with heart failure (HF) and is associated with worse outcomes. We compared the prognostic value of simple frailty screening tools against the well-validated clinical frailty scale (CFS) in patients with acute HF (AHF).

Methods: Prospective observational study on 265 consecutive patients (62% males, median age 80 (interquartile range (IQR): 72–86) years, 84% in New York Heart Association (NYHA) classes III or IV, median NTProBNP 3633 (IQR 2025–6407) ng/l) admitted to a district hospital between January 2013 and December 2014 with AHF. All patients had left ventricular systolic dysfunction. Patients were screened for frailty using the Derby frailty index (DFI) (frail vs non-frail), acute frailty network (AFN) frailty criteria (frail vs non-frail) and CFS (measured between 1–9, higher score indicates worse frailty status). Charlson comorbidity index was used to assess for comorbidities.

Results: Based on the CFS (CFS >4), DFI and AFN; 50%, 49% and 53% were frail (Figure 1). Frail patients were older, had higher Charlson score, worse NYHA class and renal function, were more likely to be anemic, and were less likely to receive an angiotensin-converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB). DFI correlated with AFN score (correlation coefficient (R) = 0.78, P <0.001) and CFS (R =0.70, p<0.001). During a median follow-up of 598 days (IQR 319–807 days), 113 patients died. Frailty was associated with mortality in univariable analysis (HR with 95% CI: 1.73 (1.56–1.92)).

Conclusion: The presence of frailty is strongly related to a poor outcome in patients with AHF. DFI and CFS both improve base model in predicting mortality in AHF patients.

P4235 | BENCH
Preserved exercise capacity in experimental heart failure by selective optogenetic recruitment of C-fibre vagal motor fibres
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Introduction: Vagus nerve stimulation (VNS) has been shown to reduce the extent of myocardial infarction (MI) and slow the progression of myocardial re-modelling and dysfunction in animal models of chronic heart failure. The precise mechanisms underlying the beneficial effect of VNS in heart failure are poorly understood. Vagus is a complex nerve containing both sensory and motor fibres, which conduct impulses from and to the majority of internal organs. It remains unclear whether the potential benefit of VNS in heart failure is due to the recruitment of afferent (sensory) or efferent (motor) vagal fibres by the stimuli delivered via implantable stimulators. Here we targeted vagal preganglionic neurones of the dorsal motor nucleus of the vagus nerve (DNVMN) to express light-sensitive optogenetic actuators and determined the effect of selective optical stimulation of vagal C-fibre efferent fibres on exercise capacity in a rat model of MI-induced heart failure.

Methods and results: Experiments were performed in accordance with the EU legislation and the UK Scientific Procedures Act 1986 and associated guidelines. In male Sprague-Dawley rats, DNVMN neurones were targeted using viral vectors to express either the light sensitive protein - Channelrhodopsin variant ChIEF, or transcontrol gene (eGFP). Four weeks later, animals underwent permanent left anterior descending (LAD) coronary artery ligation or sham surgery. Blue light stimulation (445 nm, 10 ms pulses, 15 Hz) of the transduced neurones via a pre-implanted optrode was performed under mid sedation (1% isoflurane) for 15 min every 48 h for weeks commencing 2 days after the surgery. Exercise capacity was determined using a single lane treadmill. Rats were selected for their compliance after a three-day recruitment protocol and randomized. The experimental protocol involved starting speeds of 20–30 cm/s over 5 min after 15 min acclimatisation. Speeds were then raised in increments of 5 cm/s every 5 min until the defined point of exhaustion. The calculated work (Joules, J) was used as an index of exercise capacity. After 4 weeks, left ventricular dysfunction in rats is associated with a marked reduction in exercise capacity (28±3 vs 56±8 J in sham-operated rats expressing eGFP; p=0.04, ANOVA). Optogenetic stimulation of vagal C-fibre efferents expressing ChIEF significantly enhanced exercise capacity in sham-operated animals (105±11 vs 56±8 J in sham-operated rats expressing eGFP; p=0.001, ANOVA) and preserved exercise capacity in animals with left ventricular dysfunction (56±4 vs 28±3 J in post-MI rats expressing eGFP; p=0.02; ANOVA).

Conclusion: Selective optogenetic recruitment of vagal C-fibre efferents is sufficient to preserve exercise capacity in the pathophysiological context of heart failure developing after a myocardial infarction.

Acknowledgement/Funding: Supported by The BHF (Ref: RG/14/4/30736 & PG/13/13/30429), Welcome Trust (Ref: 095064), Marie Curie Actions (Ref: 654691) and Rosetrees Trust

P4236 | BEDSIDE
Cholesterol homeostasis as a maker of early diagnosis of abdominal organs impairments in patients with non-ischemic diluted cardiomyopathy
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Background: Although low plasma total cholesterol (TC) level is known as a risk factor of heart failure (HF), alteration of its metabolism in patients with HF may be unknown. We hypothesized that alteration of TC metabolism would be a reliable maker for abdominal organs impairments due to HF, because it mainly comes from intestinal absorption and liver synthesis.

Purpose: To investigate whether reduction of TC absorption and synthesis has prognostic value in patients with non-ischemic diluted cardiomyopathy (NIDCM).

Methods: We analysed 64 patients with NIDCM (median age 57.5 years, female 31%) without lipid lowering therapy or NYHA class III/IV. All patients were examined biochemical examinations including plasma non-cholesterol sterols (Campesterol and Lathosterol as absorption markers; Lathosterol as a synthesis marker), and their serum TC, HDL-C, LDL-C were measured. We classified four subsets based on the median of Campesterol and Lathosterol as follows; Non-impaired (N-subset), Campesterol >3.6 μg/mL and Lathosterol >1.4 μg/mL; Absorption-impaired (A-subset), Campesterol ≤3.6 μg/mL and Lathosterol >1.4 μg/mL; Synthesis-impaired (S-subset), Campesterol >3.6 μg/mL and Lathosterol ≤1.4 μg/mL; Double-impaired (D-subset), Campesterol >3.6 μg/mL and Lathosterol ≤1.4 μg/mL. We followed up all patients mean of 2.4 years.

Results: The median of plasma brain natriuretic peptide (BNP) level and left ventricular ejection fraction of all the patients were 114 pg/mL and 31.4%, respectively. D-subset had the highest pulmonary capillary wedge pressure level and plasma BNP level and the lowest cardiac index among the four subsets (Table). During the mean of 2.4 years follow-up, 12 patients suffered from cardiac events, and D-subset had a significantly higher cardiac events rate (Figure). The best cut-off value of TC which discriminate D-subset was 15 mg/dL with 57% sensitivity and 92% specificity (C-statistic 0.76, 95% Cl 0.56–0.88, p<0.001).

Conclusion: Low plasma total cholesterol (TC) level is known as a risk factor of heart failure (HF), while alteration of its metabolism in patients with HF may be unknown. We hypothesis that alteration of TC metabolism would be a reliable maker for abdominal organs impairments due to HF, because it mainly comes from intestinal absorption and liver synthesis. Low plasma total cholesterol (TC) level is a maker of early diagnosis of abdominal organs impairments in patients with non-ischemic diluted cardiomyopathy. Low TC would be a reliable maker for early diagnosis of abdominal organs impairments due to HF.
BEST POSTERS IN IN TRANSFORMING UNDERSTANDING OF THE ELDERLY WITH CARDIOVASCULAR DISEASE

P4328 | BEDSIDE
Secondary versus primary stroke prevention in atrial fibrillation - Insights from the community-based darlington atrial fibrillation registry
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Background: Previous stroke is one of the strongest risk factors for recurrent stroke or thromboembolic event in patients with atrial fibrillation (AF).

Aim: To compare clinical outcomes of AF patients with versus without previous stroke in relation to stroke risk profile and antithrombotic treatment (ATT) patterns.

Methods: Retrospective analysis of an observational community study cohort of 105,000 patients from 11 general practices (GP) in Darlington, England. Follow-up period of 12 months, ATT use was assessed against 2014 NICE (National Institute for Health and Care Excellence) guidelines.

Results: Overall, 2259 (2.15%) AF patients were identified, of which 18.9% constituted a secondary prevention cohort (Table). Multivariable analyses demonstrated that non-guideline adherent ATT was associated with increased risk of stroke in primary prevention patients (odds ratio [OR] 3.25, 95% confidence interval [CI] 1.45–7.28, p=0.004 for under-treatment), while in the secondary prevention setting, guideline adherent ATT was associated with an increased risk of recurrent stroke (OR 2.57, 95% CI 1.25–5.31, p=0.01 for over-treatment) and all-cause death (OR 2.99, 95% CI 1.52–5.90, p=0.002 for under-treatment).

Table 1

<table>
<thead>
<tr>
<th>Characteristics, n (%)</th>
<th>All (2259)</th>
<th>Primary stroke prevention</th>
<th>Under-treatment</th>
<th>Over-treatment</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, mean (SD)</td>
<td>75.6 ± 12.2</td>
<td>79.6 ± 9.6</td>
<td>74.7 ± 12.6</td>
<td>74.9 ± 12.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Females</td>
<td>1041 (46.1)</td>
<td>193 (45.1)</td>
<td>848 (46.3)</td>
<td>85 (48.0)</td>
<td>0.684</td>
</tr>
<tr>
<td>CHA2DS2-VASc score, mean (SD)</td>
<td>3.5 ± 1.79</td>
<td>5.5 ± 1.28</td>
<td>3.0 ± 1.54</td>
<td>3.1 ± 1.54</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No antithrombotic therapy</td>
<td>367 (16.2)</td>
<td>26 (6.2)</td>
<td>335 (18.5)</td>
<td>25 (14.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>OAC A</td>
<td>971 (43)</td>
<td>422 (95.2)</td>
<td>446 (79.4)</td>
<td>4 (0.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>naptiapentol</td>
<td>812 (35.9)</td>
<td>370 (82.6)</td>
<td>680 (92.5)</td>
<td>3 (0.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>OAC + naptiapentol</td>
<td>109 (4.8)</td>
<td>9 (1.9)</td>
<td>92 (15.9)</td>
<td>3 (1.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Adherent antithrombotic treatment</td>
<td>1147 (50.7)</td>
<td>431 (95.2)</td>
<td>710 (95.8)</td>
<td>36 (9.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Over-treatment</td>
<td>216 (13.1)</td>
<td>216 (13.1)</td>
<td>195 (11.7)</td>
<td>1 (0.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Under-treatment</td>
<td>816 (36.1)</td>
<td>106 (24.8)</td>
<td>710 (38.8)</td>
<td>2 (0.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Recurrent/new stroke</td>
<td>67 (3.0)</td>
<td>37 (8.6)</td>
<td>30 (1.6)</td>
<td>0.33</td>
<td>0.001</td>
</tr>
<tr>
<td>Non-thromboembolic</td>
<td>4 (0.2)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0.001</td>
</tr>
<tr>
<td>All-cause death</td>
<td>214 (9.5)</td>
<td>25 (5.8)</td>
<td>189 (10.3)</td>
<td>0.33</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Conclusion: Despite a high thromboembolic risk profile, especially amongst secondary stroke prevention patients, only approximately 50% of patients are prescribed OAC in line with guidelines. Guideline-adherent ATT reduces the risk of stroke amongst primary prevention patients, but in those with prior stroke (i.e. secondary prevention), there is a significant reduction in recurrent stroke and death.

P4329 | BEDSIDE
Predictors of mortality in orthostatic hypotension among ultra-elderly: analysis of 27,031 hospitalizations
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Introduction: Ruhr University Bochum (RUB), Bochum, Germany

Aim: To study if antithrombotic treatment according to ESC guidelines is lower risks for both cardiovascular (CV) and all-cause death, but “real world” validation of the European Society of Cardiology (ESC) guidelines is needed.

Methods: To determine antithrombotic treatment had a lower rate of both CV death (3.4% vs 8.9%, p=0.024) and all-cause death (11.7% vs. 21.9%, p=0.007). Kaplan-Meier analysis showed that guideline adherent AF patients had a lower cumulative risk for both CV death (Log-Rank: 6.497, p=0.011) and all-cause death (Log-Rank: 9.631, p=0.002).

Results: Among 2,535 patients enrolled, 558 (22.0%) were discharged with a diagnosis of AF. Based on ESC guidelines, 40.9% of patients were guideline-adherent treatment, 6.8% were overtreated and 52.3% were undertreated. Logistic regression analysis [Table] found that age (p=0.010), heart failure (p=0.040), coronary artery disease (p=0.013), peripheral arterial disease (p=0.030) and comorbid neoplasms (p=0.003) were associated with non-adherence to guidelines. When compared to guidelines non-adherence, patients with guideline adherent treatment had a lower risk of both CV death (3.4% vs 8.9%, p=0.024) and all-cause death (11.7% vs. 21.9%, p=0.007). Kaplan-Meier analysis showed that guideline adherent AF patients had a lower cumulative risk for both CV death (Log-Rank: 6.497, p=0.011) and all-cause death (Log-Rank: 9.631, p=0.002).

Table 1. Logistic regression analysis

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>OR 95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per year)</td>
<td>1.03</td>
<td>0.100</td>
</tr>
<tr>
<td>Heart failure</td>
<td>0.68</td>
<td>0.440</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>1.71</td>
<td>0.013</td>
</tr>
<tr>
<td>Peripheral arterial disease</td>
<td>5.25</td>
<td>0.040</td>
</tr>
<tr>
<td>Neoplasia</td>
<td>2.31</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Legend: CI = confidence interval; OR = odds ratio.

Conclusion: Among Italian elderly AF patients, guideline non-adherence was evident for a larger proportion of patients. ESC guideline adherent treatment was independently associated with a lower risk of CV death and all-cause death.

P4330 | BEDSIDE
Adherence to ESC antithrombotic guidelines improves mortality among Italian elderly AF patients: insights from the REPOSI study
M. Proietti1, A. Nobili2, V. Raparelli3, R. Cangemi4, L. Napoleon Le4, S. Basili5, P.M. Mannucci6, G.Y.H. Lip2 on behalf of REPOSI Investigators, 1University of Birmingham, Institute of Cardiovascular Sciences, Birmingham, United Kingdom; 2IRCBS - Istituto di Ricerche Farmacologiche Mario Negri, Department of Neuroscience, Milan, Italy; 3Sapienza University of Rome, Department of Experimental Medicine, Rome, Italy; 4Sapienza University of Rome, Internal Medicine and Medical Specialties, Rome, Italy; 5Fondazione IRCSS Cà Granda, A. Bianchi Bonomi Hemophilia and Thrombosis Center, Milan, Italy

Introduction: Orthostatic AF (AF) is associated with a substantial risk of thromboembolism and mortality. Oral anticoagulation significantly reduces stroke/systemic embolism and all-cause mortality. Adherence to guidelines may lower risks for both cardiovascular (CV) and all-cause death, but “real world” validation of the European Society of Cardiology (ESC) guidelines is needed.

Methods: The REPOSI study was an observational study enrolling patients ≥ 75 years admitted to Italian internal medicine wards. The objectives were to compare “real-world” adherence to ESC guidelines in 2012 and 2014 discharged with an AF diagnosis were studied. Adherence of prescribed antithrombotic treatment, was defined accordingly to 2012 ESC guidelines.

Results: Adherence to ESC antithrombotic guidelines improves mortality among Italian elderly AF patients: insights from the REPOSI study
old patients achieved higher absolute contribution margins (2065±1033 €) than old (1804±1902; p=0.001) and young patients (1771±1902; p=0.001). However, relative contribution margins (DRG revenue per day) were significantly smaller (440±228 €) than in old (488±234; p=0.001) and young patients (484±206; p=0.001).

Conclusions: Catheterization of very elderly patients is related to lower contribution margins per patient day despite higher material and time expenditures. Since efforts to reduce the length of hospital stay are limited in these patients a competitive disadvantage of hospitals who are more affected by the demographic change may result.

BEST POSTERS IN MYOCARDITIS

P4334 | BEDSIDE
Incidence of late life-threatening arrhythmias in cardiac sarcoidosis presenting with heart block
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Purpose: According to Heart Rhythm Societys (HRS) expert consensus statement, an intracardiac cardioverter-defibrillator (ICD) should be considered (class IIa recommendation) in all patients with cardiac sarcoidosis (CS) needing device-based therapy for atrioventricular block (AVB). Yet, the risk of sudden death is unknown in patients with CS presenting with AVB free of severe left ventricular (LV) dysfunction and spontaneous ventricular tachyarrhythmias. We set out to study the incidence of late-life threatening ventricular arrhythmias in CS patients presenting with AVB.
Methods: Our work involved 67 consecutive CS patients (56 women, mean age 57 y) presenting between 1989 and 2015 with an AVB needing device-based therapy. AVB was complete in 55 patients, of 2nd degree (Mobitz II) in 7 patients and of 1st degree in a 3-fascicular block combination in 5 patients. 52 and 15 patients received a permanent pacemaker and an ICD, respectively, by the discretion of the attending cardiologist. The outcome endpoint during retrospective follow-up was a composite of sudden death, aborted sudden death due to ventricular fibrillation (VF) and sustained ventricular tachycardia (VT) needing treatment.

Results: At presentation, 10 patients had either severe LV dysfunction (ejection fraction <35%) or history of spontaneous sustained VT or VF and thus fulfilled, in retrospect, a class I indication for an ICD by the current HRS expert consensus criteria. Arrhythmic endpoint events were recorded in 5 of these 10 patients during follow-up (mean duration 56 months); 2 of the 5 events were sudden or aborted sudden deaths. From the remaining 57 patients without class I indication for an ICD, 8 individuals experienced endpoint events of which 5 were sudden or aborted sudden deaths. The figure shows the Kaplan-Meier curves for event-free survival in the two groups. The 5-year estimate for the cumulative incidence of life-threatening arrhythmias in the subgroup without class I indication was 18% (95% confidence interval, 9–31%).

Event-free survival

Conclusions: Our findings support the class IIa recommendation for an ICD to all CS patients needing device therapy for the management of AVB.

Acknowledgement/Funding: Finnish Cardiac Society, Finnish Government Research Funding

P4335 | BENCH
Myocardial expression of TLR-4 predicts the response to immunosuppressive therapy in patients with virus negative inflammatory cardiomyopathy
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Background: Immunosuppressive therapy has demonstrated beneficial effects in patients with virus-negative myocarditis, but there are still a proportion of patients who do not respond to the treatment.

Purpose: We sought to determine whether myocardial expression of Toll-like receptor (TLR) 4 may predict the response to immunosuppression.

Methods: Left ventricular endomyocardial biopsies from 30 consecutive patients with virus negative inflammatory cardiomyopathy responding to immunosuppressive therapy (group A) were analyzed for the myocardial expression of TLR 4. Group A was compared with 30 consecutive patients not responding to immunosuppression (group B) and with 30 normal controls (group C). A semi-quantitative evaluation of the immunoreactivity (grading from 0 to 4) for TLR4 and for HLA-DR was performed together with Real time PCR and Western blot for TLR4 on frozen tissue.

Results: A focal intense positive cytoplasmic immunoreactivity for TLR4 was observed in cardiomyocytes of all group A patients, with a statistically significant different (p<0.001) compared with group B and controls (panel A). Conversely, HLA-DR immunostaining did not discriminate between responders and non-responders. Real time PCR expression of TLR4 was 4 fold higher in responders than in non-responders (p<0.001) (panel B). Western blot analysis showed a 3,3 fold increase in TLR4 in group A compared with group B (panel C and D). Cell death by apoptosis was 3,5 fold higher in Group A compared with Group B, while necrosis was comparable between the two groups. After six months immunosuppression responders showed an increase in ejection fraction that correlated with the reduction in TLR4 expression.

TLR4 in virus negative myocarditis

Conclusion: TLR4 is highly expressed in human immune-mediated myocarditis responding to immunosuppression. It can be considered as a new high sensitive marker in patient selection for immunosuppressive/immunomodulatory therapy.

P4335 | BEDSIDE
Utility of plasma and endomyocardial galectin-3 levels to predict cardiac fibrosis and inflammation in patients with newly diagnosed cardiomyopathy
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Aims: Galectin (Gal)-3 is a soluble β-galactoside-binding lectin released by inflammatory cells, including macrophages, and currently intensely studied as a novel biomarker in patients with heart failure. Importantly, Gal-3 also exerts pro-inflammatory effects, at least in extracellular tissues. The aim of the present study was to characterize the relationship of plasma and myocardial levels of Gal-3 with cardiac fibrosis and inflammation in patients with newly diagnosed cardiomyopathy.

Methods: Endomyocardial biopsies from both ventricles and blood samples were obtained from 109 patients with newly diagnosed cardiomyopathy and clinical suspicion of myocarditis. According to the histological analysis, patients were classified as having inflammatory cardiomyopathy (ICMP, n=73) or dilated cardiomyopathy (DCM, n=36). Gal-3 plasma levels were quantified by ELISA; endomyocardial Gal-3 mRNA and protein levels were analyzed by PCR and immunohistochemistry, respectively. Cardiac fibrosis was assessed histologically on endomyocardial biopsy sections.

Results: In patients with ICMP myocardial Gal-3 expression significantly correlated with macrophage cell count on endomyocardial biopsy. In contrast, an inverse association was observed between myocardial Gal-3 expression and cardiac fibrosis in patients with ICMP. These results were consistent for right and left ventricular biopsy samples. In patients with DCM myocardial Gal-3 expression correlated with cardiac fibrosis on right and left ventricular biopsy. Of note, in both groups marked differences were observed between plasma and myocardial Gal-3 levels, independent of renal function.
Conclusion: The present study demonstrates for the first time that myocardial Gal-3 needs to be considered as a marker for both, cardiac inflammation and fibrosis. At least in the present cohort, plasma Gal-3 did not serve as a reliable surrogate for endomyocardial Gal-3 levels. These findings are likely of importance for studies evaluating plasma Gal-3 as a novel biomarker in patients with heart failure.

P4336 | BEDSIDE
Endomyocardial biopsy in patients with no symptoms of myocardial disease except ventricular arrhythmia
V.V. Grokhotova1, L.B. Mitrofanova2. 1 The North -Western State Medical University, Cardiac Surgery, Saint-Petersburg, Russian Federation; 2 Almazov Federal Heart, Blood and Endocrinology Centre, St. Petersburg, Russian Federation

Purpose: Idiopathic ventricular tachycardia (VT) is known to occur in structurally normal hearts. The aim of our study was to establish morphological basis for “idiopathic” ventricular arrhythmias.

Methods: 87 patients of averal age 39,9±1,7 with no clinical signs of myocardial disease and structurally normal hearts and normal ejection fraction according to echocardiography were included. 41 (53%) had sustained VT, 46 (47%) had premature ventricular beats and episodes of non-sustained VT, ventricular ectopy was monomorphic in 48 patients, pleomorphic in 21 (24%) and polymorphic in 18 (21%). Patients underwent radiofrequency ablation for ventricular arrhythmia and endomyocardial biopsy (EMB). We obtained 4–5 pieces of myocardium from right ventricle. Myocarditis was diagnosed according to histological criteria (myocyte degeneration and necrosis of non-ischemic origin) and immunohistochemistry criteria (>14 leukocytes/mm² including up to 4 monocytes/mm² with the presence of CD 3 positive T lymphocytes >7 cells/mm²). Arrhythmogenic right ventricular cardiomyopathy (ARVC) was diagnosed if there was fibro-fatty tissue replacement with residual myocytes less than 60% by morphometric analysis.

Results: 29 patients showed major criterion of ARVC. Residual cardiomyocytes were 33,3% ±15,5. Patchy or full lack of plakoglobin expression was found in 65% with ARVC. Acute myocarditis was found in 7 patients, borderline in 2, viral in all cases. VP1 antigen of Enterovirus was found in 5 patients, NS3 antigen of hepatitis C virus in 1 patient and antigen of Parovirus B 19 in 2 persons. Average area of lipomatosis was 34,3±1,4%, in patients with ARVC and myocarditis - 42,1±2,5%, in patients without myocarditis -32,7±13,4%. ARVC + myocarditis specimens appeared to have more severe fibrosis - 37,2±17,2% versus those with ARVC only -30±15%. 34 patients had myocarditis only, 21% -viral myocarditis specimens appeared to have more severe fibrosis - 37,2±17,2% versus those with ARVC only -30±15%. 34 patients had myocarditis only, 21% -viral myocarditis specimens appeared to have more severe fibrosis - 37,2±17,2% versus those with ARVC only -30±15%. 34 patients had myocarditis only, 21% -viral myocarditis specimens appeared to have more severe fibrosis - 37,2±17,2% versus those with ARVC only -30±15%. 34 patients had myocarditis only, 21% -viral myocarditis specimens appeared to have more severe fibrosis - 37,2±17,2% versus those with ARVC only -30±15%.

Conclusion: EMB can reveal myocardial disease in patients with ventricular arrhythmias even if non-invasive methods cannot. Detection of myocarditis and ARVC is of diagnostic importance because it can influence treatment tactics. Myocarditis often accompanies ARVC, inducing myocyte damage and necrosis, thus worsening the disease.

BEST POSTERS IN ANTITHROMBOTIC: FROM THE BENCH TO THE BEDSIDE

P4338 | BEDSIDE
Composite of platelet receptors genes and cytochrome p450 genes polymorphisms is the possible predictor of cardiovascular events after coronary artery bypass grafting
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Background: The identification of cardiovascular events (CVE) predictors after coronary artery bypass grafting (CABG) remains up-to-date.

Purpose: To investigate the association of single nucleotide polymorphisms (SNPs): rs2046934, rs1226643 (C607T, Phe224Phe) on ITG2A [encoding collagen receptor] (n=87); rs5918 (176 T→C, Leu33Pro) on ITG3 [encoding fibrinogen receptor] (n=91); rs6065 (Thr145Met) on GP1BA [encoding platelet receptor for Von Willebrand factor] (n=114); rs4244285 (2) (n=84) and rs4986893 (3) (n=83) on CYP2C19 [encoding cytochrome P450 activity].

Results: The prevalence of SNPs rs5918, rs6065, rs4244285, rs4986893, rs2046934 did not differ significantly between patients and healthy volunteers. The mutant allele (T) of ITG2A was detected more often in healthy volunteers: 67,2% vs 51,7% (p=0,021). Before and after CABG there was no significant difference in the platelet aggregation between carriers of the mutant ITG2A allele and non-carries. During follow-up period 12 CVE were registered: 3 strokes, 6 MI, 3 deaths. Patients with composite mutant alleles of ITG3B+CYP2C19*2 or CYP2C19*2+ITG2A, and with the mutant allele (2) of CYP2C19 met end points more often than patients with other gene combinations (wild type homozygous, presence of one mutant allele of ITG3B or ITG2A, the composite of mutant alleles of ITG3B+ITG2A or ITG3B+ CYP2C19*2 (HR=4, 95% CI: 2,19–7,29, p=0,008). Carriers of ITGB3 mutant allele showed higher AA-induced platelet reactivity values on the 1st-3rd day after CABG. Amplitude of platelet aggregation in mutant allele carriers was 27.5% vs 12.7% in wild type (p=0.016). No differences in platelet reactivity among carriers of other mentioned mutant alleles and wild types were observed.

Conclusion(s): Carriage of the combination of mutant alleles ITGB3+CYP2C19*2 or CYP2C19*2+ITG2A is a possible predictor for CVE in patients after CABG.
stated for validation by means of qRT-PCR. Interestingly, among the miRNAs showing the largest modulation, we found that the platelet miR-223 (p = 0.006) and miR-129-3p (p < 0.001), as well as the miR-100 (p < 0.001), associated with plaque vulnerability, and the miR-1973 (p < 0.001) were significantly up-regulated. On the contrary, the miR-650 (p < 0.001), miR-219-5p (p = 0.001) and miR-1248 (p < 0.001), associated to reduced cardiac function were found to be significantly down-regulated, together with the antiatherogenic miR-32 (p < 0.001) and the miR-129-5p (p < 0.001), involved in cell-to-cell communication in cardiovascular diseases. Target and network analyses performed with Ingenuity Pathway Analysis and Gomir revealed that the modulated miRNAs are involved in key intracellular signaling pathways, including ERK, Runx-1, p53 and NFAT.

Conclusions: The differential miRNA expression profile in intra-coronary thrombi from NR patients suggests that both platelets and cells of the vessel wall could be involved in the pathophysiology of NR. Future studies will test their mechanistic involvement in experimental models.

P4340 | BEDSIDE
Pro-coagulant activity during exercise testing in patients with coronary artery disease
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Background: Strenuous exercise may trigger myocardial infarction through increased pro-coagulant activity. We intended to investigate whether patients referred for exercise testing, who were found to have angiographically verified coronary artery disease (CAD), have a more hypercoagulable profile during exercise testing compared to those without CAD.

Materials and methods: 106 patients (82 males, mean age 62±10 years) with symptoms suggestive of stable CAD were examined with exercise electrocardiography on bicycle ergometer. Venous blood samples were taken at rest and within 5 minutes after end of exercise. The following haemostatic variables were analysed: tissue factor pathway inhibitor (TFPI) activity and antigen, prothrombin fragment 1+2 (F1+2), D-dimer and endogenous thrombin potential (ETP). The latter was measured by the calibrated automated thrombogram (CAT) assay and the others with ELISAs. All participants underwent conventional coronary angiography. CAD was defined as having any degree of atherosclerosis.

Results: Out of 106 patients enrolled, 70 were found to have angiographically verified CAD. Mean exercise duration was 10:06±4:11 min and mean metabolic equivalent (MET) 6.7±1.8, with non-significant differences between the two groups. A significant increase from baseline to after exercise testing was observed in all measured markers in the total population (p < 0.002 for all). The increase remained significant in all markers except for D-dimer (p = 0.071) when adjusting for change in hematocrit. In patients with angiographically verified CAD, total TFPI was significantly lower at baseline compared to patients without CAD (median value 67.4 and 78.6 ng/ml respectively, p = 0.027). However, no significant differences in changes of the measured markers during exercise were observed between the two groups.

Conclusion: Pro-coagulant activity increased during exercise testing in patients with symptoms suggestive of CAD, but the hypercoagulable state observed after undergoing strenuous exercise, was not more pronounced in patients with CAD than in patients without CAD.

P4341 | BEDSIDE
A novel score that includes thrombogenicity and central pulse pressure enhances the prediction of long term ischemic outcomes
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Background: Conventional cardiovascular risk stratification scores are mainly based on demographic characteristics and lipids but ignore thrombogenicity and vascular function.

Methods: Laboratory, angiographic, and clinical variables were collected in 411 patients with documented coronary artery disease undergoing elective cardiac catheterization and followed for 3 yrs for composite endpoint (CE) (CV death, MI or IS) and total ischemic event (TIE) (CE+ hospitalization for recurrent ischemia). Lipid profile, and thrombin-induced platelet-fibrin clot strength (TIP-FCS) were determined prior to catheterization and central pulse pressure (CPP) was obtained during catheterization. A scoring model was proposed to predict ischemic event occurrence based on multi-regression analysis.

Results: There were 22 CEs and 82 TIEs. The most predictive factors for CE were CPP, age, TIP-FCS, prior PCI or CABG, and diabetes. 54%, 36% and 10% had risk scores of low, moderate and high risk respectively. The CE frequency was 1%, 4%, and 36% in patients with low risk, moderate risk, and high risk, respectively (table).

Conclusion: Inclusion of CPP and an assessment of thrombogenicity in a novel risk score enhance the identification of patients with documented CAD who are at risk for ischemic events.

POSTER SESSION 5
ECHO VENTRICULAR FUNCTION

P4342 | BEDSIDE
Relationship of left ventricular hypertrophy to vascular events in patients with non-valvular atrial fibrillation: the ARAPACIS study
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Background: Left ventricular hypertrophy (LVH) is associated with a higher risk of adverse events and mortality in both the general population and hypertensive patients. Limited data are available on adverse outcomes in AF patients with LVH.

Purpose: To study clinical features associated with severe LVH amongst AF patients. Second, we would determine the relationship of LVH with adverse outcomes.

Methods: The ARAPACIS study is a nationwide observational study of Italian non-valvular AF patients. LVH was evaluated according to left ventricular mass indexed (LVMi) according to body surface area. Severe LVH was defined as LVMi ≥ 142 g/m2 for women and ≥ 149 g/m2 for men. Vascular events (composite outcome of vascular death, any myocardial infarction and any stroke or transient ischemic attack) were evaluated after 36-months follow-up.

Results: Of 1,087 (53.6%) patients had reliable echocardiographic data. LVH was reported in 53.0% (n=576) and severe LVH was recorded in 20.3% (n=221). Logistic regression analysis found that age (odds ratio [OR]: 1.05 per year, 95% CI: 1.00–1.10, p = 0.001), history of diabetes mellitus (OR: 1.87, 95% CI: 1.33–2.63, p < 0.001) and vascular disease (OR: 1.53, 95% CI: 1.08–2.18, p = 0.017) were associated with the presence of severe LVH. A total of 75 (6.9%) events were collected during a median [IQR] 36 [21–36] months follow-up. Patients with severe LVH had a higher rate of vascular events compared to those with “mild” and “moderate LVH”, as well as “no LVH” (12.2% vs. 3.3%, 6.4% and 6.3% accordingly; p = 0.002).

Kaplan-Meier curves for vascular events

Table 1

<table>
<thead>
<tr>
<th>Ischemic risk model</th>
<th>Hazard ratio</th>
<th>P value</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPP, mmHg &lt; 60</td>
<td>7.1</td>
<td>0.0001</td>
<td>0</td>
</tr>
<tr>
<td>CPP, mmHg ≥ 60</td>
<td>2</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Age &lt;65 yrs</td>
<td>6.8</td>
<td>0.0001</td>
<td>2</td>
</tr>
<tr>
<td>Age ≥65 yrs</td>
<td>2</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>TIP-FCS &lt;69 mm</td>
<td>6.8</td>
<td>0.0001</td>
<td>2</td>
</tr>
<tr>
<td>TIP-FCS ≥69 mm</td>
<td>2</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Prior PCI or CABG</td>
<td>3.5</td>
<td>0.006</td>
<td>1</td>
</tr>
<tr>
<td>History of diabetes</td>
<td>2.6</td>
<td>0.03</td>
<td>1</td>
</tr>
</tbody>
</table>

Low risk level 0-2

Medium risk level 3-5

High risk level 6-8
Strain echocardiography predicts early death in ST-elevation myocardial infarction after primary percutaneous coronary intervention

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Background: Speckle tracking derived myocardial strain is a sensitive reflector of myocardial deformation and shown to be superior to wall motion analysis. The value of strain in post-infarction is uncertain relative to well-known clinical variables.

Purpose: The aim was to evaluate the clinical value of strain echocardiography in early death after myocardial infarction.

Methods: Clinical, laboratory, electrocardiographic, angiographic, and conventional and strain echocardiographic parameters were collected in 539 patients (mean age 60±14 years; 85% men) with ST-elevation myocardial infarction (STEMI) and status-post primary percutaneous coronary intervention (PCI). 2-dimensional speckle tracking method was used to assess left ventricular (LV) global longitudinal strain (GLS). Door to balloon interval, QRS interval, and echocardiographic parameters were collected in 539 patients (mean age 60±14 years; 85% men) with ST-elevation myocardial infarction (STEMI) and status-post primary percutaneous coronary intervention (PCI). 2-dimensional speckle tracking method was used to assess left ventricular (LV) global longitudinal strain (GLS). Door to balloon time, QRS interval, and echocardiographic parameters were collected in 539 patients (mean age 60±14 years; 85% men) with ST-elevation myocardial infarction (STEMI) and status-post primary percutaneous coronary intervention (PCI).

Results: During follow-up (mean 3 years), 62 deaths occurred (Fig). There were 39 (63%) deaths within 2 months, defined as early death. No difference in gender, age, Killip class, history of hypertension, diabetes mellitus, chronic kidney disease, previous MI and heart failure, peak cardiac enzyme, culprit vessel, TIMI flow, stent deployment, intraaortic balloon pumping or extracorporeal membrane oxygenation was noted between early and late death. However, there was significant difference in QRS interval, door to balloon time, left main disease, LV ejection fraction, and GLS. The receiver operating characteristic analysis demonstrated that GLS ≤ -11.9 predicted early death with sensitivity 0.82 and specificity 0.61, better than other variables (Tab). The multivariable analysis showed that GLS was better than left main disease to predict early death as well.

Conclusion: Speckle tracking derived GLS is a strong and independent predictor of early death in patients with STEMI post primary PCI. The prognostic value of GLS is superior to other clinical variables, including angiographic ones.

<table>
<thead>
<tr>
<th>Early death (n=39)</th>
<th>Late death (n=25)</th>
<th>P value</th>
<th>Area under curve</th>
</tr>
</thead>
<tbody>
<tr>
<td>QRS interval (ms)</td>
<td>122±32</td>
<td>97±21</td>
<td>0.003</td>
</tr>
<tr>
<td>Door to balloon time (min)</td>
<td>124±115</td>
<td>102±166</td>
<td>0.01</td>
</tr>
<tr>
<td>Left main disease</td>
<td>7 (18%)</td>
<td>0 (0%)</td>
<td>0.04</td>
</tr>
<tr>
<td>LV ejection fraction (%)</td>
<td>38±15</td>
<td>48±16</td>
<td>0.02</td>
</tr>
<tr>
<td>GLS (%)</td>
<td>−9±4</td>
<td>−14±5</td>
<td>0.0006</td>
</tr>
</tbody>
</table>

![Survival curve](https://example.com/survival_curve.png)

Conclusion: Speckle tracking derived GLS is a strong and independent predictor of early death in patients with STEMI post primary PCI. The prognostic value of GLS is superior to other clinical variables, including angiographic ones.
Objective: To evaluate in stable outpatients with systolic heart failure, and on optimal therapy, if the GS is superior to LV ejection fraction (LVEF) in predicting long term survival.

Population and methods: 232 consecutive outpatients, LVEF < 40%, clinically stable in "dry-state", on optimal HF therapy were followed-up for 3 years in a HF Unit. End-point was all-cause death. Clinical stability: no change in NYHA, therapies including diuretics, no decompensation or hospitalization. GS, LVEF, LAVi and TAPSE evaluated off-line (Vivid 7, Ecospace 12). GS was categorized according to the median (<26). Cox regression model adjusted for confounders including clinical profile, therapeutics, NYHA, LVEF, TAPSE and LAVi.

Results: (1) GS correlated significantly with LVEF (r = -0.69, p < 0.001). (2) Decreased had worse GS (9.18±3.4 vs. -7.5±2.7; p < 0.025). LVEF (28.8±8.6 vs 25.9±8.3; p = 0.023), TAPSE (20.4±4.8 vs. 15.2±4.9; p = 0.003) and LAVi (29.3±17.2 vs 49.2±19.2; p = 0.001). (3) The ROC curve for death was associated with GS (AUC 0.63 95% CI 0.56–0.71; p = 0.002), with optimal cut-off > -9.51. (4) GS > -8.26 (HR = 2.2, 95% CI 1.0–4.72; p = 0.041) was associated with increased death risk, after adjustment for all significant confounders.

Conclusion: In stable outpatients with systolic heart failure and on optimal therapy, global strain evaluation improves survival prediction beyond conventional echocardiographic parameters.

P4346 | BEDSIDE

Differences in the regional and global changes in speckle tracking analysis after radiotherapy in the early left-sided versus right-sided breast cancer patients

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Background: Radiotherapy (RT) in the thoracic region increases late cardiovascular morbidity and mortality. The impact of the breast cancer laterality on cardiac function is largely unknown. The aim of this prospective study was to compare RT-induced changes in left-sided and right-sided breast cancer patients by speckle tracking echocardiography (STE).

Methods: Twenty eligible patients with right-sided and sixty patients with left-sided breast cancer were evaluated before and immediately after RT. None received chemotherapy. A comprehensive echocardiographic examination included 3D measurements and STE of the left ventricle.

Results: The global longitudinal strain (GLS) was reduced from -18.3±3.1 to -17.2±3.3 % (p < 0.003) after RT and regional analysis showed reduction in the apical strain from -18.7±5.3 to -16.7±4.9 % (p < 0.002) and increase in basal values from -21.6±5.0 to -23.3±4.9 % (p < 0.024) in patients with left-sided breast cancer. Patients with right-sided breast cancer showed deterioration in basal anterior segments by STE and pulsed tissue Doppler. The decline in GLS was associated with increased myocardial mass (r = 0.357, p < 0.002) and atrial size (r = 0.361, p < 0.002). The decline in the apical STE values was associated with several maximal RT values and with delayed apical rotation (r = 0.4, p < 0.001). RT caused no significant changes in the conventional systolic or STE circumferential measurements.

Conclusions: RT induced regional changes corresponding to the RT fields and the changes were opposite in left- and right-sided breast cancer. Patients with left-sided breast cancer experienced apical impact and global decline whereas patients with right-sided breast cancer showed basal chances with apical sparing.

Acknowledgement/Funding: Paavo and Elia Salonen Legacy, Ida Montin Fund, the Finnish Foundation for Cardiac Research.

P4347 | BEDSIDE

Validation of incremental value of speckle tracking echocardiography to predict CRT responders

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Background: A dysynchrony parameter by speckle tracking echocardiography (STE) may be useful to predict cardiac resynchronization therapy (CRT) responders. However, it has not been well studied whether a STE parameter improves the diagnostic accuracy beyond the already documented diagnostic information. Therefore, we hypothesized that a multivariate diagnostic model associated with CRT responders might be helpful to quantify the incremental value of a STE parameter.

Methods: One hundred eighty patients with CRT were enrolled. A responder to CRT was defined as a patient with a >15% reduction of left ventricular end-systolic volume at 6 months after CRT. A standard deviation of time from QRS onset to first peak of circumferential strain in the LV 6 segments (TSD) was used as the dysynchrony parameter. A logistic regression analysis with forward step method was used to determine independent parameters, and compared the probability of multivariate models between without TSD (model 1) and with TSD (model 2). In addition, the MADIT score also was compared. The incremental value of STE was assessed using a c-statistics, the net reclassification improvement (NRI), integrated discrimination improvement (IDI), and net benefit using decision curve analysis.

Results: 109 patients were identified as responders to CRT. Left bundle branch block (LBBB), mitral regurgitation (MR) index <40%, use of beta blocker, blood urea nitrogen (BUN) <30mg/dL, LV end-systolic dimension (LVED) ≤50mm, and TSD >116ms were significantly associated with responders. In the comparisons of the multivariate model and model 2, the c-statistics of the model 2 were significantly higher than the model 1 (0.86 vs. 0.77, p < 0.001). In addition, the NRI of model 2 for model 1 was 0.19 (p < 0.001), and the IDI was 0.17 (p < 0.001). Based on the model 2, a point of LBBB and MR index <40% were assigned a numeric value of 2, use of beta blocker, BUN ≤30mg/dL and LVED ≤50mm was 3 each, and TSD >116ms was 4 in our score system. The c-statistics of our score system was higher than MADIT score system (0.86 vs. 0.66, p < 0.001). The NRI of our score system for MADIT score system was 0.45 (p < 0.001), and the IDI was = 0.15 (p < 0.001). On the decision curves, net benefit was higher with threshold probabilities >0.2 by the our score system approach with TSD than the MADIT score system approach (Figure).

Conclusions: This study revealed the incremental value of a STE parameter to predict CRT responders beyond the already documented diagnostic information by novel statistical methods.

P4348 | BEDSIDE

Left ventricular geometry and cardiopulmonary exercise performance in apparently healthy individuals at cardiovascular risk: an analysis of the EUROEX trial

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Background: Left ventricular hypertrophy (LVH) and altered geometry are predictors of adverse cardiovascular (CV) events. 4 patterns of LV chamber remodeling were identified in apparently healthy individuals at cardiovascular risk: an analysis of the EUROEX trial.

Methods: 185 healthy subjects (47% males), mean age 62.3±13.4 years, with CV risk factors (20.5% diabetes; 23.8% tobacco use; 51.4% dyslipidemia; 70.3% hy-
Strain echocardiography demonstrates alterations in left ventricular deformation in preadolescents with previous fetal growth restriction

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Background: Fetal growth restriction (FGR) affects about 5 to 10% of new-borns and is associated with increased cardiovascular mortality in adulthood. FGR might induce primary cardiac alterations, explaining susceptibility for cardiovascular disease later in life.

Purpose: Our goal was to assess LV deformation by 2D speckle-tracking strain echocardiography in preadolescents with previous FGR.

Methods: Within a cohort of fetuses with FGR identified in fetal life and followed-up into preadolescence, echocardiography was performed in 58 preadolescents with FGR (defined as birthweight below 10th centile) and 94 preadolescents with normal birthweight centile. Peak systolic longitudinal strain was assessed in 18 LV segments and peak systolic circumferential and radial strain were assessed in 6 LV segments and were averaged to global longitudinal strain (GLS), global circumferential strain (GCS) and global radial strain (GRS), respectively. The presence of post systolic shortening, a marker of increased afterload, was also investigated in the LV segments.

Results: GLS was significantly decreased (Figure) while GCS and GRS were similar (Table).

Conclusions: Our results suggest that primary cardiac alterations are present in preadolescents with previous FGR. Although, longitudinal LV function was preserved due to increase in circumferential and radial deformation. Nevertheless, these subclinical alterations may explain the increased predisposition to cardiovascular disease in adulthood.

P4349 | BEDSIDE
Prognostic value of echocardiographical diastolic dysfunction parameters in a large population based cohort: a long term (7 year) follow up study

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Introduction: Diastolic dysfunction is associated with increased morbidity and mortality. Relationship between echocardiographical diastolic dysfunction parameters and total mortality in a large randomly selected population based cohort is largely unknown.

Aim: The aim of this study was to determine the relationship between echocardiographical measurements indicating diastolic dysfunction and total mortality in subjects of HAPPY (Heart Failure Prevalence and Predictors in Turkey) cohort whose total mortality and echocardiographical data could be obtained.

Methods: HAPPY is a population-based, cross-sectional study of heart failure residents, aged >35 years were enrolled. Baseline echocardiographical measurements and total mortality data could be obtained for 277 patients. Left ventricle end systolic volume (LVESV), left ventricle end diastolic volumes volume (LVEDV), left atrial volume index (LAVI), mitral E and A velocities, mitral E to A velocity ratio (Mitral E/A), mitral E velocity to mitral annulus E velocity ratio (E/e), left ventricular ejection fraction (LVEF), left ventricular isovolumetric relaxation time (LVIRVT) and left ventricle mass index (LVMI) values were compared between subjects that were alive and dead.

Results: Mean age was 51.5±11.21 years, 157 subjects (56.7%) were female, 168 subjects (60.6%) had hypertension, 21 subjects (7.6%) had a history of coronary heart disease. Mean follow up was 81.3±11.57 months. 20 subjects (7.2%) died during follow up. Mean LVEF, E/e, LAVI, LVIRVT and LVMI were significantly higher and mean LVEF was significantly lower in the subjects who died compared to the subjects who survived (Figure 1). Binary logistic regression analysis revealed E/e as independent predictor for total mortality. [OR:1.17 (1.01–1.37, 95% CI), p=0.04]

Echocardiographic parameters

<table>
<thead>
<tr>
<th>Controls (n=14)</th>
<th>FGR (n=58)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV ejection fraction, %</td>
<td>58 (56–60)</td>
<td>58 (57–62)</td>
</tr>
<tr>
<td>LV cardiac index, L/min/kg</td>
<td>2.9 (2.5–3.4)</td>
<td>3.1 (2.6–3.4)</td>
</tr>
<tr>
<td>LV global longitudinal strain, %</td>
<td>-22±1.37</td>
<td>-21±1.16</td>
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<tr>
<td>LV global circumferential strain, %</td>
<td>-22±2.62</td>
<td>-24±2.52</td>
</tr>
<tr>
<td>LV global radial strain, %</td>
<td>46±1.46</td>
<td>54±1.16</td>
</tr>
</tbody>
</table>

Presence of post systolic shortening, n (%) | 20 (21) | 19 (22) | 0.04 |

Data expressed as mean ± SD, median (interquartile range) and n (%). Right column shows P-value for Student’s t, non-parametric and Chi square tests. FGR, fetal growth restriction; LV, left ventricular; E/e, mitral E velocity to mitral annulus E velocity ratio; Mitral E/A, mitral E velocity to mitral annulus E velocity ratio; LVIRVT, left ventricular isovolumetric relaxation time; LVMI, left ventricle mass index

Conclusion: In study population baseline mean ESV-LV, E/e and LAVI measurements were significantly higher in subjects who died during long term follow up. E/e was an independent predictor of long term total mortality.
P4351 | BEDSIDE
Improvement of arterial stiffness, LV myocardial deformation and endothelial glycosalyx in patients with poorly controlled diabetes mellitus type 2 after optimization of antidiabetic medication
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Arterial stiffness is associated with increased risk for cardiovascular disease. The purpose of this study is to investigate changes in arterial stiffness, LV myocardial deformation and endothelial glycosalyx in patients with diabetes mellitus type 2 before and after glycemic control by optimal medication.

Methods: In 75 patients with uncontrolled type 2 diabetes (age:49±12 years) and 25 controls of similar age and sex and no atherosclerotic risk factors we measured at baseline and 9 months after control glycemic control: a) flow-mediated vasodilatation (FMD) as percentage difference between peak twisting and untwisting at mitral valve opening (%dpTw−UtwFMD); b) %dpTw-UtwPEF (r=−0.55), %dpTw-UtwEDF (r=−0.74) respectively. Reduced BP (PASP) ≥2); right ventricular systolic dysfunction (tricuspid annular plane systolic excursion (TAPSE) <17 mm), pulmonary artery systolic pressure (PASP) >35 mmHg. Criteron for abnormal LUS was a total number of B-lines >10 at anterior and posterior chest scan.

Results: Compared to controls, diabetics had higher PWV (10.3±2.6 vs. 8.1±1.9m/sec), AI (25.1±29.4 vs. 19.4±14.7%), PVWc (12.3±2.9 vs. 8.8±3.1m/sec), cSBP (134±20 vs. 119±18mmHg), PBR (2.17±0.2 vs. 1.89±0.1m/sec) and lower GLS (−15.6±3 vs. −18.3%), LongSr (−0.8±1 vs. −0.95±0.2lsecp), LongSrE (0.79±0.27 vs. 1.2±0.3lsecp), S’, E’ and A’/m of mitral annulus by Tissue Doppler; c) LV systolic strain (GLS), diastolic function (E/e’ ≥14% elevated PASP; 11% diastolic dysfunction, 5% reduced PASP). The sublingual arterial microvessels (ranged from 5–25μm) using Sideview, Darkfield imaging (Microscan, Glycocheck). Increased PBR is considered an accurate index of reduced endothelial glycosalyx thickness because of a deeper RBC penetration in the glycocalyx (r=−0.5, p<0.01)

Conclusions: Cardiopulmonary abnormalities are very frequent in SSc patients, irrespective of symptoms. An integrated one-stop shop TTE and LUS evaluation is feasible, avoiding the inaccuracies, delays, costs, and risks of a fragmented multi-imaging, multi-site, and multi-days approach.

P4353 | BEDSIDE
Analysis of vortex flow in the left ventricle during ejection period may be used as a new tool for noninvasive assessment of LV systolic dysfunction

Background: It has been shown that various cardiac diseases affect intracardiac flow. Analysis of intracardiac flow, especially vortex formation may be useful for the assessment of left ventricular (LV) function. Vector flow mapping (VFM) based on Doppler echocardiography and tissue tracking method provides quantitative assessment of the vortex formed in LV cavity by showing streamline and vorticity derived from intracardiac flow vector.

Purpose: The purpose of this study was to examine how LV systolic dysfunction affect vortex formation in LV cavity during ejection period.

Methods: The study population consists of 33 subjects; 11 patients with severe LV dysfunction (group-S, EF <35%), 12 patients with moderate LV dysfunction (group-M, EF 41–44%), and 10 healthy volunteers without LV dysfunction (group-N, EF 66±4%). Apical long-axis view was recorded by color Doppler echocardiography for off-line analysis using VFM (DAS-RS1, Hitachi-Aloka Medical Systems).

Results: From the images showing streamline and vorticity in LV cavity, we assessed detection ratio of vortex in basal and mid-apical LV during ejection period, duration of vortex formation, average vortex area and average circulation (integral of vorticity) during its appearance in each group.

Conclusions: Examples of VFM showing streamline and vorticity from group-N and group-S are shown in figure A and B, respectively.

1) Detection ratio of vortex formation in basal LV cavity was significantly lower in group-S (64%, p<0.01 vs group-M and N) while it was visualized in all cases in group-M and N (p<0.01 vs group-S).
2) There was no significant difference in average vortex area in mid-apical LV among group-S, M, and N (212±116, 207±183, and 207±183 mm²), respectively) compared with group-N (0.77±0.29).
3) Ratio of basal LV vortex appearance time to ejection duration was significantly smaller in group-S and group-M (0.40±0.10 and 0.49±0.20, p<0.01 vs group-N, respectively), compared with group-S (0.27±0.29).
4) Although there was no significant difference in average vortex area in basal LV among group-S, M, and N (212±116, 207±183, and 207±183 mm²), average circulation (integral of vorticity) of basal vortex was more reduced in group-S compared with group-M (-4.9±1.8 vs -7.5±3.2×10⁻⁶ m²/s, p<0.01) and group-M compared with group-N (-7.5±3.2 vs -10.7±5.8×10⁻⁶ m²/s, p<0.01).
5) There was no significant difference in average vortex area in mid-apical LV between group-S and group-M (433±277 and 496±319 mm²)

Downloaded from https://academic.oup.com/eurheartj/article-abstract/37/suppl_1/599/2197552 by guest on 18 April 2019
**Table 1.** Level and layer specific global peak systolic left ventricular longitudinal strain divided by longitudinal strain in older individuals while the magnitude in apical level increased < mid and apical levels (-16.4±4.2%, -18.2±4.2%, -21.4±7.5%; p<0.001, respectively).

<table>
<thead>
<tr>
<th>Layer</th>
<th>Age categories (years)</th>
<th>Total group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Basal</td>
<td>Mid</td>
</tr>
<tr>
<td></td>
<td>(n=63)</td>
<td>(n=66)</td>
</tr>
<tr>
<td>GLS (%)</td>
<td>55.4±7.1</td>
<td>59.3±5.9</td>
</tr>
<tr>
<td></td>
<td>65.7±7.5</td>
<td>69.9±5.7</td>
</tr>
<tr>
<td></td>
<td>75.7±7.5</td>
<td>81.0±5.9</td>
</tr>
<tr>
<td>P value</td>
<td>0.001</td>
<td>0.001</td>
</tr>
</tbody>
</table>

**Conclusions:**
- Normative values of LV longitudinal strain on a level and layer-based analysis show an increase in magnitude from basal to apical levels and from epi- to endocardial layers. These patterns were not significantly different across age categories.

Acknowledgement/Funding:
- The department of cardiology received research grants from Biotronik, Edwards Lifesciences, Medtronic, Boston Scientific.

**P4356 | BEDSIDE**

Long-term impact of cardiac contractility modulation on left ventricular function and remodeling

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**Purpose:**
Cardiac contractility modulation (CCM) has emerged as an effective device treatment for advanced systolic heart failure (HF) with normal QRS duration and its long-term benefit on quality of life and exercise capacity. The aim of this study was to explore the long-term impact of CCM therapy with comprehensive echocardiography on left ventricle (LV) geometry, function and reverse remodeling.

**Methods:** Thirty-two consecutive HF patients (age 62±9 years; 87.5% male) with LV ejection fraction (EF) <35%, New York Heart Association (NYHA) class III or IV and NYHA ≥2-3 were included. Two-dimensional echocardiography was performed (GE Vingmed Ultrasound AS, Horten, Norway) at baseline and long-term follow-up (4.8±1.9 years) to determine LV volumes and LV mass. LV global longitudinal strain was assessed with automated function imaging (AFI).

During long-term follow-up, LV reverse remodeling was evident with a significant reduction in LV end-systolic volume (133±44 ml vs 102±61 ml, P<0.001) and a gain in LV ejection fraction (28.5±6% vs 38±12.9%, P<0.001). Myocardial contraction was significantly improved as reflected by an increase in global longitudinal strain (7.1±2.4% vs 8.3±3.6%, P=0.037). Of note, LV mass at long-term follow-up was also markedly reduced (234±71 g vs 187±49 g, P<0.001).

**Conclusions:** CCM therapy resulted in LV reverse remodeling with improvement from epi- to endocardial layers and reduction of LV mass at long-term follow-up.

Acknowledgement/Funding:
- This project was supported by a research grant from Hong Kong Research Grant Council (RGC grant number 749709).

**P4357 | BEDSIDE**

Assessment of myocardial fibrosis using multi-slice speckle tracking in patients undergoing chemotherapy: A comparison of two vendors

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**Background:**
Global longitudinal strain (GLS) using single layer tracking is recommended for early cardiotoxicity detection in patient receiving chemotherapy. The purpose of this study was to investigate intervendor variability when measuring GLS from epicardial to endocardial layers for the two vendors in each apical view (4c, 3c and 2c) and for each layer (epicardial, mid and endocardial) using Vivid 9 (Vendor A) and SC 2000 ultrasound systems for each patient. We assessed myocardial fibrosis by using their respective speckle tracking software (AFI) for the VIVID E9 system and Vector VVI for SC 2000 system for strain multilayer measurement. Thus, we compared GLS multilayer values for the 2 vendors in each apical view (4c, 3c and 2c) and for each layer (epicardial, mid and endocardial) to compare the vendors used evaluating intra class correlation coefficient (ICC).

**Results:** Eighty cancer patients were prospectively included between February and June 2015. Mean age was 55±6.3 years and 61% of the studied population were female. Mean left ventricular ejection fraction was 52% (57–66%). Results of GLS multilayer values according to vendor, incidence, layer and their comparison are summarized in Table 1. There was a poor agreement between GLS multilayer as measured with GE system and Siemens system, whatever the layers, the incidence and the vendor.

**Table 1.** Values of GLS according to vendor, layer and views.

<table>
<thead>
<tr>
<th>Vendor</th>
<th>Layer</th>
<th>View</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>4c</td>
<td>GLS endo</td>
<td>20.7 (18.5–23.5)</td>
</tr>
<tr>
<td>B</td>
<td>4c</td>
<td>GLS mid</td>
<td>18.2 (16.1–20.5)</td>
</tr>
<tr>
<td></td>
<td>4c</td>
<td>GLS epi</td>
<td>15.9 (14.1–17.9)</td>
</tr>
<tr>
<td></td>
<td>3c</td>
<td>GLS endo</td>
<td>22.8 (19.8–25.7)</td>
</tr>
<tr>
<td></td>
<td>3c</td>
<td>GLS mid</td>
<td>19.2 (17.3–22.3)</td>
</tr>
<tr>
<td></td>
<td>3c</td>
<td>GLS epi</td>
<td>16.9 (15.4–18.3)</td>
</tr>
<tr>
<td></td>
<td>2c</td>
<td>GLS endo</td>
<td>21.7 (19.0–24.1)</td>
</tr>
<tr>
<td></td>
<td>2c</td>
<td>GLS mid</td>
<td>19.3 (17.0–21.8)</td>
</tr>
<tr>
<td></td>
<td>2c</td>
<td>GLS epi</td>
<td>17.3 (15.1–19.4)</td>
</tr>
</tbody>
</table>

**Acknowledgement/Funding:**
- This study was funded by grants from Biotronik, Edwards Lifesciences, Medtronic, Boston Scientific.
Conclusion: There was a poor agreement for layer specific strain evaluation between GE and Siemens system using their dedicated software for strain multi-layer assessment. These results suggest that in patient receiving chemotheraphy the same system and software from the same vendor should be used for longitudinal follow-up.

Results: Using the bull’s eye view of the regional longitudinal strain (LS) values, we found a cut off value of -9% to differentiate between ischemic and non-ischemic segments, yielded moderate agreement between the predicted and actual culprit artery (kappa coefficient = 0.482). We could predict culprit LAD with a reasonable sensitivity and specificity (77% and 83% respectively). The highest specificity was for prediction of culprit RCA (96.2%), albeit at a low sensitivity. At baseline, both ejection fraction and global LS correlated significantly with the number of segments with PSS (r = 0.7, P value = 0.05; r = 0.56, P value=0.01, respectively). The baseline indexed number of segments with PSS in the culprit territory (RLS/PSSI) was the only significant predictor of Δ regional strain by univariate analysis (r=0.65, P=0.008).

Conclusion: STE can accurately predict culprit LAD in NSTEMI. PSSI is simple, non-invasive tool that can be useful to predict recovery of regional systolic function following successful revascularization.

P4360 | BEDSIDE
Clinical significance of global longitudinal strain of the left ventricle in patients with heart failure with reduced ejection fraction


Background: Global longitudinal strain of the left ventricle (GLSLV) can measure LV myocardial mechanics objectively. We studied the clinical significance of GLSLV in patients with heart failure with reduced ejection fraction (HFREF).

Methods: We studied 487 consecutive HFREF patients, we divided them into two groups according to the presence of functional recovery in a follow up echocardiography (LVEF >55%). They were followed for mean 36 months for checking major adverse cardiovascular events (MACE). Results: We studied total 786 patients (490 men, 64±14 years old) and 377 patients (48%) had significant CAD. Baseline LVEF was 33±8% and GLSLV was -6.8±2.4%. Of them, 204 patients (26%) showed functional recovery. In patients with functional recovery, there were significantly higher incidence of non-ischemic cause, higher diastolic blood pressure, and higher heart rate. Lower LV dimensions, smaller LV volumes, higher LVEF and lower GLSLV also associated with MACE (HR=1.147, P=0.005). During the follow-up, 186 patients experienced more than one MACE (120 deaths and 91 admission for heart failure). Higher GLSLV also associated with MACE (HR=1.147, P=0.005).

Conclusions: Baseline GLSLV was statistically significantly associated with the improvement of LVEF and long term prognosis. It can be used as a prognostic marker in HFREF patients.

P4361 | BEDSIDE
LV dysynchrony and factors related to its severity

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The role of mechanical dysynchrony (MD) in the selection of patients suitable for CRT is not well-established and still a matter of debates in current guidelines. Aim: To compare the value of 2D- and 3D-echo in the diagnosis of intraventricular diastessynchrony (IVD) and to identify factors related to its severity.

Methods: 164 patients (110 men, 54.8±10.1 yrs) with left bundle branch block (LBBB) on the ECG were enrolled into the study. 52 of them (31.7%) had dilated, and 19 (11.6%) ischemic cardiomyopathy; 43 patients (26.2%) had a history of previous myocardial infarction and/or myocardial revascularization; 7% had hypertension as a primary diagnosis, and the remaining 7% (4.2%) had a history of previous myocardial infarction; and 41 (26%) had a history of previous myocardial revascularization. At baseline, 30% was 95.4%, but only 14.8% in patients with EF <50%.

Conclusion: 2D-echo obtained detecting IVD accurately in only 40% of patients with LBBB, mainly due to the presence of severe wall motion abnormalities (a-, hypo-, dyskinesias), and inability to obtained an adequate echo image. 3D-echo revealed IVD in 87% of the total cohort of patients with LBBB. The incidence of IVD in patients with EF <30% was 95.4%, but only 14.8% in patients with EF >50%.

Multiple linear regression analysis was used to identify factors associated with the severity of IVD. Twenty six parameters were analyzed altogether. The severity of
TMSV Sel-SD (the maximum value of dysynchrony between randomly selected segments) was related to the distance of 6-minute walk test (p < 0.006), and the points score of the Minnesota questionnaire (p < 0.05). LVEF was the only predictor of TMSV 16-SD severity (all segments except the apex of LV, p = 0.006), TMSV 6-SD (dysynchrony between the basal segments of LV, p = 0.001), and it showed a tendency for TMSV Sel-SD as well (p = 0.056).

**Conclusions:** 3D-echo reveals IVD in 87% of patients with LBBB, with the incidence of 95.4% in patients having EF < 30%. EF value, and signs of CHF determined the severity of IVD.

**P4362 | BEDSIDE**

**The systolic paradox in hypertrophic cardiomyopathy, normal ejection fraction and decreased longitudinal function**

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**Background:** Patients with hypertrophic cardiomyopathy (HCM) typically have normal ejection fraction (EF), despite a decreased longitudinal function.

**Purpose:** We explored HCM related changes in cardiac volumes and the effects on systolic function in 180 phenotype positive HCM patients (HCMP+), 100 geno-

**Methods:** End-diastolic (EDVI) and end-systolic (ESVI) volume index, EF and maximum wall thickness (MWT) were measured by echocardiography. Left ventricular (LV) global longitudinal strain (GLS) was assessed from 16 LV segments compared to healthy (57±14 ml/m² and 23±9 ml/m², both p < 0.001) in all groups, despite significantly worse GLS in the HCMP+ compared to HCMP+P- and healthy (-16.4±3.7% vs. -21.3±2.4% vs. -22.3±3.7%, p < 0.001). In the total HCMP population, the decrease in ESVI was closely correlated to EF (R²=0.19, p < 0.01) as expected, but not to GLS (R²=0.01, p=0.08). Worse GLS correlated significantly with increased MWT (R²=0.56, p < 0.001), but with no correlation observed between EF and MWT (R²=0.01, p=0.24).

**Conclusion:** HCMP+ patients with normal EF and reduced GLS had small cardiac volumes compensating the EF equation. Greater MWT correlated with worse GLS, but not with EF. Our results demonstrate that HCM result in loss of longitudinal function and that smaller volumes normalize EF.

**P4363 | BEDSIDE**

**Right ventricular outflow tract systolic excursion and fractional shortening: can these echocardiographic parameters be used for assessment of right ventricular function?**

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**Background:** Echocardiographic RV function assessment is difficult and still a grey area despite rapid advancement of imaging modalities. Most recent modalities for assessing RV function depends on the inflow free wall segments missing the outflow tract and the septal contribution to the overall RV function. Additional measurements of RV outflow tract function may add great value.

**Purpose:** The aim of this study is to assess the role of echocardiographic RVOT fractional shortening (RVOT FS) and RVOT systolic excursion (RVOT SE) in assessment of RV function.

**Methods:** 90 subjects divided equally in two groups. A control group included 45 normal healthy adult subjects. The patient group included 45 adult patients (22 males & 23 females) with RV dysfunction (i.e. both tricuspid annular plane systolic excursion<16 mm & RV fractional area change<35%). RV function was assessed in both groups using transthoracic echocardiogram for following parameters: Tricuspid Annular Plane Systolic Excursion, right Ventricular Fractional Area Change. Peak systolic velocity of the lateral tricuspid annulus (S') using pulsed tissue Doppler and all were compared with RVOT FS and RVOT SE.

**Results:** RVOT FS was found significantly lower in patients than in controls and RVOT FS <32% was 93% sensitive and 98% specific to identify patients with impaired RV function. RVOT SE was also significantly lower in patients than in controls and RVOT SE <5 mm was 80% sensitive and 76% specific to identify patients with impaired RV function.

**Conclusion:** RVOT FS is simple valuable parameter that can be used for RV function assessment. However, RVOT SE is less accurate than RVOT FS in RV function assessment.

**Acknowledgement/Funding:** Am shams university

**P4364 | BEDSIDE**

**Quantitative comparison between amyloid deposition detected by 99mTc-Diphosphonate imaging and myocardial deformation evaluated by strain echocardiography in transthyretin-related cardiac amyloidosis**

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**Background:** The clinical course of cardiac amyloidosis (CA) is strongly related to amyloid deposition.

**Purpose:** The aim of our study is to assess the effects of amyloid deposition on myocardial function.

**Methods:** 28 patients with transthyretin mutation and a control of 14 controls underwent echocardiography to quantify left ventricular (LV) dimensions and function, and global (G) longitudinal (L), radial (R) and circumferential (C) strain (S). 99mTc-3,3-diphosphono-1,2-propanodicarboxylic-acid-scintigraphy (99mTc-DPD) was used to quantify CA.

**Results:** 99mTc-DPD revealed accumulation in 14 of 28 patients (CA-group) and no accumulation (no CA-group) in 14 patients. Cardiac accumulation was mild-moderate in 5 (mild-moderate CA-group) and severe in nine patients (severe CA-group). Severe CA-group showed higher values of LV septal thickness (LVST), posterior wall thickness and E/E' ratio than the no CA-group and the control group (adj. p < 0.05). Ejection fraction was similar among groups (p = 0.65). GLS was lower (-19.3±3.0) in severe CA-group (-12.2±4.5) respect to no CA-group (-19.3±3.0) and to the control group (-20.9±2.5). On the contrary, GCS and GRS were lower (p < 0.05) in mild-moderate CA-group (-10.8±4.1 and 9.5±5.7, respectively) respect to the severe CA-group (-18.9±5.1 and 23.9±6.3 respectively), no CA-group (-18.2±4.1 and 28.4±10.2, respectively) and the control group (-23.9±4.4 and 29.9±8.7, respectively). A correlation was found between the scintigraphic heart retention (HR) index and LVST (ρ=0.72; p=0.001) and E/E' (ρ=0.46; p=0.03). An inverse tendency was observed between HR and GLS (ρ=0.40; p=0.06).

**Conclusion:** 99mTc-DPD HR is well correlated with LVST, diastolic and longitudinal systolic dysfunction.
Evaluation of myocardial degeneration and prognosis using speckle-tracking echocardiography in hypertrophic cardiomyopathy

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Purpose: In patients with hypertrophic cardiomyopathy (HCM), the left ventricular (LV) ejection fraction is usually normal or increased, but myocardial hypertrophy and fibrosis contribute to regional impairment of myocardial function. The utility of late gadolinium enhancement (LGE) by cardiac magnetic resonance (CMR) for detecting myocardial fibrosis and predicting adverse cardiovascular events in HCM is established. The objective of this study is to investigate (1) the association between strain by speckle-tracking echocardiography (STE) and LGE by CMR in HCM patients, (2) the utility of strain by STE in patients with HCM for the prediction of cardiovascular events.

Methods: We performed STE and CMR in 35 HCM patients (age: 59±13 years). Segmental and global longitudinal strain (LS) on 12 segments of the apical 4-chamber and 2-chamber views and circumferential strain (CS) on 16 segments of the basal, mid-, and apical short-axis views were measured by STE. Simultaneously, CMR was performed in 26 patients. Segmental LGE (LGE+) or minus (LGE−) was determined by CMR. Results: LS was determined in 88 (21%) of 420 apical 4-chamber and 2-chamber segments, and in 127 (23%) of 560 basal, mid-, and apical short-axis segments. In apical view's segments, LS was reduced significantly in the LGE+ segments compared with LGE− segments (−22.4±9.9 vs. −36.1±5.5%, P=0.001). In short-axis view's segments, CS was significantly lower in the LGE+ segments compared with LGE− segments (−10.9±6.0 vs. −18.8±4.0%, P=0.001). During 2 years follow-up, cardiac events (heart failure and ventricular tachycardia) occurred in 10 of 35 patients (28.5%; CE group). Number of segments with LGE+ was significantly higher in CE group than non-CE group (12±4 vs. 2±6 segments, P=0.001). Global LS (−9.5±4.6 vs. −19.4±4.6%, P=0.0001) and global CS (−24.1±10.2 vs. −40.5±9.1%, P=0.001) were reduced significantly in CE group compared with the other patients.

Conclusions: Strain by STE was important index for noninvasive evaluation of myocardial degeneration and prognosis in patients with HCM.

P4367 | BEDSIDE
Correlation of right ventricular strain imaging parameters with cardiac magnetic resonance imaging parameters in the assessment of right ventricular function among repaired tetralogy of Fallot patient

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Background: The ratio of early mitral inflow velocity (E) to global diastolic strain rate (+E/e') was proposed as a marker of diastolic dysfunction. Although the early active relaxation and the effective chamber compliance may be affected by myocardial ischemia, the predictive ability of myocardial strain analysis on the presence of coronary artery disease (CAD) in patients with suspected stable block remains unknown.

Objective: We hypothesized that the E/e' ratio would be independently associated with the presence of CAD and has superior predictive ability to +E/e'.

Methods: From January 2012 to September 2015, we retrospectively investigated 200 suspected CAD patients with preserved LVEF (ejection fraction >50%). All patients underwent echocardiography with comprehensive diastolic evaluation including E/e' and coronary angiography. Echocardiograms obtained in patients with atrial fibrillation, paced rhythm, congestive heart failure, severe heart valve disease, acute coronary syndrome and history of cardiac surgery were excluded from the analyses. Two-dimensional strain echocardiography was performed in the 3 apical projections and E/e' was measured in 18 myocardial sites and averaged. Coronary angiograms were obtained for each coronary vessel in ≥2 projections within a month of the echocardiogram. Patients with an arterial lumen area stenosis ≥70% in ≥1 epicardial coronary artery were categorized as having significant CAD.

Results: Eighty-nine patients had significant CAD. E/e' was significantly higher in patients with CAD compared with patients without (1.01±0.55 versus 0.89±0.39, P<0.001) and remained an independent predictor of CAD after multivariable adjustment for conventional coronary risk model (HR: 4.31, 95% CI: 1.53–12.1, P=0.006). C-statistics for predicting significant CAD were calculated for two models; conventional risk model (age, hypertension, diabetes mellitus, hyperlipidemia, chronic renal failure, chest pain, body mass index and smoking) and conventional risk model + E/e'. There was no statistical significant difference in c-statistics between these two models (0.71 vs 0.74, P=0.13), but net-reclassification improvement (NRI) was significant when E/e' was added to conventional risk model (95% CI: 0.07–0.61, P=0.015). Compared with conventional risk model + E/e', conventional risk model + E/e' showed significantly better predictive ability (NRI: 0.38, 95% CI: 0.11–0.65, P<0.006).

Conclusion: In patients with suspected CAD, E/e' is an independent predictor of significant CAD and had an incremental predict ability. Furthermore, E/e' might be superior to E/e' as a metric of diastolic dysfunction to identify significant CAD.

P4368 | BEDSIDE
Do we overestimate left ventricular ejection fraction by two-dimensional echocardiography in patients with left bundle branch block?

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Background/Introduction: Especially in patients with regional wall motion abnormality, 2D based calculation of LVEF could be less accurate than three-dimensional (3D) based measurements. Although it is not considered as a wall motion abnormality, left bundle branch block (LBBB) causes dysynchronous contraction of LV due to abnormality in the sequence of activation. Therefore, LVEF derived by conventional 2D echocardiography may be less reliable by conventional 2D echocardiography in this particular population.

Purpose: Our aim was to evaluate the role of systolic dysynchrony index measured by 3D echocardiography in assessment of LVEF and left ventricular volumes accurately in patients with LBBB.

Methods: In this cross-sectional study, we included 52 patients with LBBB and normal LV or non-ischemic cardiomyopathy. Measured LVEF and volumes using 2D (modified Simpson's rule) and 3D (tour beats full volume analysis) echocardiography were compared. Systolic dysynchrony indices (SDI) and ORS durations were also calculated and their possible effects on results were investigated.

Results: Twenty-eight patients had LVEF equal or more than 50% [56.00% (40.00–58.25); p=0.002]. In short-axis view's segments, CS was significantly lower in the LGE+ segments compared with LGE− segments (−22.4±9.9 vs. −36.1±5.5%, P=0.001). Global LVEF values [(54.50% (49.00–59.00) vs 54.25% (40.00–58.25), p=0.193] calculated by 2D and 3D echocardiography, respectively. LV diastolic volumes were not different between two modalities while systolic volumes were underestimated by 2D strain measurements.

Conclusions: LVEF derived by 2D and 3D echocardiography was significantly different [46.00% (29.50–52.50) vs 37.60% (24.70–45.15); p<0.001] between 2D and 3D echocardiography, respectively. In patients with SDI >6%, there were no significant difference between mid segment strain determined cut-off was −16.58% which showed sensitivity of 88.83% and a specificity of 100%, PPV of 100%, NPV of 88.83%, right ventricular free wall CS (−10.9±4.6 vs. −23.8±3.15%, P=0.019) was calculated by 2D and 3D echocardiography, respectively.
P4369 | BENCH
Characteristic changes of systolic and diastolic function in rat models of type 1 versus type 2 diabetes mellitus assessed by speckle-tracking echocardiography

Left ventricular (LV) dysfunction is a frequent consequence of diabetes mellitus (DM) even in the absence of coronary artery disease. Comparison of animal models of type 1 and type 2 DM may contribute to a deeper pathophysiologic understanding of diabetic cardiomyopathy. Gold standard LV pressure-volume (PV) analysis provides a detailed hemodynamic characterization, however, the non-invasive speckle-tracking echocardiography (STE) may be a powerful method to assess the deterioration of systolic and diastolic function.

Therefore, we aimed to comparatively investigate diabetic cardiomyopathy by PV analysis and STE in rat models of type 1 and type 2 DM. Rat models of type 1 (8 weeks after DM induction in Sprague-Dawley rats by streptozotocin, n=8) and type 2 DM (inbred Zucker Diabetic Fatty rats at the age of 32 weeks, n=7) and corresponding control animals (n=5 and n=8, respectively) were compared. Echocardiography was performed using a 13MHz linear transducer to obtain LV short-axis recordings for STE analysis (EchoPAC). Beyond global circumferential strain (GCS), peak strain rate values in systole (SrS), isovolumic relaxation (SrIVR) and early diastole (SrE) were measured. LV PV analysis was performed to calculate load-independent contractility indices (i.e. preload recruitable stroke work [PRSW]), time constant of LV pressure decay (tau), and diastolic stiffness parameters (i.e. slope of end-diastolic PV relationship [EDPVR]).

In type 1 DM, contractility and active relaxation were deteriorated to a greater extent compared to type 2 (relative impairment type 1 vs. type 2 DM: PRSW 46±13 vs. 64±6%, tau: 21±14 vs. 17±9%) (all p<0.05). In contrast, diastolic stiffness was impaired more in type 2 DM (EDPVR: 22±11 vs. 46±17%, p<0.01). Correspondingly, STE described more severe systolic dysfunction in type 1 (type 1 DM vs. control; GCS: −13±1±18 vs. −16±9±3%, SrS: −2.48±0.37 vs. −4.58±0.18 1/s, both p<0.01) compared to type 2 DM (2.2×±18 vs. −16±9±2.1%, NS; SrS: −2.88±0.35 vs. −3.22±0.17 1/s, p<0.05; relative impairment type 1 vs. type 2 DM: SrS: 46±8±17 vs. 17±11%, p<0.01). Among diastolic STE parameters, SrIVR was more decreased in type 2 DM rats (2.68±0.35 vs. 3.22±0.17 1/s, p<0.001), while SrE referring to diastolic stiffness was expressed by SDTTPS (Table). Women had significantly higher values for LVendo strain rate compared to men (50% vs. 44%, p<0.01), while in type 2 DM rats SrE was closely related to LVendo strain rate (r=0.729, p<0.05), while in type 2 DM rats SrE was closely related to LVendo strain rate (r=0.729, p<0.05).

Conclusion: Normal pattern of mitral inflow indicates good prognosis in cardiovascular events in middle- and advanced-age subjects.

P4370 | BEDSIDE
Normal pattern of mitral inflow indicates good prognosis in cardiovascular events in middle- and advanced-age subjects
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Background: Although the change of mitral inflow pattern from normal pattern (E/A=1) to abnormal relaxation pattern (E/A<1) is according to aging in healthy subjects, it maintains the normal pattern in some cases. However, it remains unclear whether the prognosis of cardiovascular events is different between the normal pattern and the abnormal relaxation pattern in middle- and advanced-age people.

Purpose: We investigated whether the normal pattern of mitral inflow indicates good prognosis in cardiovascular events in middle- and advanced-age subjects.

Methods: We enrolled 475 subjects with sinus rhythm (280 men, 62.5±1.8 years) (60–65 years). Exclusion criteria were patients with paroxysmal atrial fibrillation (AF), moderate to severe valvular heart disease and left ventricular systolic dysfunction (LVEF<50%). All subjects were divided into two groups according to mitral inflow pattern, i.e., the normal pattern group (n=80); E/A>1, left atrium volume index (LAVI) <30ml/m² and a ratio of early diastolic trans mitral velocity to early diastolic mitral annular velocity (E/e') <15, the abnormal relaxation pattern group (n=395); E/A<1. The cardiac events were defined as cardiac death, nonfatal myocardial infarction, unstable angina pectoris, heart failure, paroxysmal or persistent AF, and fatal arrhythmias.

Results: At the baseline, there were no differences in age, sex, LVEF, LAVI and E/e' between the two groups. In the normal pattern group compared to the abnormal relaxation pattern group, the prevalence was significantly lower in hypertension (37.5 vs. 58%, P<0.01) and chronic kidney disease (2.5 vs. 9.4%, P<0.01). The left ventricular mass index was also significantly lower in the normal pattern group (161±26 vs. 95±26 g/m², P<0.001). During the follow-up period (4.9±1.8 years, 1–6 years), there were 38 events (AF 12, cardiac death 11, unstable angina pectoris 7, nonfatal myocardial infarction 4, heart failure 3, and fatal arrhythmia 1). In the normal pattern group compared to the abnormal relaxation pattern, the hazard ratio for cardiac events was 0.25 (95% CI 0.04–0.84).

Conclusion: Normal pattern of mitral inflow indicates good prognosis in cardiovascular events in middle- and advanced-age subjects.

P4371 | BEDSIDE
New multi-layer approach of left and right ventricular myocardial deformation by 2D speckle tracking imaging in a large group of normal subjects
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Background: There are limited data regarding intrinsic functional changes of the left and right ventricles. Recently, advancements in the area of speckle tracking echocardiography (STE) to characterize longitudinal deformation of each layer of the LV and RV, as well as the global deformation of the entire ventricle, have been reported.

We used a new multi-layer approach by 2D speckle tracking echo (STE) to characterize longitudinal deformation of each layer of the LV and RV, and global synchonosity of the LV and RV in a large group of normal subjects. 151 normal subjects (19–79 years, 99 women) were evaluated by 2D multilayer STE. They were divided in 4 groups: <40yrs (28), from 41 to 50 yrs (36), from 51 to 60 (32), and >61 yrs (47). Systolic longitudinal function was evaluated by global endocardial (LV/RV endo) and epicardial strain (LV/RV epi). A LV dyssynchrony index was defined as standard deviation of all LV myocardial times to peak strain from each segment (SDTTPS).

Results: In all 4 groups, similarly for men and women, a subendocardial to subepicardial gradient was present in both LV longitudinal (4.65±0.9%) and RV longitudinal strain (4.42±2%) (both p<0.001), with higher values in the subendocardial layer. There were no differences in deformation with age in all layers, for both ventricles. However, we found a significantly increased dyssynchrony with age, expressed by SDTTPS (Table). Women had significantly higher values for LVendo (-24.2±6 vs. -22.8±3), LVepi (-19.3±3.2 vs. -18.1±2.4), and UMDiv (-21.5±2.3 vs. -20.5±2.8) (all p<0.05), but similar strain values for the RV.

Conclusion: Normal pattern of mitral inflow indicates good prognosis in cardiovascular events in middle- and advanced-age subjects.
gender; LV dyssynchrony increases with age. Our study provides reference values for the deformation of each LV and RV layer, which can be further used when assessing subclinical dysfunction in different myocardial diseases.

**Conclusions:**

Fibrosis and aging of the heart might explain these findings. Further studies were divided into 2 groups according to the reported history of paroxysmal AF. Left ventricular (LV) and LA volumes, LV ejection fraction and LA ejection fraction were estimated using 2D echocardiography. E/e was evaluated by Doppler echocardiography. LA longitudinal Strain (LA pump function) and LA longitudinal Strain Rate (LA pump function) were obtained using 2D speckle tracking echocardiography. Analysis before and after chemotherapy was also analyzed. None of the echocardiographic parameters showed significant alteration after two and four cycles of chemotherapy compared with those at baseline (P>0.05 for all). At the end of the therapy (after six cycles of ATC treatment), there was no statistically significant difference on tissue Doppler data as well as strain measurements (P>0.05 for all). However, the RAEDA (6.5±1.9 cm2 vs. 7.7±4.2 cm2) and RAESA (8.8±2.5 cm2 vs. 10.8±2.8 cm2) revealed obvious dilatation after six cycles of the regimen compared with those at baseline (both P<0.01). Similar morphologic characteristics were found on the RVEDA (14.1±3.4 cm2 vs. 16.2±3.7 cm2) and RVESQA (7.9±1.9 cm2 vs. 9.0±2.2 cm2) (both P<0.01) simultaneously. Furthermore, RVEDV (29.8±10.5 ml vs. 37.0±12.7 ml) and RVESQA (12.7±5.4 ml vs. 15.0±5.2 ml) as well as RVEF (59.4±5.8% vs. 56.4±5.8%) in patients with lymphoma presented statistically significant difference between baseline and after six cycles of ATC (P<0.05). Meanwhile, no marked change was detected on left ventricular ejection fraction at follow up (P>0.05).

**Conclusions:**

Echocardiography can be used easily and noninvasively to assess right ventricular subclinical dysfunction. ATC-induced cardiotoxicity has been recently shown to have incremental value in atrial fibrillation (AF) prediction. We evaluated the possible association of these biomarkers with standard echocardiographic and novel 2DSTE indices, focusing on a possible role in the risk stratification of such a cohort.

**Methods:**

Seventy-four patients with lymphoma who accepted ATC treatment were enrolled. Each patient underwent transthoracic echocardiographic examination before chemotherapy as well as after two, four and six cycles of ATC. Right and left ventricular function should be taken into account in the assessment of ATC-induced cardiotoxicity. We sought to assess the subclinical dysfunction in different myocardial diseases. Fibrosis and aging of the heart might explain these findings. Further studies are needed in order to test the hypothesis that these biomarkers may play a role in AF prediction and risk stratification of variable patient cohorts.

**Results:**

Both right and left ventricular function at follow up (P<0.05 for all). At the end of the therapy (after six cycles of ATC treatment), there was no statistically significant difference between baseline and after six cycles of ATC treatment.

**Conclusions:**

Echocardiography can be used easily and noninvasively to assess right ventricular subclinical dysfunction. ATC-induced cardiotoxicity has been recently shown to have incremental value in atrial fibrillation (AF) prediction. We evaluated the possible association of these biomarkers with standard echocardiographic and novel 2DSTE indices, focusing on a possible role in the risk stratification of such a cohort.
and stiffness were improved after dialysis. LV function in dialysis patients may be noninvasively and comprehensively evaluated by 3D-STE.

P4376 | BEDSIDE
Reference values and determinants of right ventricle outflow tract acceleration time in healthy adults by two-dimensional echocardiography
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Background: Right ventricle outflow tract acceleration time (RVOT-AT) provides an estimate of pulmonary hemodynamics and a clear correlation with mean pulmonary arterial pressure. The aim of this study was to define reference values and determining factors of RVOT-AT in a large population of healthy subjects and by values found in the literature.
Methods: In the first part of the study, 1029 healthy subjects [mean age 45.6±16.0 years, range 16 to 92; 565 (54.7%) females] were prospectively assessed. In the second part, we performed a pooled analysis of published studies describing RVOT-AT in healthy subjects (8 studies, n=450). Statistical analysis included the calculation of 95% quantiles for defining reference values and analysis of determining factors.
Results: RVOT-AT showed a significant correlation with age (r: −0.207; p<0.001). RVOT-AT correlated also significantly with Body Mass Index, systolic and diastolic blood pressure, heart rate and left ventricular (LV) E/A ratio (all p<0.001). No differences were found with regards to gender. In a synopsis of both data sets, 5% quantile for RVOT-AT was 104.7ms (95% confidence interval, 98.2–110.1).
Conclusion: Our study is in line with the cut-off value proposed by European guidelines. Age, Body Mass Index, systolic and diastolic blood pressure, heart rate and LV diastolic function were determinants of RVOT-AT.

P4377 | BEDSIDE
Tricuspid annular plane systolic excursion inaccuracy to assess right ventricular function in patients with previous tricuspid annuloplasty
Introduction: The clinical and prognostic usefulness of tricuspid annular plane systolic excursion (TAPSE) is well established. However, the ability of TAPSE to assess right ventricular (RV) function in patients with previous tricuspid valve annuloplasty is controversial. This study examined the TAPSE suitability in patients with previous tricuspid valve annuloplasty using right ventricular fractional area change (RVFAC) as reference method.
Methods: We retrospectively analyzed 53 consecutive patients who underwent tricuspid valve annuloplasty at our hospital between 2010 and 2015. TAPSE and RVFAC were obtained in preoperative and postoperative periods in the usual manner.
Results: Mean age was 68±12 years and 34 patients (64.1%) were women. TAPSE decreased significantly after surgery in comparison with pre-surgical values (17±4.2 Vs 12.9±4.1 mm, p<0.001). However, in postoperative period TAPSE correlated weakly with RVFAC (r=0.38, p=0.005). Good intra- and interobserver agreement for TAPSE and RVFAC were obtained, with intraclass correlation coefficients of 0.97 and 0.92 for TAPSE; and 0.90 and 0.85 for RVFAC, respectively.

Conclusions: This findings suggests TAPSE is not suitable after tricuspid valve annuloplasty and it leads to an underestimation of RV systolic function. It seems to be appropriate to rely on echocardiographic parameters of global RV function such as RVFAC in this context.

P4378 | BEDSIDE
Cost-effectiveness of TYRX antibacterial envelope compared to standard of care for cardiovascular implantable electronic device (CIED) infection prevention
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Background: Infection is a major complication of cardiovascular implantable electronic device (CIED) surgery that usually requires device extraction and is associated with high morbidity and mortality. The TYRX Antimicrobial Envelope is a polymer film that stabilises the CIED and elutes antibiotics, minocycline and rifampin, to reduce the risk of post-operative infection.
Purpose of study: An economic model was developed to assess the cost and health-related quality of life (HRQoL) impact of TYRX versus standard of care (SOC) Her the model projects the incremental cost-effectiveness of using TYRX in patients at increased risk of post-operative infection in terms of an incremental cost-effectiveness ratio (ICER).
Methods: A decision tree was developed to model the initial 12 months following the CIED surgery with estimates of lifetime costs and HRQoL benefits assigned to those patients who survived to 12 months. The model is parameterised for a United Kingdom (UK) National Health Service (NHS) perspective. Standard of care was defined as pre-operative antibiotic prophylaxis. Model probabilities were derived from clinical data. Resource use included drug acquisition and administration, hospitalisation, adverse events, device extraction and replacement. ICERs were calculated using estimates of direct costs and quality-adjusted life-years (QALYs). Deterministic and probabilistic sensitivity analyses were conducted.
Results: Within the initial 12 month period, the reduced healthcare resource utilisation associated with TYRX was sufficient to offset the additional cost of the envelope. As such, TYRX was marginally less costly (saving £9) and more effective (0.004 additional QALYs) than SOC and hence dominated SOC. Over a lifetime time horizon, TYRX use was associated with an ICER of £7,137 per QALY relative to SOC. This was attributed to improved survival which increased both lifetime costs and HRQoL. Deterministic sensitivity analyses showed that the lifetime ICER was robust to a number of scenarios. The ICER was most sensitive to the probability of infection with SOC, TYRX infection with SOC, TYRX efficacy (0.004 additional QALYs) than SOC and hence dominated SOC. Over a lifetime time horizon, TYRX use was associated with an ICER of £7,137 per QALY relative to SOC. This was attributed to improved survival which increased both lifetime costs and HRQoL. Deterministic sensitivity analyses showed that the lifetime ICER was robust to a number of scenarios. The ICER was most sensitive to the probability of infection with SOC, TYRX infection with SOC, TYRX efficacy (0.004 additional QALYs) than SOC and hence dominated SOC. Over a lifetime time horizon, TYRX use was associated with an ICER of £7,137 per QALY relative to SOC. This was attributed to improved survival which increased both lifetime costs and HRQoL. Deterministic sensitivity analyses showed that the lifetime ICER was robust to a number of scenarios. The ICER was most sensitive to the probability of infection with SOC, TYRX infection with SOC, TYRX efficacy (0.004 additional QALYs) than SOC and hence dominated SOC.
Conclusion: TYRX is associated with lower infection rates than SOC, resulting in reduced levels of healthcare resource utilisation even at an initial increase in cost. The ICERs generated by the model are below the accepted willingness-to-pay thresholds used by decision-makers in the UK. TYRX therefore represents a cost-effective treatment option for CIED patients at high-risk of post-operative infection.
Acknowledgement/Funding: Study was funded by Medtronic

P4379 | BEDSIDE
Beat-to-beat heart rate detection by smartphone accelerometers
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Purpose: Mobile phones offer the possibility to monitor and track health parameters, thanks to externally-connected devices or to embedded sensors technology. In particular, technological improvements and miniaturization in the embedded accelerometers sensors allow nowadays to obtain information about cardiac activity. Our aim was to test the feasibility and accuracy of measuring beat-to-beat heart rate using smartphone accelerometers by recording the vibrations generated by the heart during its function and transmitted to the chest wall, i.e. the so-called seismocardiographic signal (SCG).
Methods: 12 healthy volunteers (1 female, age 25±2, BMI 23±3 kg/m2) were studied while supine with a smartphone (iPhone 6, Apple or G3, LG) positioned on the chest in corresponding to the cardiac apex, and then on the abdomen. For each position, the three orthogonal components (head-to-foot, antero-posterior, left-to-right) of the SCG signal were recorded (100 Hz sampling rate) for 3 minutes during spontaneous respiration, synchronous with 3-leads ECG (2048 Hz sampling rate). Using a novel fully automated algorithm based on amplitude thresholding after rectification, the characteristic peak of the wave with maximum amplitude was detected in the head-to-foot component of the SCG signal, and used to compute beat-to-beat heart duration, to be compared with corresponding RR intervals directly extracted from the ECG.
Results: For the cardiac apex position (APP), a total of 2023 beats were accurately (100%) detected by the automated algorithm, while for the navel position (NAP) the accuracy was 99% (1950/1958). Linear correlation (r2) with RR was
very high (0.99) for both APP and NAP. Bland-Altman analysis showed no bias and narrow limits of agreement (±2SD: APP ±0.33 msec, NAP ±0.34 msec).

**Conclusions:** Obtained results proved the feasibility of the proposed approach and the robustness of the applied algorithm in measuring the beat-to-beat heart rate from smartphone-derived SCG, with high accuracy compared to conventional ECG-derived measure. This fact put the basis for easy, fast, and accurate multiplex self-evaluation of resting heart rate using smartphone accelerometers, thus increasing patient empowerment, with potential benefits in both patient monitoring and cardiac disease prevention.

**Acknowledgement/Funding:** Study supported by the Italian Space Agency (contract 2013-064-R.0, recipient EG Caiani).

**P4380 | BEDSIDE**

**Clinical usefulness of a mobile application for the appropriate selection of the antiarrhythmic device in heart failure**

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**Background:** Appropriate selection of implantable cardioverter/defibrillator (ICD) or cardiac resynchronization therapy (CRT) device can be challenging in patients with left ventricular dysfunction.

**Purpose:** To this regard, we wanted to evaluate the role of a medical application, called e-CRTD, in helping physicians to choose the most useful device.

**Methods:** We developed a medical application that provides guidelines-based algorithms for helping doctors in decision process using the Apache Cordova API. The digital medical application is available on two main online stores as free-of-charge download in the App StoreTM for iOS and in the Google PlayTM for Android. The App e-CRTD was tested in 36 consecutive patients (age 66.4±8.5 yrs, 31 males) with diagnosis of heart failure addressed to electrophysiology laboratory for evaluation of ICD (N=18) or CRT-D (N=18) implantation. Two separate teams evaluated each patient independently: expert electrophysiologists (group A); cardiologists in training using the App (group B).

**Results:** The outcomes of the clinical evaluation performed by groups A and B were similar in 100% patients in terms of classes of recommendations to device (class I in 8 cases, class III in 7 cases, class III in remaining 21). Surprisingly, the majority of indications from the general practitioners to cardiac device were inappropriate (N=7 ICD, N=4 CRT-D, class III); nevertheless, the e-CRTD helped group B (non-expert cardiologists) in excluding all these cases.

**HYPERTENSION-HAEMODYNAMICS AND GENETICS**

**P4381 | BEDSIDE**

**Characterization of premature arterial aging by the reservoir wave analysis in different stages of chronic kidney disease**

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**Objectives:** Declining renal function may cause premature arterial aging with loss of the reservoir function and exacerbation of wave motions. Recently, the reservoir wave analysis (RWA) was developed to construct the reservoir pressure (Preservoir) and a pressure due to wave motions (Pexcess). We aimed to investigate the parameters derived from RWA in different stages of chronic kidney disease (CKD).

**Methods:** Carotid pressure waveforms and aortic flow waveforms were recorded using tonometry and Doppler echocardiography respectively in a cohort of 99 CKD patients. RWA was performed from the calibrated pressure and flow waveforms to generate 6 parameters, namely peak of Preservoir (Max), pulse pressure of Preservoir (PPR), Pexcess integral (XSPI), Preservoir integral (PRI), systolic rate constant (SC) and diastolic rate constant (DC). ARterial stiffness was assessed using carotid-femoral pulse wave velocity (PWV) measured by arterial tonometry.

**Results:** There were no significant differences in brachial blood pressures or PWV among patients with different stages of CKD. Conversely, increasing PPR, XSPI, PRI and DC were associated with more advanced stages of CKD (trend P values: PPR = 0.040, XSPI = 0.011, PRI = 0.034, and DC = 0.014). The dose-response trend persisted with further adjustments for sex, and mean arterial blood pressure (trend P values: PPR = 0.001, XSPI = 0.003, PRI = 0.008 and DC = 0.021).

**Conclusions:** Parameters derived from RWA may be useful to characterize the premature arterial aging process associated with the deteriorated renal function.

**Acknowledgement/Funding:** Taipei Veterans General Hospital, Taipei, Taiwan

**P4382 | BEDSIDE**

**Associations of microRNAs gene expression in peripheral blood mononuclear cells and left ventricular global longitudinal strain in patients with essential hypertension**

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**Purpose:** MicroRNAs (miRs) modulate cardiovascular development and disease by post-transcriptional gene expression regulation and thus they are emerging as potential biomarkers and therapeutic targets in cardiovascular disease. It has been shown that miRs expression is modified in hypertensives and this is correlated with left ventricular hypertrophy. We evaluated the associations of miR-208b, miR-499, miR-21, miR-1, miR-133a and miR-26b gene expression levels in peripheral blood mononuclear cells in patients with essential hypertension in relation with left ventricular global longitudinal peak strain (GLGPS).

**Methods:** We assessed the expression levels of the miR-208b, miR-499, miR-21, miR-1, miR-133a and miR-26b, in 43 patients with essential hypertension (29 men, mean age 65.5±11.7 years). All patients underwent a serial assessment with standard conventional transthoracic and a two-dimensional speckle tracking echocardiography at baseline and at 12 months follow-up. MiRs expression levels were compared in men with cardiac device were in-100% patients in terms of classes of recommendations to device (class I in 8 cases, class III in remaining 21). Surprisingly, the majority of indications from the general practitioners to cardiac device were inappropriate (N=7 ICD, N=4 CRT-D, class III); nevertheless, the e-CRTD helped group B (non-expert cardiologists) in excluding all these cases.

**Results:** GLGPS did not show any significant difference during the 12 months follow-up (from -15.7 ± -4.3% at baseline to -14.5 ± -5.4%, p> NS). However, miR-21 gene expression levels at baseline revealed a significant positive correlation with the reduction of GLGPS (r = 0.53, p<0.05) and a moderate negative correlation between miR-499 gene expression levels and the reduction of GLGPS (r = 0.45, p<0.05). These correlations were independent of the patients’ clinical parameters.

**Conclusions:** Our data reveal that miR-21 and miR-499 might have a prognostic value of the deterioration of left ventricular GLGPS in essential hypertension. In addition, they may be involved in the pathophysiology of hypertension heart disease and may be promising therapeutic targets.

**P4383 | BEDSIDE**

**Assessments of associations between clinical and echocardiographic parameters and microRNAs expression in peripheral blood mononuclear cells and left ventricular global longitudinal strain in patients with essential hypertension**

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**Purpose:** Aim of our study was to determine the relationship between Scheie functional classification and left ventricular hypertrophy in newly diagnosed essential hypertension patients.

**Methods:** We studied 780 consecutive newly diagnosed, never-treated, non-diabetic, hypertensive patients stage I-III (51±13 years, 45.3±23% females). Echocardiographic left ventricular mass calculation was performed from parasternal long axis and normalized for height in meters to the power of 2.7 (LVM). Using established normal values (m2.7 for females), the study population was split in two groups: normal LVMI (n=649) and increased LVMI (n=131). All patients underwent fundoscopic examination and alterations were classified according to Scheie grading system, as 0, 1, 2 and 3.

**Results:** Compared to hypertensives without LVH, patients with LVH were older (53±13 vs. 51±13, p=0.018), with higher gestational and abdominal obesity, metabolic profile and target organ damage frequency and severity, while there was no difference regarding gender (females 43.7 vs. 45.6, p=0.693). Fundoscopic grade severity was significantly correlated with age (r=0.189, p<0.001), flow-mediated dilatation of brachial arteries (r=-0.15, p=0.045) and aortic velocity (r=-0.183, p=0.039), carotid IMT (r=0.212, p<0.001), HDL and Triglyceride ratio (r=0.110, p=0.022), pulse pressure amplification ratio radial to central (r=-0.140, p=0.042), 24 hour SAP (r=0.119, p=0.011), 24 hour pulse pressure (r=0.128, p=0.006) and BP severity (r=0.170, p=0.001). Prevalence of grades 0 and 1 was higher in patients with no LVH (45.3% vs. 36.1% and 31.8% vs. 23.6%, respectively), while grades 2 and 3 were more prevalent in patients with LVH (20.1% vs. 33.3% and 2.9% vs. 5.6%, respectively), p<0.007 for all.
Conclusion: In the early course of essential hypertension, advanced arteriolar retinal damage is associated with left ventricular hypertrophy.

P4384 | BEDSIDE
Pulmonary hypertension and pregnancy outcome: data from the cardiac disease in maternity grootse schuur cohort study
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Background: Pulmonary hypertension (PH) is unequivocally considered to pose an extreme risk of maternal death and women are advised to avoid pregnancy. Prospective, contemporary data on the management of pregnant women with various forms of PH are limited. The aim of the study is to describe the outcome of pregnancy in 32 women with PH included in the prospective, single center South African Cardiac Disease in Maternity Grootse Schuur Cohort Study.

Methods and results: The Cardiac Disease in Maternity Grootse Schuur Cohort Study was initiated in 2010 and consecutive patients with all forms of cardiovascular disease, presenting with pregnancy, were enrolled with the aim to investigate maternal and offspring outcome. Blood sampling was performed at baseline and four times during pregnancy at 28, 34, 37 weeks and 24 hours after delivery. This cohort included 32 women with PH, including PH due to left heart disease (LHD-PH) (43.7%), Pulmonary Arterial Hypertension (PAH) (37.5%) including iPAH, PH associated with congenital heart disease (CHD-PAH) or PH due to other conditions (oPAH). Mean maternal age was 30±4.9 years and 40% were nulliparous. The degree of PH was mild (RVSP—50mmHg) in 63% of patients, moderate (RVSP—70mmHg) in 31% and severe (>70mmHg) in 3%, assessed by echocardiography at baseline. In more than 56% of patients the diagnosis of PH had been made prior to pregnancy. During pregnancy death up to delivery occurred in 1 patient (3%), with another dying within 6 months after delivery. During pregnancy heart failure occurred in 44%. Caesarian section was performed in 47%. Therapeutic abortion was performed in 6%. Offspring complications were fetal mortality (0%), miscarriage (0%), neonatal mortality (3%), premature delivery (22%) and low birth weight of <500 g (19%). Most patient received diuretics (84%) and 3 of the patients were managed with advanced PH therapy, such as sildenafil, during pregnancy. Mortality in this group of patients with various forms of pulmonary hypertension was lower than previously reported as specialized care during pregnancy and delivery were available. However, maternal and fetal morbidity remains prohibitively high. Early advice on contraception, pregnancy risk and fetal outcome remains paramount.

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Impact of left ventricular systolic stress on torsion and twist in hypertensive heart failure: results observed by real-time one-beat three-dimensional speckle tracking echocardiography with high volume rates
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Introduction: Left ventricular (LV) twist and torsion caused by contraction of inner and outer oblique muscle may reflect LV systolic function and contribute a part of stroke volume. LV peak twist is defined as a maximum difference in rotation angle between base and apex and LV peak torsion is defined as LV peak twist divided by LV long axis length. LV outer muscle plays a predominant role in torsion and inspiration of inner muscle results in increase of torsion. LV remodeling such as hypertrophy, fibrosis and dilation caused by pressure overload may result in significant alterations of LV performance including torsion. However, the impact of systolic stress on LV torsion in patients with hypertension (HTN) and hypertensive heart failure (HHF) has not been fully examined by echocardiography.

Purpose: The aim of this study was to noninvasively evaluate LV systolic stress and examine the impact of LV stress on LV twist and torsion in HTN and HHF by 3-dimensional speckle tracking echocardiography with high volume rates (3D-STE).

Methods: We examined LV ejection fraction (EF), systolic stress, twist and torsion in 53 controls (age: 67±10), 50 patients with HTN but without LV hypertrophy (LVH) (age: 72±16), 50 patients with LVH (age: 70±11) and 48 patients with HHF (age: 72±16). Time-LV torsion curve was derived from time-twist curve and integrated by long axis length for every instance in time by 3D-STE with high volume rates of 70–80fps. LV systolic stress was calculated by LV force divided by LV cross-sectional area. LV ejection fraction (EF), LV volumetric and mass indexes and LV loading gradient were calculated from echocardiographic data. LV systolic stress was defined as peak systolic pressure divided by LV wall thickness at end diastole/LV end-diastolic dimension (pressure gradient ≈30mmHg) during late diastole. *P<0.01, †P<0.05 vs Non-concentric.

Echocardiographic data of subjects

<table>
<thead>
<tr>
<th>Non-concentric (n=23)</th>
<th>Concentric (n=15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV mass index, g/m²</td>
<td>86.4±15.5</td>
</tr>
<tr>
<td>IVSd, mm</td>
<td>9.3±1.3</td>
</tr>
<tr>
<td>IVPG, after nitroglycerin, mmHg</td>
<td>2.4±2.0</td>
</tr>
<tr>
<td>IVPG, after dobutamine, mmHg</td>
<td>3.2±1.9</td>
</tr>
<tr>
<td>IVPG, after peak dose of dobutamine, mmHg</td>
<td>49.5±33.0</td>
</tr>
<tr>
<td>IVQ, n (%)</td>
<td>14 (61%)</td>
</tr>
</tbody>
</table>

LV in concentric group preserved LVEF and torsion in HTN with LVH was preserved, whereas LVEF in HHF reduced associated with increased stress. There was significant negative correlation between torsion and stress in the total group (r=−0.23, p<0.05), and negative correlation was also found in HHF group (r=−0.34, p<0.01). On the other hand, no significant correlation was found between twist and stress. LV torsion had significant correlation with LV twist (r=0.61, p<0.01) and with LVFP (r=0.40, p<0.05), whereas no correlation was found between twist and LVFP. Conclusion: LVFP and torsion but not twist in HHF decreased associated with increased LV stress. This suggests that LV torsion but not LV twist may play an important role to maintain the LV performance to some extent against increased LV systolic stress and that deterioration of torsion may result in HHF with reduced EF.

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Association of left ventricular concentric geometry and dynamic intraventricular obstruction in patients with hypertension: a dobutamine stress echocardiography study
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Background: Dynamic intraventricular obstruction (IVO) may be responsible for unexplained dyspnea or chest discomfort on exertion especially in the elderly patients with hypertension.

Purpose: We assessed the left ventricular (LV) geometry and dynamic IVO using dobutamine stress echocardiography (DSE) with the provocation of preload reduction by nitroglycerin.

Methods: We enrolled 38 hypertensive elderly patients over 60 years (mean age 66 years) referred for DSE with unexplained dyspnea or chest discomfort. Concomitant LV geometry and LV systolic wall thickness (RWT>2.6, posterior wall thickness at end diastole/LV end-diastolic dimension) over 0.42. The patients with transmural infarction, significant valvular heart disease, atrial fibrillation, beta-blocker therapy, and induced ischemia during DSE were excluded. IVO during DSE was defined as a late-peak intraventricular pressure gradient (IVPG) >30mmHg.

Results: The patients with RWT >0.42 (n=15, concentric group) and with RWT ≤0.42 (n=23, non-concentric group) were not different in terms of age, gender, smoking history, diabetes and used anti-hypertensive drugs. Concentric group had smaller LV cavity and volume, and more increased interventricular septum and basal septal thickness than non-concentric group. At rest, during peak dose of dobutamine, and after nitroglycerin, IVO was higher in concentric group. The development of dynamic IVO during DSE was much more in concentric group (p<0.05).

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The impact of resting heart rate on left atrial volume: findings from NAMBU HEART study
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Background: Elevated resting HR is associated with an increased likelihood of new-onset atrial fibrillation (AF) in patients with essential hypertension. Left atrial (LA) size increases with an increasing electrical burden of AF. There is no evidence evaluating the association between resting HR and LA morphology. The aim of this study is to demonstrate the association between resting HR and LA volume.

Methods: This study is echo lab based cross-sectional analysis to evaluate the association between resting HR and LA morphology. Resting HR and LA morphology were assessed by echocardiography and simultaneous electrocardiogram recording. LA morphology was evaluated by LA volume index. Patients with atrial fibrillation were excluded.

Results: Among 1885 consecutive patients examined echocardiography in 2015, 1188 patients without atrial fibrillation (582 men, 606 women, 72.1 [14.5] years) were evaluated. Approximately 80% of them had hypertension, 33% with diabetes, 24% with coronary artery disease, 33% with stroke, and 24% with
heart failure. The mean resting HR, LA volume index of these patients were 69 (14) bpm and 27 (10) ml/m² respectively. In this study, LA volume index more than 32 ml/m² is considered as dilated LA. Approximately 77% of these patients had normal LA volume, and 23% with dilated LA. Resting HR was negatively associated with LA volume index (R²=0.04, p<0.0001) (Figure). Logistic regression analysis indicated that every 10 bpm HR increase was associated with a 22% decrease in the risk of dilated LA (95% confidence interval: 0.70–0.88) after adjusted for age, sex, body height, body weight, diabetes, hypertension, dyslipidemia, and coronary artery disease.

**Discussion:** Inconsistent with evidences so far, elevated resting HR was associated with lower LA volume. HR lowering might not be beneficial for LA morphology as well as the LV morphology.

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On-treatment blood pressure values and cardiac organ damage in hypertensive patients


**Objective:** The recent results of the SPRINT study suggest that “intensive” reduction of systolic blood pressure (BP) (to less than 120 mmHg) might provide greater cardiovascular protection as compared to less intensive (≈140 mmHg) reduction of BP, at least in some subsets of patients. Only few studies, have investigated the possible effect of tight blood pressure control on indices of left ventricular hypertrophy, and have been mainly based on electrocardiography. Aim of our study was to evaluate cardiac organ damage according to “on treatment” blood pressure values in a large cohort of hypertensive patients undergoing echocardiography (2D, M-mode with conventional and tissue Doppler analysis) at the echo-lab of a centre in Italy.

**Design and method:** The analysis included 976 treated hypertensive patients (43% female, 58±12 yrs, age range 15–90). Patients were subdivided in three groups according to BP values at the time of the echocardiogram, defined as follows: uncontrolled (UC; SBP > or equal to 140 mmHg), controlled <140 (C140; SBP between 139 and 120 mmHg) and controlled <120 (C120; SBP ≤ 120 mmHg).

**Results:** In 407 patients (42%) SBP values were > 140 mmHg, 449 patients (46%) had SBP between 139 and 120 mmHg (C140) and in 120 (12%) SBP was < 120 mmHg (C120).

Left ventricular mass (LVM) and LVM index (LVMI) were progressively lower in UC, was 0.001). No significant difference was observed for relative wall thickness. Left atrial volume was measured in all participants.

**Results:** In logistic regression analysis LV was inversely correlated with LVM index (normal LVM index, LVH) and further subdivided according to carotid IMT (normal IMT and high IMT) (figure). In analysis of covariation TT levels were significantly lower in the group of patients with both LVH and high IMT (n=24) compared to all the other groups (F=5.678, P=0.006, left plot). As figure shows (right plot) one out of two hypertensive males with both high IMT and LVH had testosterone deficiency (TT<3 ng/ml).

**Conclusion:** Elevated resting HR was associated with lower LA volume.

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Endogenous testosterone levels in hypertensive patients with target organ damage

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**Background/Introduction:** Vascular dysfunction, low-grade inflammation and arterial stiffening are associated with adverse cardiovascular outcome, while left ventricular hypertrophy (LV hypertrophy) is an independent risk factor.

**Purpose:** In this study we examined the interrelationship between augmented LV mass, high-sensitivity C-reactive protein (hs-CRP), asymmetric dimethylarginine (ADMA), osteoprotegerin (OPG) and arterial stiffness in essential hypertensives.

**Methods:** Our population consisted of 195 newly diagnosed untreated non-diabetic hypertensive patients with stage I or II essential hypertension (107 men, mean age=51 years, office blood pressure (BP)=149±96 mmHg) that underwent echocardiographic examination and according to gender-specific criteria were divided into those with LV hypertrophy (LVH) and those with normal LV mass (n=122). Arterial stiffness was evaluated on the basis of carotid to femoral pulse wave velocity (PWV), by means of a computerized method.

**Results:** Patients with LV hypertrophy compared to those without LV hypertrophy were older (53±5 vs 44±6 years, p<0.005) and had greater 24-h systolic and diastolic BP (139±10 vs 132±12 mmHg and 91±7 vs 85±9 mmHg, respectively; p<0.001 for both cases). In the total population hs-CRP was associated with body mass index (r=0.278, p<0.0001), 24-h systolic BP (r=0.146, p<0.05), ADMA (r=0.188, p<0.05) and PWV (r=0.244, p<0.0001). Moreover, PWV was associated with age (r=0.371, p<0.0001), 24-h systolic BP (r=0.248, p<0.0001) and ADMA (r=0.281, p<0.0001). Although the two groups did not differ regarding body mass index, smoking status and lipid levels (p>NS for all), hypertensives with LV hypertrophy as compared to those without exhibited higher levels of hs-CRP (3.1±0.5 vs 2.2±0.4 mg/l, p<0.05), ADMA (0.58±0.05 vs 0.50±0.04 µmol/l, p<0.0001), OPG (5.71±3 vs 4.2±0.6 pmol/l, p<0.05) and PWV (8.7±1.1 vs 7.6±1.3 m/sec, p<0.05). Analysis of covariance revealed that hs-CRP, ADMA, OPG and PWV values remained significantly different between groups after adjustment for confounders (p<0.05).

**Conclusions:** LV hypertrophy in essential hypertensives is accompanied by pronounced inflammatory activation, endothelial/vascular dysregulation and impaired arterial properties. These findings may partially explain the augmented risk associated with LV hypertrophy in this setting.
Arterial hypertension is the most important modifiable cardiovascular risk factor. Effective treatment of hypertension is a tempting strategy of reducing the risk of life-threatening complications. Despite the vast information on the association between genetic variants and hypertension obtained by genome-wide association studies, the identified loci explain only a small fraction of blood pressure variability. This may be due to epistasis, i.e., interactions between genes that remain undetected by genome-wide studies, and reflect population-specific patterns of linkage disequilibrium between the variants. In this study, we aimed to evaluate the predictive value of genotype and/or allelic combinations of the polymorphic loci associated with essential hypertension, and compare it with the predictive ability of the same loci analyzed separately.

We performed the analysis of association between polymorphic variants in 10 genes implicated in the pathogenesis of hypertension (EDN1, EDNRA, EDNRB, ACE1, ADRB1, ADRB2, ADRB3, VEGFA, ICAM1, VCAM1) in the ethnic group of Tatars from the Republic of Bashkortostan, Russia (N=530). A Markov chain Monte-Carlo-based approach (APSampler) was applied to identify genotype and/or allele combinations associated with hypertension. We detected 1287 unique genetic patterns, 50 of which remained significant after the correction for multiple comparisons (Bengamini-Hochberg test) was applied. We found that the analysis of gene-gene interactions increased the predictive ability of the candidate genes loci. For example, we demonstrated that the carriers of the EDNRA*A/A genotype have a much more moderate risk score (OR=3.94, P<0.001), while the individual analysis have shown that EDNR*A/A genotype has a much higher moderate risk score (OR=9.52, P<0.001), but just one-fifth of side branch supplied %FMM

Most side branch supplied %FMM ≥10% in 482 LM bifurcations (N=467, 97%), but just one-fifth of side branch supplied %FMM ≥10% in 2,448 non-LM bifurcations (N=510, 21%, p<0.001). Regardless of bifurcation location, %FMM ≥10% could be estimated accurately by vessel length: 73 mm (c-statistics = 0.91 to 0.99, p<0.001). In 604 vessels interrogated by FFRA, main vessels showed significantly higher %FMM and higher FFR–0.8 compared with side branches (41.0% versus 19.7%; 49.5% versus 28.2%, p<0.001, all), but similar angiographic diameter stenosis (55.4% versus 53.0%, p=NS).

Conclusions: This study established specific values for regional myocardial mass subtended by main vessel and side branch. Only one out of every five non-LM bifurcation side branch supplies clinically significant amount of myocardial mass defined by %FMM ≥10%, which could be identified by vessel length ≥73 mm with high accuracy. Lower %FMM of side branch may explain less functional significance of stenosis in side branch compared with main vessel.

Conclusions: The implications of these variants for the Romanian population need to be further analyzed, replication studies having to be undertaken for confirmation. Acknowledgement/Funding: Acknowledgements. The research is part of EU FP7 ProMark project.
Results: In total, 1339 (84.5%) stents were available for evaluation. As regards ISR, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were 94.5%, 94.2%, 82.9%, and 98.3%. Evaluable rate of stent fracture (6.2%) using MSCT were more frequent than those on coronary angiography. Stent fracture was associated with stent type, longer stent and excessively tortuous lesions. The incidence rate of stent fracture was more frequent in RCA ostial lesion (14.2%) and mid-distal LCX lesion (7.6%). RCA ostial lesion was the highest risk factor of in stent restenosis due to the stent fracture (p<0.001).

Conclusions: 256-MSC T angiography has high diagnostic value for detection of coronary stent fracture and in stent restenosis.

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Coronary calcium deposits in cardiac computed tomography
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Background: Coronary calcification can represent a challenge for percutaneous coronary intervention. Cardiac computed tomography (CT) is well established to assess coronary disease, with superior accuracy compared to other imaging modalities. The total coronary calcium score calculated by CT thus far is limited to the area of calcified plaques within the coronary lumen. Measurement of coronary calcium deposits that was confirmed histologically. We sought to define a cut off value for coronary calcium on the Hounsfield unit (HU) scale that best reflects the true size and shape of calcium deposits seen in CT using OFDI as a reference.

Methods: We retrospectively analysed all patients who underwent both CT and OFDI, during the last 2 years at our institution. Calcium deposits had to be fully traceable in both examinations and the maximum area within the frames was identified. Side branches were used as landmarks to correctly match the position of each calcium deposit in both examinations. In CT, the area of each deposit was assessed with different HU cut-off values ranging from 300 to 900 HU at intervals of 100 HU. For determination of the cut-off value that identically depicets the reference area seen in OFDI, the lowest and upper cut off HU values were identified and their weighted average calculated in each patient. The calculated cut off value was further analysed in relation to the peak HU value recorded from each calcium deposit.

Results: Within 80 patients analysed 24 fully traceable calcium deposits in 18 patients were detected. The mean area of calcium deposits in OFDI was 2.81 ± 1.75 mm², best reflected by a calculated mean HU cut off value of 649 ± 79 in CT. Mean in-segment peak HU value was 1114 ± 276. Linear regression analysis revealed a significant correlation between calculated cut off HU values and peak HU values (R² = 0.6372). According to the regression line the cut off HU value can be calculated as follows: 0.223 x in-segment peak HU + 395.62.

Conclusion: The cut off HU value which displays the true size of coronary calcium deposits in CT strongly correlates with the peak HU value. Therefore the cut off HU value can be calculated as 0.223 x in-segment peak HU + 395.62.

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Coronary Artery computed Tomography as the first-choice imaging diagnostics in patients with high probability of Coronary Artery Disease (CAT-CAD study) - preliminary results
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Background: Current recommendations indicate invasive coronary angiography (ICA) as the first choice anatomiical diagnostics in patients with high probability of stable coronary artery disease (CAD), evaluated based on sex, age, symptoms, and stress test results. However, this approach may effect in a high proportion of expendable ICAs, i.e. those not followed by further therapeutic procedures. The reasons include the lack of significant stenoses, the presence of significant stenoses ineligible for interventional treatment, or inadequate patient preparation for ad-hoc procedures. We hypothesized the use of coronary computed tomography angiography (CCTA) as the first choice anatomical diagnostic method in this population may reduce the number of expendable invasive diagnostic procedures.

Purpose: To evaluate the efficacy, and the safety of CCTA as the first choice anatomiical diagnostic method in patients with high probability of CAD.

Methods: This is a prospective, randomised, open-label, single center trial. The study is planned to include 120 patients randomised 1:1 to either group A - ICA or group B - CCTA. Depending on the primary diagnostic study results patients are qualified for further procedure, further invasive tests, interventional treatment (PCI/CABG). All patients are monitored for the occurrence of possible end points during diagnostic and therapeutic cycle (up to 3 months).

The primary efficacy outcome includes the average number of invasive proce-
dures, the safety outcomes include contrast and radiation dose during 3 months following enrolment. Clinical Trials NCT02591992.

Results: Between May 1, 2015 and November 20, 2015 we randomised 42 pa-
tients to group A (mean age of 66.8±9.5, 69% male) and 36 patients to group B (mean age of 66.0±7.3, 61% male). Patients from both groups did not differ significantly with regard to clinical characteristics, angina symptoms and stress test results (p>0.05 for all characteristics). The total number of separate invasive studies in classic ICA group was 53, and in CCTA group it was 11. The average number of the invasive procedures in ICA group was significantly higher than in CCTA group (1.26±0.25 vs. 0.31±0.52, p<0.0001). The number of expendable ICAs (not accomplished with invasive treatment) was also substantially higher in group A than in group B (29 vs. 3, p<0.0001). During the diagnostic process, there were no significant differences between both groups with regard to the doses of contrast (75.0ml [50.0–100.0] vs. 80.3ml [67.0–162.5], p=0.0580), and radiation (9.5mGy [5.4–14.3] vs. 8.9mGy [7.4–21.3], p=0.2066).

Conclusions: Preliminary study results strongly suggest that CCTA as the first choice anatomiical diagnostics in patients with high probability of CAD may result in significant reduction of invasive procedures. The trade-off may include trend towards slightly more contrast volume in CCTA group. The ultimate results will be provided after the study completion planned on May 2016.

Acknowledgement/Funding: Funded by Institute of Cardiology in Warsaw, Poland

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Correlation between noninvasive Doppler data of coronary arteries at rest and wall motion abnormality during exercise
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Several recent studies have reported the opportunity for diagnosing significant narrowing of the coronary arteries without stress testing using local flow acceleration measurements. The aim of our study was to define how often patients with increased coronary flow velocities at rest (< 0.70 m/s) have a positive exercise echocardiography test.

Methods: One hundred and fifty patients scheduled for exercise echocardiography were studied using transthoracic Doppler echocardiography in order to assess coronary artery flow velocity before exercise in left main (LM), proximal parts of left anterior descending (pLAD) and left circumflex arteries (pLCx). A significant correlation was observed between the value of the maximal velocity in LM/pLAD and the ejection fraction at the peak of exercise (r=0.000006), the value of the maximal velocity in LM/pLAD and index of wall motion abnormalities (iWMA) at the peak of exercise (r=0.04, p<0.000001). The percentage of stress echocardiography tests, had a velocity more than 0.70 m/s in the left main, proximal parts of left anterior/left circumflex arteries. Afterwards severe ischaemic stress echocardiography tests were observed in this group. The average iWMA of these tests found to be 2.3. Sixty-two angiograms were available for comparison with Doppler data. The cut-off velocity 70 cm/s in LM was defined as significant. Sensitivity, specificity, and accuracy were 78%, 100%, 90%, respectively, for predicting significant stenoses in LM/pLAD. The sensitivity, specificity, and accuracy for predicting significant lesions in pLCx were 7%, 25%, 63%, respectively.

Conclusion: Scanning of coronary flow before stress echocardiography can detect significant lesions in the left main, proximal segments of left anterior/left circumflex arteries can select high risk patients without the need for a more stress inducing ischemia.

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Coronary magnetic resonance imaging allows noninvasive evaluation of vascular patency and hemodynamics after implantation of bioreosorable vascular scaffolds
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Introduction: Bioreosorable Vascular Scaffolds (BVS) are a rapidly develop-
ing technique in interventional cardiology. The polylactate-based backbone of the BVS is dissolved after 2–3 years, leaving behind a vessel without metal reinforcement from the large number of patients with post-procedural angina pectoris after the BVS is implanted. Post-procedural angina pectoris after BVS implantation is a potential advantage of BVS over metal-based stents in order to noninvasively evaluate vessel patency, since polylactate does not cause metal artefacts in magnetic resonance imaging (MRI). Therefore, we used post-interventional MRI to evaluate patency of the BVS, as well as flow measurements for quantification of myocardial blood flow as a possible parameter influencing post-interventional angina, which has been previously described to be reduced after implantation of a BVS.

Methods: 50 patients with coronary vascular disease were randomized to receive either BVS (n=25) or a bare metal stent (n=25). MRI scanning was performed 6 months after implantation. Coronary MR images were acquired in 3D flash sequences for myocardial blood flow measurement using an accumulation of 4 scans per slice. Functional data was processed using the random displacement model for myocardial blood flow analysis.

Results: MRI flow measurements were performed in 11 patients on a 3 Tesla (T) system within two days after coronary intervention, including patients receiving one or more BVS in proximal segments of the coronary arteries. Initial presentation of patients was mixed, including stable/unstable angina, NSTEMI, and STEMI. For

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the assessment of coronary patency, a 3D bright-blood FLASH as well as a 2D dark-blood TSE sequence were acquired along the course of the vessel. Time-resolved blood flow velocity quantification was done via phase-contrast MRI, using a cross-sectional 2D single slice with through-plane velocity-encoding positioned proximal to the scaffolded vessel area. Finally, the ejection fraction was measured with a routinely used multi-slice cine-SSFP sequence.

**Results:** In all patients the scaffolded coronary arteries could be imaged without limitations. Reformatted 3D bright-blood and dark-blood images demonstrated the well-perfused BVS lumen in all patients. Luminal characteristics corresponded well between images obtained during the coronary angiography and post-interventional MRI. No susceptibility or RF-shielding artifacts from the BVS were seen in both gradient-echo and spin-echo images at 3T. In a subgroup of 6 patients, blood flow and blood flow velocity diagrams showed physiological flow patterns. In contrast to segments containing BVS, metal-based stents implanted in another subgroup of patients caused strong artifacts, which did not allow for any judgement of in-stent luminal patency.

**Conclusion:** Artifact-free coronary MRI is feasible and safe in patients after implantation of BVS in a mixed setting of clinical presentations. Judgement of luminal patency is possible in segments treated with BVS, whereas segments treated with metal stents show the typical metal-induced artifacts in MRI. Furthermore, measurement of blood flow and blood flow velocity is feasible in segments proximal to BVS implantation. Follow-up of patients will aim for characterizing resorption kinetics as well as changes in flow patterns, potentially helping to explain clinical findings such as post-interventional reduction of angina after BVS implantation.

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Incomplete stent apposition after everolimus-eluting stent implantation: a serial optical coherence tomography analysis

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**Background:** Incomplete stent apposition (ISA) is related to stent thrombosis, which is a rare complication but may lead to serious adverse events. Currently, there are few studies assessing the time-course of ISA after 2nd generation everolimus-eluting stent (EES) implantation.

**Objectives:** Aim of this study was to evaluate the time-course of acute ISA after EES implantation with optical coherence tomography (OCT) assessment.

**Methods:** Patient who underwent percutaneous coronary intervention (PCI) with implantation of an EES in one or two de novo stenosis (≥75%) of a native coronary artery were enrolled. OCT imaging was performed at baseline and follow-up. Follow-up was performed at 6–8 months (group A), 9–11 months (group B), and 12 months (group C). Stents were assessed according to the presence of the malapposition and coverage.

**Results:** At baseline, 20 lesions in 18 patients (505 frame, 4,896 struts) were analyzed. ISA was 1.4% as well as changes in flow patterns, potentially helping to explain clinical findings such as post-interventional reduction of angina after BVS implantation.

**Conclusions:** ISA at baseline ≥1.7% ISA group A (n = 7), 4.3% in group B (n = 4), and 3.9% in group C (n = 7). At follow-up, corresponding 20 lesions in 18 patients (504 frame, 5,554 struts) were analyzed. ISA was present in 0.05%, 0.13% and 0.10% respectively in group A, B and C. There was significant decrease in the frequency of ISA at follow-up compared to group A, 1.7% vs. 0.05% (p < 0.001), group B: 4.3% vs. 0.13% (p < 0.001), and group C: 3.9% vs. 0.1% (p < 0.001). In group A, acellular ISA was not found. All ISA struts at baseline were covered at follow-up. Longer follow-up was associated with a significant decrease in the number of uncovered struts: 4.4% at 6–8 months, 0.8% at 9–11 months, and 0.39% at ≥12 months (p < 0.003). However, there were no differences in the number of persistent ISA struts between groups.

**OCT findings for strut level analysis**

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of the struts at baseline</td>
<td>4986</td>
<td>1723</td>
<td>1525</td>
<td>1646</td>
</tr>
<tr>
<td>ISA at baseline</td>
<td>1160 (3.3%)</td>
<td>30 (1.7%)</td>
<td>66 (4.3%)</td>
<td>64 (3.9%)</td>
</tr>
<tr>
<td>Number of struts at follow-up</td>
<td>5554</td>
<td>1985</td>
<td>1532</td>
<td>2037</td>
</tr>
<tr>
<td>ISA at follow-up</td>
<td>5 (0.09%)</td>
<td>1 (0.05%)</td>
<td>2 (0.13%)</td>
<td>2 (0.10%)</td>
</tr>
<tr>
<td>Late acquired ISA</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Uncovered struts at follow-up</td>
<td>48 (0.86%)</td>
<td>27 (1.4%)</td>
<td>13 (0.85%)</td>
<td>8 (0.39%)</td>
</tr>
</tbody>
</table>

Numbers are % (count/sample size). *p* < 0.001, comparison of baseline vs. follow-up. ISA = incomplete stent apposition.

**Conclusions:** In patients undergoing PCI with 2nd generation EES and OCT imaging assessment, ISA at follow-up significantly decreased when compared to baseline procedure. Healing of acute ISA in EES is excellent, but it should be noted that there were a few persistent ISA after 12-month follow-up.

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**P4401 | BEDSIDE**

Two (or four)-week interval optical coherence tomography imaging evidence on neointimal coverage completion after implantation of the Xience Everolimus-eluting stent

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**Objectives:** In this study we sought to evaluate coverage and apposition of Everolimus eluting stent at 2.4, and 12 weeks after implantation.

**Background:** Despite the fact that the completion of neointimal coverage (NIC; the percentage of stent strut coverage and thickness of the formed neointima) is a cardinal process in the pathomechanism of late stent thrombosis, a major concern about the drug eluting stent (DES), little imaging modalities information is available on morphological changes thereof on a short-time interval basis.

**Methods and results:** 28 patients (with De-novo coronary artery disease) receiving elective PCI with Everolimus eluting stent (EES) were enrolled from November 2014 to October 2015. OCT was performed at weeks 2, 4 and 12 after EES implantation. NIC and malapposition were analyzed at each stent strut of cross-sectional OCT images with 1.0-mm intervals. In total, 699 cross-sectional OCT images, which depicted 8002 stent struts, were analyzed. The mean percentages of stent strut coverage at weeks 2, 4 and 12 after EES implantation were 24.0, 80.3, and 99.6%, respectively; a marked increase was found between weeks 2, 4 and 12. The mean thicknesses of the formed neointima were 37.5, 74.9, and 97.8 μm at respective weeks. The incidence of malapposition at post-intervention and 12 weeks was 6.0% and 0%, respectively.

**Conclusions:** The everolimus-eluting stent is associated to a high degree of intimal coverage and apposition within 12 weeks. Therefore, the current study demonstrated that EES might have a favorable in vivo vascular response within 12 weeks after stent implantation.
P4402 | BEDSIDE

Use of intravascular ultrasound in the modern percutaneous coronary intervention: a report from a Japanese multicenter registry

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Background: Since its introduction, intravascular ultrasound (IVUS) has been widely implemented. Increasing data suggests that IVUS benefits in improving outcomes after percutaneous coronary intervention (PCI). However, its safety and efficacy has not been extensively investigated in real-world practice.

Purpose: Our aim was to evaluate its use and effect on procedure time and PCI-related complications.

Method: We analyzed the data from 11,712 consecutive patients undergoing PCI between 2009 and 2014 in Japan from JCD-KiCS registry. IVUS was used in 9,940 patients (84.9%). PCI-related complications, such as coronary dissection or perforation were assessed via logistic regression models.

Results: Compared to IVUS group, non-IVUS group was older (68.7±11.3 v. 67.9±10.5 years, P<0.004) and had more risk factors, comorbidities and severe presentation status. Notably, IVUS was used extensively in elective PCI (90.8 v. 81.9% in urgent/emergent PCIs, P<0.001). In-hospital outcomes were shown in the table. Fluorescent times were not different between 2 groups (P>0.1).

Conclusion: IVUS was extensively used during the study period, particularly in elective PCIs. Its use was associated with less in-hospital complications such as coronary dissection or perforation, without increase in the fluoroscopy time.

Acknowledgement/Funding: This research was supported by a grant from the Ministry of Education, Culture, Sports, Science, and Technology, Japan (KAKENHI No. 25460360 and 254601)

P4403 | BEDSIDE

Impacts of lesion angle and hinge motion on drug-eluting stent implantation assessed by optical coherence tomography

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Background/Introduction: Tortuous lesion, which is often associated with hinge motion, has been reported to have adverse outcomes after bare metal stent implantation.

Purpose: We assessed the tortuous lesion characteristics and vessel wall injuries after stent implantation using optical coherence tomography (OCT) to investigate the impact of lesion angle and hinge motion on DES.

Methods: We enrolled 101 lesions (97 patients) revascularized with a single DES (64 platinnum-cromium everolimus-eluting stents (PDE-EES) and 37 bioresorbable-polymer sirolimus-eluting stents (BP-SES)). We measured the angle of lesion from the end diastole and systole before procedure on angiogram, and calculated ∠angle as the difference between these angles. The angled-group was defined as lesion with maximal angle ≥45° and with ∠angle ≥16°. Stent characteristics and vessel wall injuries both in the proximal and distal edge of the stent after implantation were assessed by OCT and compared among these groups.

Results: Thirty-two (27 PDE-EES and 12 BP-SES) and 20 lesions (15 PDE-EES and 5 BP-SES) were assigned to the angled-group and the hinge-group, respectively. OCT analysis revealed that the angled-group had higher rate of incomplete stent apposition (ISA) in the distal edge of PDE-EES compared with the hinge-group (36.4% vs 9.5%, P<0.01), while there was no significant difference in the proximal edge of both PDE-EES and BP-SES (31.8% vs 33.3%, P=0.90 and 41.7% vs 38.0%, P=0.74, respectively). In the angled-group, comparison between PDE-EES and BP-SES with regard to the incidence of ISA in the distal edge made no significant difference (36.4% vs 16.7%, P=0.21). In the hinge-group, there was no significant difference between ISA in both PDE-EES and BP-SES. The impact of lesion angle and hinge motion on the incidence of stent-edge dissection, protrusion and thrombosis had no significance both in the distal and proximal edge of PDE-EES and BP-SES.

Conclusion: Tortuous lesion may disturb optimal stent apposition in the distal edge of P-EES.

P4404 | BEDSIDE

Optical coherence tomography assessment of coronary evaginations after successful implantation of bioresorbable vascular scaffolds

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Background: Coronary evaginations have been proposed to represent a pathological vessel healing after drug-eluting stent implantation. The vascular healing after implantation of an everolimus-eluting Absorb bioresorbable vascular scaffold (BVS) can be assessed with optical coherence tomography (OCT).

Purpose: To evaluate the vascular healing at 9-month and 24-month after Absorb BVS implantation.

Methods: Serial OCT was performed in 20 patients with stable angina after Absorb BVS implantation, at 9-month and after 24 months. Dynamic changes in scaffold structure and major coronary evaginations were evaluated. Coronary evaginations were classified when the maximal depth of outward bulges of the luminal contour between scaffold struts were >150 μm and major evaginations (ME) as presence of evaginations in >3 consecutive analyzed frames, with a prominent bulge of more than 10% of the nominal scaffold diameter.

Results: The lesion length was 14.4±3.4 mm and the scaffold length was 19.7±4.2 mm. The scaffold size was 3.0±0.3 mm, maximum balloon size was 3.3±0.3 mm and maximum balloon pressure was 14.5±2.6 atm. Baseline, 3,745 struts were analyzed. The median percentage of uncovered struts was 5.1% [25th-75th percentiles: 0.5–10.0%] after 9 months and 0.0% [0.0–0.0%] after 24 months. Completely covered scaffolds were seen in 3 patients (16.7%) after 9 months and in 17 patients (94.4%) after 24 months (p<0.001). The mean neointimal thickness increased from 9-month: 95 μm [70–116 μm] to 24-month: 120 μm [100–170 μm] (p<0.001). The minimum lumen area (MLA) decreased from baseline to 9-month (5.2 mm² [5.0–5.8 mm²] vs. 4.5 [3.8–4.9 mm²] p<0.001), whereas no further decrease in MLA was observed at 24-month (4.5 mm² [3.6–4.9 mm²], p=0.001).

MEs were seen in seven patients (38.9%) at 9-month follow-up and resolved in six out of these seven patients after 24 months. The median MLA length was 4.0 mm [3.0–5.0 mm], the MLA volume was 1.4 mm³ [1.1–6.3 mm³], the maximal evagination area was 0.8 mm² [0.6–0.9 mm²], and the maximal evagination depth was 0.5 mm [0.4–0.8 mm].

Conclusion: Almost complete scaffold strut coverage was present at 24 months without causing long-term lumen area reduction. Late scaffold enlarge- ment was seen after 24 months and lumen area remained stable after 9 months. Major coronary evaginations were frequently seen after 9 months and mainly resolved after 24 months.

P4405 | BEDSIDE

In coronary culprit lesions fibrous cap thickness but not calcification is associated with the presence of diabetes: an optical coherence tomography study

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Background: Patients with type 2 diabetes are at a high risk for cardiovascular events, which usually arise from the rupture of a vulnerable coronary plaque. The minimal fibrous cap thickness (FCT) overlying a necrotic lipid core is an established predictor for plaque rupture. Recently, coronary calcification has been discussed as a further risk factor of coronary plaque vulnerability. To date, the association between type 2 diabetes and these morphological plaque parameters is largely unexplored.

Purpose: The aim of this study was to compare the differences of coronary plaque morphology in patients with and without type 2 diabetes, with a special focus on coronary calcification.

Methods: Plaque morphology and calcification of coronary culprit lesions of patients with stable coronary artery disease (n=45) and without (n=49) diabetes were analysed using optical coherence tomography (OCT) prior to coronary intervention. OCT was performed in type 2 diabetes on these morphological plaque parameters is largely unexplored.

Results: Patients with diabetes had a lower minimal FCT (82.0±27.5 μm vs. 106.9±27.8 μm, p<0.005) and a higher per cent area stenosis (71.8±18.6% vs. 71.7±11.3%, p=0.003) compared to non-diabetic subjects. However, diabetic
and non-diabetic patients had a similar amount of calcifications (3.7±2.6 vs 4.2±3.1, p=ns) and no significant difference was detected in the number of microcalcifications (0.36±0.83 vs. 0.31±0.71, s.poty (2.07±1.89 vs. 2.37±1.6) or macrocalcifications (1.31±1.57 vs. 1.51±0.97, all p=ns). The average calcium arc (74.7°± 34.8° vs. 73.7°± 31.6°), the average thickness of calcification (0.52±0.127 mm vs. 0.50±0.146 mm), the mean calcified area (0.89±0.49 mm² vs. 0.78±0.66 mm²), the mean depth of calcification (0.184±0.212 mm vs. 0.164±0.078 mm) and the cap thickness overlying the calcification (41.4±37.4 μm vs 53.1±41.4 μm) showed no significant differences between the two groups (all p=ns).

Conclusion: Type 2 diabetes is associated with increased plaque vulnerability and has an impact on the minimal fibrous cap thickness of the coronary culprit lesion, but not on the morphology and the extent of calcification.

P4400 | BEDSIDE
Comparison of in-stent neoahterosclerosis between drug-eluting stents and bare metal stents observed by optical coherence tomography
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Background and purpose: Previous pathological studies have described that atheroma with some lipid core can be formed within in-stent neointima, which is called as neoahterosclerosis, and that in-stent neoahterosclerosis might be related to very late stent thrombosis. However, comparisons of incidence and characteristics of neoahterosclerosis between drug-eluting stent (DES) and bare metal stents (BMS) have not been sufficiently examined. Therefore, the present study was to compare neoahterosclerosis between DES and BMS by optical coherence tomography (OCT).

Methods: We analyzed the incidence of neoahterosclerosis in patients who underwent routine follow-up coronary angiography after stent implantation. Neoahterosclerosis was defined as the tissue including lipid component between the luminal border and the inner border of the stent struts according to OCT findings. Then, maximum lipid arc (Larc) and minimal thickness of fibrous cap (Lfc) within neoahterosclerosis were measured by OCT in DES and BMS group.

Results: We performed follow-up OCT study for 567 stents in 291 patients from 2012 to 2015. Neoahterosclerosis was found in 32 stents (5.6%, 19DES, 13BMS). There was no significant difference of Larc within the neoahterosclerosis between DES group and BMS group. However Tfb was significantly thinner in DES group than in BMS group (0.16 (0.13–0.22) vs 0.22 (0.16–0.37) mm, p<0.03). Moreover, neoahterosclerosis was found significantly earlier in DES group than in BMS group (1148 (510–2093) days vs 2194 (1381–4337) days, p<0.020).

Conclusions: Neoahterosclerosis of neointima within DES might be more vulnerable than that within BMS.
the treatment of coronary atherosclerotic lesions. Their distinguishing feature is the disappearance of the foreign implant in two years, bringing the potential benefits of eliminating the risk of late stent thrombosis and the restoration of physiological vasomotion. Due to the limited experience with BVS it is not yet clear what will be the further development of the initially treated, hemodynamically significant, atherosclerotic plaque and its removing the mechanical support of a stent.

Purpose: To perform an analysis of atherosclerotic plaque using intracoronary spectroscopy in the site treated with a biodegradable BVS. Intra coronary spectroscopy is a method capable of detecting lipid core of a vulnerable plaque (VP).

A numerical representation of the presence of a lipid core is the lipid core burden index (LCBI).

Methods: Spectroscopic analysis was performed in 8 patients 2 years after implantation of BVS. The results were compared with a control group of 12 patients in whom the spectroscopic analysis was performed before and after percutaneous coronary intervention (PCI).

Results: Median maximum LCBI (25th, 75th percentile; LCBI(max)) before PCI was 280.5 (75.5, 409.5). We observed a statistically significant reduction of LCBI(max) to 57 (1.86; p<0.02) after PCI. The values of LCBI(max) during the two years follow-up did not differ significantly from the values after PCI (LCBI(max)=213; 115: 240; p~ns). In 2/8 of the patients a lipid core was not observed (LCBI(max)=0) and in 2/8 of the patients we detected LCBI(max) greater than the median LCBI(max) before PCI (LCBI(max)=291; p=0.417). The value of LCBI(max)=417 was associated with a 27% reduction of the vessel lumen.

Conclusion: Our results suggest that in the majority of patients the significant reduction of the lipid core, which occurs after PCI, persists even after the biodegradation of BVS. At the same time the risk plaque progression at the site of the initial intervention due to neatherosclerosis is not eliminated.

INSIGHTS INTO CORONARY MORPHOLOGY AND PHYSIOLOGY

P4411 | BEDSIDE
Comparison of FFR and IFR Measurements in Patients with and without Severe Aortic Valve Stenosis
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Background: Fractional flow reserve (FFR) and instantaneous wave-free ratio (iFR) have not been extensively studied in patients affected by severe aortic valve stenosis (AVS) and concomitant coronary artery disease (CAD).

Purpose: The aims of the present study were to test the FFR and iFR performances in a population of patients with severe AVS, to compare them with a population of CAD patients without AVS and to correlate them with quantitative coronary angiography (QCA) parameters.

Methods: In this prospective observational study FFR and iFR were measured in the three major coronary artery branches of patients undergoing diagnostic coronary angiography as part of the workflow for TAVI. QCA was performed blinded of the FFR and iFR results. During the same period, patients referred to our cathlab for suspected CAD, both stable and unstable, and no signs of valve heart disease were assessed in the same manner. Only patients with normal left ventricular function and without previous myocardial infarction were included.

Results: Between January 2015 and December 2015 a total of 175 patients with 337 coronary lesions were included in the study. Among these, 41 patients (105 lesions) were affected by symptomatic severe AVS, while the remaining 134 were patients with stable CAD without AVS. Correlation between FFR-iFR and QCA parameters was modest but remains constant in patients with AVS (r=0.61; p<0.001). FFR-iFR correlation was poorer in CAD patients compared with AVS patients (r=0.86; p<0.001) however the iFR accuracy for predicting FFR was similar between both groups (an AUC of 0.95 (0.89-0.98) vs 0.94 (0.88-0.98); p for interaction=0.8). At ROC curve analysis the best cut-off of iFR predicting FFR <0.8 was lower in patients with AVS compared with CAD patients (0.85, p=0.001 vs 0.86, p=0.001). However the iFR accuracy for predicting FFR <0.8 was similar between the two groups (an AUC of 0.95 (0.89-0.98) vs 0.94 (0.88-0.98); p for interaction=0.8). At ROC curve analysis the best cut-off of FFR predicting FFR <0.8 was lower in patients with AVS compared with CAD patients (0.85, p<0.001 vs 0.86, p<0.001) however the iFR accuracy for predicting FFR <0.8 was similar between the two groups (an AUC of 0.95 (0.89-0.98) vs 0.94 (0.88-0.98); p for interaction=0.8). Using the established cut-off point of 0.9 for IFR the false positive rate was 23% in the AVS group compared to 12% in the CAD group (p<0.1).

Conclusion: AVS may influence functional assessment of concomitant coronary artery disease. The correlation between FFR and IFR in AVS is poorer compared with CAD patients. IFR in patients with AVS may overestimate the functional significance of coronary lesions.

P4412 | BENCH
Endothelial glycoalkalx and arterial elasticity are severely impaired in patients without cardiac causes of cryptogenic stroke
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Background: Approximately 30–40% of ischemic strokes remain without a clearly defined cause after extensive workup and are described as cryptogenic. Impaired arterial hemodynamic properties and endothelial dysfunction could shed light into the pathogenesis of these cerebrovascular accidents. In this respect, we investigated the arterial stiffness and glycoalkalx integrity in patients with cryptogenic stroke.

Methods: We measured a) the aortic PWV (PWVao), central systolic blood pressure (SBPao), central pulse pressure (PPao), and augmentation index (AIxao) by Arteriograph; and b) the perfusion boundary region (PBR–micrometers) of the sublingual arterial microvessels, a valid marker of endothelial glycoalkalx thickness, (ranged from 5 to 25 micrometers) using Sideview, Darkfield imaging (Microscan, Glycocheck), in 40 patients with cryptogenic stroke and 40 healthy controls (mean age 44,4 years). Only patients with negative findings in an extensive workup including 24h ambulatory ECG monitoring and transosophageal echocardiography were assessed in the same manner. Thus, arrhythmic and thrombotic etiologies of coronary origin had been ruled out.

Results: PWVao (11.8±0.8 vs 9±0.9; p=0.001), SBPao (137±3.7 vs 117±4.6; p=0.002), PPao (51±2.2 vs 40±2.8; p=0.004), AIxao (32±25 vs 20±3.2; p=0.005), PBR–5 (2.6±0.2 vs 5.0±0.3; p=0.04) and PBR–5 >9 (1.29±0.02 vs 1.13±0.02; p<0.001) were higher in patients with cryptogenic stroke compared to healthy controls. Furthermore, there was a significant positive correlation of glycoalkalx thickness with PWVao (p=0.036). These findings provide evidence that arterial stiffness and endothelial function are impaired in and might be causally associated with strokes of undetermined etiology.

Conclusions: Increased arterial stiffness and impairment of endothelial glycoalkalx could serve as pathophysiologic substrates of cryptogenic strokes.

P4413 | BEDSIDE
How does coronary microvascular dysfunction affect fractional flow reserve measurement?
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Background: A discrepancy between coronary angiography and fractional flow reserve (FFR) has been observed in some clinical settings. Coronary microvascular dysfunction (CMD) may cause the FFR to be overestimated, since the FFR is assumed to be correct when minimal resistance at maximum hyperemia is available.

Purpose: The purpose of this study was to investigate how CMD affects FFR measurement.

Methods: The FFR and a novel index of microcirculatory resistance (IMR) were simultaneously measured using a pressure/temperature sensing coronary guide wire in non-obstructed coronary arteries (% diameter stenosis <50%). The FFR was measured after inducing maximal hyperemia using an intravenous infusion of adenosine triphosphate (180µg/kg/mL); then, room temperature saline was injected into the coronary artery to calculate the IMR. The FFR and IMR values were assessed to evaluate their potential correlation.

Results: In 123 consecutive patients, (1) the mean FFR value was 0.86±0.10 (mean±SD), (2) the mean IMR value was 17±6.6, (3) a significant correlation was observed between the FFR and the IMR (r = 0.30, P<0.001; FFR = 0.78 ± 0.04 × IMR), and (4) no significant correlations were observed between the FFR values and several patient characteristics (age, sex, coronary risk factors, and medications) according to a multivariate analysis.

Conclusions: Our results have shown that the FFR increases as CMD develops. Specifically, the FFR can be expected to increase by 0.05 when the change in the IMR exceeds 2 standard deviations. Since CMD may have an important effect on FFR measurement, CMD should be taken into account when a discrepancy occurs between FFR and coronary angiography findings.

P4414 | BEDSIDE
Feasibility of additional intracoronary adenosine administration on top of standard intravenous adenosine infusion for assessment of coronary fractional flow reserve

Background: Achievement of maximal hyperemia of coronary microcirculation is a prerequisite for correct fractional flow reserve (FFR) measurement. However, concern exists as to whether a maximal hyperemia is achieved with standard continuous infusion of adenosine.
Purpose: Our aim was to address feasibility of additional intracoronary adenosine administration to achieve maximal hyperemia and compare its efficacy between forearm and venous venous infusion.

Methods: Hyperemia was induced by continuous intravenous (IV) infusion of adenosine (140 μg/kg/min) through either the forearm vein with 20-gauge cannula or the femoral vein with 5-Fr sheath. The first FFR value (FFRIV) was obtained after achieving steady-state hyperemia with IV infusion. Then, an additional intracoronary adenosine was administered (60 μg for the left coronary artery, 36 μg for the right coronary artery) to obtain the second FFR value (FFRaddIC).

Results: One hundred forty five paired recordings (116 forearm and 29 femoral venous access) were taken from 93 patients (mean age of 64.6±10.8 years). Mean values of FFRIV and FFRaddIC were 0.81±0.08 and 0.81±0.08 (paired t-test; p<0.001) with forearm venous infusion and 0.86±0.08 and 0.85±0.08 (paired t-test; p=0.001) with forearm venous infusion, respectively. Significantly higher FFR compared to the FFRaddIC, defined as the difference between them was >0.02, was observed in 33 (28%) cases with forearm venous infusion, which led to reclassification of five cases (from ≥0.80 to <0.80). There was no such a case with femoral venous infusion. There were 7 transient AV block related to intracoronary bolus of adenosine.

Conclusions: FFRIV with forearm venous infusion was significantly higher than FFRaddIC in 28% of cases. The femoral venous infusion was preferred for correct FFR measurement. Additional intracoronary injection of adenosine might be a feasible option to ensure the achievement of maximal hyperemia when the forearm vein was used as infusion route.

P4416 | BEDSIDE
Inhibition of renal sympathetic nerve activity via electrical stimulation of the urinary tract
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Background: Efferent renal sympathetic nerve activity (RSNA) plays an important role in the control of renal function and hemodynamics by its actions on renal blood flow, renin release and the regulation of sodium and water balance. Increased RSNA is known to be a critical factor in fluid retention, may contribute to kidney injury and is associated with challenging and costly clinical conditions.

Purpose: The aim of this study was to test the effect of electrical stimulation of the urinary tract on RSNA, renal blood flow (RBF) and hemodynamics in a large animal model using a novel stimulation catheter.

Methods: In five sheep anaesthetised with isoflurane, electrical stimulation (frequency 5 and 10 Hz, pulse duration 2 msec) of the bladder neck and proximal urethra was performed using a Foley-like, urinary catheter imprinted with electrodes and wired to an external pulse generator. Direct RSNA (recorded via intravesical electrodes inserted into the left renal nerve, RBF (via a transit-time flow probe placed on the left renal artery) and arterial pressure were recorded continuously. RSNA was quantified using Burst area under curve (AUC), the rectified integrated signal normalized to the level of the basal activity, and Spike Frequency, the number of activity spikes exceeding threshold per unit time. The stimulation sessions were of two minutes duration separated by 10 minutes for washout of any residual effects. Each animal served as its own control and the values used for each parameter were the mean of the two minute periods from before, during and after stimulation. A total of 14 stimulation sessions were conducted (two to three such stimulation sessions for each sheep). Additional stimulation sessions in each sheep using a range of stimulation amplitudes were used to test amplitude dependency. Results are shown as means±SD.

Results: Electrical stimulation of the urinary tract inhibited RSNA in a controllable ON-OFF fashion. Burst AUC, serving as a surrogate for overall magnitude of nerve firing, decreased by 15.6±17.2% (p<0.01) and RSNA Spike Frequency decreased by 3.8±7.1% (p=0.066) from baseline values. RSNA returned to baseline after cessation of stimulation (p<0.001 for Burst AUC and p<0.01 for Spike Frequency). Mean arterial pressure (MAP) decreased by 5.0±3.7 mmHg (p<0.001) and heart rate by 2.12±0.5 beats/min (p<0.01). A key indicator of renal hemodynamic state, renal vascular resistance (RVR), was reduced by 6.3±5.4% (p<0.001). Both the decrease in MAP and HR were stimulation amplitude dependent (p=0.03 and p<0.02 for MAP and HR, respectively).

Conclusions: In healthy anaesthetised sheep, electrical stimulation of the urinary tract produced a reversible inhibition of RSNA, which was associated with decreased RVR. The stimulation also resulted in systemic effects with reduction in MAP and HR. Urinary tract stimulation may have potential benefits as a new modality for treating pathological states associated with elevated RSNA.

Acknowledgement/Funding: The study was funded by Nephera Ltd.
cardiac coronary artery. It is unknown how FFR evolves over time at coronary stenoses with deferred intervention and if these changes are related to clinical or angiographic features.

**Purpose:** To describe the longitudinal evolution of FFR (dFFR = FFR follow-up – FFR baseline), explore its clinical significance and correlation with angiographic indices and identify predictors of dFFR in coronary stenoses with deferred intervention.

**Methods:** Patients who had undergone FFR assessment of the same coronary stenosis at the occasion of 2 repeated coronary catheterizations > 1 year apart were retrospectively included. FFR evolution was defined as "worsening" if dFFR < 0.04, "stable FFR" if dFFR = 0.04 to 0.04 and "improving FFR" if dFFR > 0.04. Age and sex-matched coronary artery stenosis was also evaluated by changes in percent diameter stenosis (d%DS) and minimum lumen diameter (dMLD). Correlations between dFFR, d%DS and dMLD were calculated using Spearman’s ρ. Multiple linear regression analysis with stepwise elimination was performed in order to identify the independent predictors of FFR follow-up: age, sex, smoking, hypertension, diabetes mellitus, dyslipidemia, PCI at non-reference vessel, use of aspirin, clopidogrel, beta-blockers, statins, ACEI, ARBS, CCBs and baseline FFR, %DS and MLD values were entered as independent variables. ROC analysis for the discrimination ability of FFR baseline to predict FFR follow-up < 0.04 was performed.

**Results:** 126 patients with 147 lesions were studied; time interval between measurements 15.5 (18.4, 39.8) months; FFR baseline was 0.86 (0.81–0.90) and FFR follow-up was 0.84 (0.79–0.90) (P = 0.001). DFFR was observed in 51 (34.7%) lesions, stable FFR in 76 (51.7%) lesions, and in 20 (13.6%) lesions FFR improved over time. The number of clinically significant lesions (e.g. FFR ≤ 0.75) was higher at follow-up compared to baseline (30.6% vs. 18.4%, P < 0.05), dFFR did not correlate with changes in angiographic indices (d%DS, dMLD; P = NS for both). In multiple linear regression analysis, FFR was the only independent predictor of FFR follow-up (R 2 = 0.155, B = 0.587, P < 0.001).

**Conclusion(s):** FFR baseline, but not angiographic indices or clinical characteristics, is the only predictor of significant longitudinal arteriosclerosis progression, probably for which reasons will require revascularization.

**Acknowledgement/Funding:** P. Xaplanter is supported by an EAPCI intervention cardiology research grant and a Hellenic Cardiological Society (HCS) grant for 2016.

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**P4418 | BEDSIDE**

**Coronary Pulse Wave Velocity: insight from a first routine assessment in humans**

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**Background:** Little is known about biomechanical properties of coronary arteries, although they may have important clinical consequences. One way is to assess vascular compliance by measuring pulse wave velocity (PWV). The prognostic impact of aortic PWV on coronary events has been extensively documented but, to our knowledge, coronary PWV has never been measured in routine.

**Objectives:** To propose this routine method to assess coronary PWV (cPWV) based on the use of a pressure wire and to describe conditions which will require revascularization.

**Methods:** This is the first report on real-time simultaneous LV-coronary haemodynamics and correlations with 3DSTE, examining myocardial-coronary interdependence at rest, exercise and in ischaemia in a cohort of patients with IHD and preserved systolic function.

**Results:** 42 patients consented and 25 with known stable angina and preserved LV function completed the protocol (Fig A) with 3DSTE datasets acquired (15) followed by invasive catheter lab measurements in the same patients (rest, exercise and ischaemia) with coronary blood flow (CBF) assessment (sensor pressure-flow wire) in coronary artery and electronically routing into the intracardiac analyser, via which LV haemodynamics – using pressure-volume (PV) loop catheter in LV apex - were measured enabling simultaneous real-time recordings. Global LV longitudinal, circumferential, and radial strain was compared with simultaneous CBF, wave intensity analysis and LV PV loops were analysed with custom in-house software (Fig B).

**Conclusion(s):** cPWV baseline, for 2016.

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**P4420 | BEDSIDE**

**Presence of cardiac autonomic dysfunction in patients with coronary vasospasm**

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**Background:** Coronary artery vascular tone is partly controlled by autonomic nervous system and important pathophysiology for coronary vasospasm. Nevertheless, the association between microvascular coronary and cardiac autonomic function has not been studied. In present study, we investigated the relation between CAS and autonomic dysfunction by assessing the heart rate and blood pressure recovery after exercise.

**Methods:** 358 patients (M/F=233, mean age=59±10.1 years) who presented with chest pain in outpatient clinic and who underwent a symptom-limited treadmill exercise test (TET) and coronary angiography were included. Coronary artery stenosis (>50% narrowing of at least one coronary artery) was detected...
in 146 patients (37.4%). In remained 242 patients, coronary spasm provocation test was performed in 230 patients (58.3±9.9 years). CAS was defined as >90% narrowing induced by intra-coronary acetylcholine injection. Delayed HR was defined as ΔHR1min -18.1 min (ΔHR1min: Maximal HR-HR at 1 minute after exercise termination). A ratio systolic blood pressure (SBP) after 3 minute of recovery to peak exercise SBP:0.95 was defined as delayed BP response.

Results: CAS by provocation test was seen in 97 among 230 patients (42.2%). The presences of classical cardiovascular risk factors (age, smoking, diabetes, hypertension, dyslipidemia) were not different between patients with and without CAS. There were no difference in the exercise duration (P=0.14) and the percent of ischemic ST changes during TET (P=0.94) between patients with and without CAS. The mean ΔHR1min was lower in patient with CAS than that in patients without CAS (38±17.8 vs 45±18.9, P=0.007), BP recovery after exercise in patients with CAS was also less than that of patients without CAS. (The mean of SBP ratio after 3 minute of recovery/peak exercise, 1.02±0.23 vs 0.95±0.19, P=0.019). The prevalence of autonomic dysfuction was higher in patients with CAS than in patients without CAS (delayed HR: 16.7% vs 5.6% P<0.011, delayed BP response 60.4% vs 42.0% P=0.009).

In multivariate regression analysis, the delayed HR and BP response was independently related with CAS: OR: 3.15, P=0.043, CI: 1.04–9.53, and OR: 1.86, P=0.037, 95% CI: 1.07–3.46, respectively, after adjusting classical cardiovascular risk factors.

Conclusion: Abnormal cardiac autonomic dysfunction defined as diminished HRR and BPR after exercise were associated with coronary spasm. These findings suggest that autonomic instability might be involved in the pathophysiology of coronary spasm.

**P4421 | BEDSIDE**

The influence of elective percutaneous coronary intervention on microvascular resistance: a serial assessment using the index of microcirculatory resistance
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Background: The effect of epicardial coronary artery stenosis on hyperemic microvascular resistance (MR) is controversial, and the influence of elective coronary intervention (PCI) on MR remains unclear. This study investigates whether MR is influenced by elective PCI, by using the index of microcirculatory resistance (IMR).

Methods and results: Seventy-one consecutive patients with stable angina pectoris undergoing elective PCI for focal de novo stenoses were prospectively studied. IMR was measured before, after, and at the 10-month follow-up of elective stenting. There was a trend but no significant difference in IMR between pre- and post-PCI (mean difference, -2.8±1.7; P=0.051), however a significant decrease was observed between pre-PCI and follow-up (mean difference, -5.4±12.4; P=0.001). Forty-six vessels showed a decrease and 25 showed an increase in IMR until long-term follow-up. Pre-PCI IMR significantly correlated with change in IMR between pre- and post-PCI (r =-0.66, P<0.001) and between pre- and follow-up (r =-0.86, P<0.001). There was no significant difference in clinical variables and physiological parameters between the vessels with IMR increase and decrease, except for pre-PCI IMR and pre-PCI mean transit time (Tmn) which has been validated to correlate with inverse value of absolute coronary flow after PCI. In all patients we measured FFR with a pressure wire under maximal hyperemia and if pre-PCI fractional flow reserve (FFR) or IMR predicts the post-PCI change in hyperemic coronary flow. FFR measurements. Receiver operating characteristic curve analysis revealed that the optimal pre-PCI IMR and pre-PCI FFR cut-off values to predict an increase in hyperemic coronary flow after PCI were 12.7 (AUC, 0.76; P<0.001) and 0.73 (AUC, 0.72; P<0.001), respectively. In multivariate analysis, factors significantly associated with increased post-PCI IMR were pre-PCI IMR (odds ratio [OR], 1.13; 95% confidence interval [CI], 1.08–1.19; P<0.001) and angiographic reference diameter (OR, 2.44; 95% CI, 1.99–5.48; P=0.03). Factors significantly associated with increased coronary flow post-PCI were pre-PCI IMR (OR, 1.15; 95% CI, 1.08–1.23; P<0.001) and pre-PCI FFR (OR, <0.001; 95% CI, 0.000–0.003; P<0.001). When the vessels were divided into 4 categories based on FFR and IMR cut-off values, the frequencies of increased coronary flow after PCI were significantly higher for vessels with a high IMR than for those with a low IMR, given the same FFR value, and significantly higher for vessels with a low FFR than for those with a high FFR, given the same IMR value.

Conclusion: Hyperemic coronary flow after successful PCI increased in the majority of target territories, and the pre-PCI physiological indices of FFR and IMR may predict an increase in coronary flow after PCI.

**P4422 | BEDSIDE**

Preprocedural fractional flow reserve and microvascular resistance predict increased hyperaemic coronary flow after elective percutaneous coronary intervention
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Aims: Epicardial focal coronary artery stenosis, diffuse coronary disease, and microvascular resistance (MR) may limit coronary flow. The purpose of percutaneous coronary intervention (PCI) is to increase coronary flow by targeting epicardial lesions. After PCI, MR might change and affect coronary flow. We investigated whether PCI influences the index of microcirculatory resistance (IMR) and if pre-PCI fractional flow reserve (FFR) or IMR predicts the post-PCI change in hyperemic coronary flow.

Methods and results: This prospective study included 245 vessels from 229 patients with stable angina pectoris undergoing elective PCI. Finally, 182 vessels in 176 patients without peri-procedural myocardial infarction fulfilled the inclusion criteria and were included in the final analysis. FFR and IMR were measured before and after PCI. Post-PCI increase in hyperaemic coronary flow was assessed using the change in thermolumination-derived transit time (pre-PCI Tmn – post-PCI Tmn). IMR significantly decreased after PCI (median 1.9; interquartile range, 4.9–10.1) and was significantly associated with pre-PCI IMR (r=0.70, P<0.001). Coronary flow increased, as indicated by a decrease in Tmn, in 141 territories and decreased in 41 territories after PCI. Increased coronary flow was significantly correlated with pre-PCI IMR (r=0.62, P<0.001) and pre-PCI FFR (r=0.51, P<0.001). ROC curve analysis revealed that the optimal pre-PCI IMR and pre-PCI FFR cut-off values to predict an increase in hyperemic coronary flow after PCI were 12.7 (AUC, 0.76; P<0.001) and 0.73 (AUC, 0.72; P<0.001), respectively. In multivariate analysis, factors significantly associated with decreased post-PCI IMR were pre-PCI IMR (odds ratio [OR], 1.13; 95% confidence interval [CI], 1.08–1.19; P<0.001) and angiographic reference diameter (OR, 2.44; 95% CI, 1.99–5.48; P=0.03). Factors significantly associated with increased coronary flow post-PCI were pre-PCI IMR (OR, 1.15; 95% CI, 1.08–1.23; P<0.001) and pre-PCI FFR (OR, <0.001; 95% CI, 0.000–0.003; P<0.001). When the vessels were divided into 4 categories based on FFR and IMR cut-off values, the frequencies of increased coronary flow after PCI were significantly higher for vessels with a high IMR than for those with a low IMR, given the same FFR value, and significantly higher for vessels with a low FFR than for those with a high FFR, given the same IMR value.

Conclusion: Hyperemic coronary flow after successful PCI increased in the majority of target territories, and the pre-PCI physiological indices of FFR and IMR may predict an increase in coronary flow after PCI.
tain an initial Pd/Pa=1. We systematically checked the Pd/Pa value after FFR measurement at the same position. We defined drift as a difference of Pd/Pa after FFR to determine FFR value during the procedure.

**Results:** In our study FFR measurement is accurate in 86% of the cases and 100% of the cases after a second equalization when a drift of more than 0.02 is observed without attributable reasons. Drift check changed the revascularization indication in 3 patients (2%). Drift should be systematically checked after FFR measurement of a borderline value.

**Conclusion:** The discordance between FFR and CFR changes after percutaneous coronary intervention.

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**Background:** Discordance of coronary flow reserve (CFR) and fractional flow reserve (FFR) has been reported to originate from patient coronary pathophysiology, mainly due to the difference in the degree of microvascular dysfunction. The purpose of percutaneous coronary intervention (PCI) is to increase coronary flow by targeting epicardial lesions, resulting in FFR improvement, although the relationship between the changes in FFR and CFR after PCI remains elusive. We sought to investigate if FFR change after PCI correlates with CFR change.

**Methods:** This retrospective study included 261 vessels from 252 patients with stable angina pectoris undergoing elective PCI. FFR, CFR, and CMR calculated by transit time based on the thermo-dilution method were measured before and after PCI. The study population included patients treated with PCI with a wide range of CFR including those with FFR < 0.80. The relationship between the changes in FFR and CFR was investigated, and patient characteristics and physiological indices between the two groups divided by the increase or decrease in CFR were compared. Furthermore, multivariate analysis was performed to identify the predictors of greater CFR increase after PCI.

**Results:** Median FFR value was 0.74 (0.67–0.81), and the prevalence of lesion severity of FFR > 0.80 was 21% in the present study. After PCI, median FFR increase was 0.14 (IQR: 0.07–0.21), CFR change from -8.0 to +10.0, and mean difference was +1.1. There was no significant relationship between post-PCI FFR and post PCI CFR, although significant relationship was observed between pre-PCI FFR and pre PCI CFR. Decrease in CFR was found in 97 (37%) and CFR improvement was observed in 164 (63%). CFR increase after PCI was significantly associated with high pre-PCI CFR, low pre PCI FFR, low pre-PCI CFR, high pre-PCI % diameter stenosis, and greater stent size. In multivariate analysis, pre-PCI FFR (OR: 0.69; 95% CI: 0.58–0.82 P < 0.001), and stent size (OR: 3.18; 95% CI: 1.60–6.29 P < 0.001) were independent predictor of CFR increase after PCI.

**Conclusion:** FFR and CFR showed a different response after PCI. Concordant improvement correlates with pre-PCI physiological indices.

**P4424 | BEDSIDE**

**Impact of additional intracoronary nicorandil administration during fractional flow reserve measurement with intravenous adenosine 5'-triphosphat infusion**

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**Background:** Fractional flow reserve (FFR) is a useful index for determining the functional severity of epicardial coronary artery stenosis as an invasive physiologic method. Although intravenous adenosine 5'-triphosphat (ATP) is generally used as a hyperemic agent for FFR measurement there are some concerns about the presence or measurement of ATP in urine, effects on coronary artery (change).

**Aim:** It is difficult to confirm sufficient maximal hyperemia after ATP infusion. Recent studies reported nicorandil (NIC) could be an alternative to ATP as a hyperemic agent.

**Purpose:** We evaluated FFR changes with additional intracoronary (IC) NIC administration during intravenous (IV) ATP infusion with intermediate coronary artery stenosis.

**Methods:** Patients who underwent FFR measurements of angiographically intermediate lesions were included. All patients were asked to refrain from caffeine-containing products more than 12 hours before FFR measurements. All patients first received IV ATP infusion (180mg/kg/min) via cubital vein for 3 minutes to measure FFR (ATP-FFR). After additional IC NIC administration (2mg/30sec) during ATP infusion, FFR was measured again (NIC-FFR). To check cyclic change in FFR, we measured minimum and maximum FFR values during both ATP and NIC hyperemic phase.

**Results:** In this study, 94 patients (age 70±9 years, 71 male) with 94 lesions were enrolled. IV ATP infusion produced significant decreases in systolic (15%), diastolic (12%), and mean blood pressure (12%), but a significant increase in heart rate (4%) compared to baseline. Moreover, additional IC NIC administration produced a further drop of blood pressure (systolic: 3%, diastolic: 5%, mean: 4%) compared to IV ATP infusion. Mean FFR value was 0.81±0.10 in ATP-FFR and 0.80±0.09 in NIC-FFR, respectively. ATP-FFR and NIC-FFR had strong correlation on the whole (r=0.92, p<0.001). In 18 patients (19%), FFR values were significantly lower in NIC-FFR than in ATP-FFR (0.88±0.08 vs 0.79±0.06; p<0.0001).

One third of those patients (6%) were possible to change therapeutic strategy from deferral range (≤0.80) to interventional range (≥0.80) after NIC-FFR measurement. Furthermore, cyclic change in FFR during measurements was smaller in NIC-FFR than in ATP-FFR (0.03±0.02 vs 0.06±0.05; p<0.0001).

**Conclusion:** Additional IC NIC might be useful to confirm sufficient maximal hyperemia after IV ATP infusion in daily clinical practice. Furthermore, additional IC NIC might reduce cyclic change in FFR, thus physicians might find it easier to determine FFR value during the procedure.
Methods: We investigated 24 vessels with indication of coronary physiology due to fluoroscopic stenosis of uncertain relevance. A pressure wire was used in order to register pressure and temperature distal to a coronary artery stenosis (PD) under conditions of hyperemia, induced by regadenoson (Rapiscan 400μg). FFR was measured 11 times in RIVA, 4 times in RCX and 9 times in RCA. After injection of regadenoson, markers of drug effect in terms of time to symptom onset and onset of systemic hypotension as well as duration of symptoms and of systemic hypotension were recorded. Transit mean time (Tm) was assessed by thermodilution method, injected 3ml NaCl of 20 °C at 3 times through the guiding catheter to receive an average value. CFR was calculated as the ratio of Tm under hyperemic and baseline conditions. IMR was calculated by multiplying PD with average Tm under hyperemia. The calculation was made by RadiAnalyzer Xpress software.

Results: Coronary physiology assessment was technically feasible in all cases. Mean time from infusion of regadenoson to symptom onset was 20±10s. Mean time from induction of hyperemia to baseline conditions was 2±0.9 minutes. Within this duration the injection of 3 ml NaCl was possible in 23/24 cases. The mean standard deviation of 3 baseline Tm measurements was 0.13±0.12s, while it was 0.08±0.06s under regadenoson hyperemia (p<0.10). Values of CFR were positively correlated to FFR in 11 cases, where FFR was <0.8 (r=0.87, p<0.05). In 8 cases of patients with non-significant stenosis, but increased LVEDP and meandering vessel shape in fluoroscopy, CFR displayed values of 0.24. In those cases IMR increased to 4.9±2.53.

Conclusion: Coronary physiology assessment is feasible during regadenoson-induced hyperemia as it provides reasonable values for FFR, CFR and IMR.

P4428 | BEDSIDE
Coronary flow reserve correlates with mean pressure gradient and indexed mass of left ventricle in severe aortic stenosis

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Background/Introduction: Aortic stenosis is the most common valve dysfunction, however underlying mechanisms involving microcirculatory dysfunction in hypertrophic ventricle are still not clear.

Objective: The aim of the study was to investigate relations between coronary flow reserve, severity of aortic stenosis and level of left ventricle hypertrophy in patients scheduled for aortic valve replacement (AVR).

Methods: In this prospective study CFR was measured non-invasively by Doppler echocardiography, calculating maximal flow velocity in left anterior descending artery (LAD) at rest and after inducing full hyperemia with adenosine administered intravenously with dose of 140 μg/kg of body weight per minute. Measurements of CFR, as well as indexed left ventricle mass and mean aortic valve gradient were repeated at baseline (before surgery), 3, 6 and 12 months after AVR. Significant LAD stenoses were excluded based on angiography made before AVR qualification.

Results: 36 patients with severe aortic stenosis were prospectively included into the study. Mean age of patients was 56.7 years (SD=12.6), 50% of patients were women, and 78% were current or former smokers. Mean aortic valve gradient (mean PG) at baseline was 63±59Hg (SD=18). After 3, 6 and 12 months mean gradient was significantly lower (p<0.001), respectively 17.8±13Hg (SD=18,3), 16.8±16Hg (SD=16,6). Mean CFR before surgery was 1.61±0.27, and after 3, 6 and 12 months increased to 2,28 (SD=0,32), 2,22 (SD=0,49) and 2,31 (SD=0.42) respectively (Friedman ANOVA p<0.001), while their association became stronger at 3, 6 and 12 months increased to 0.12±0.09s, 0.13±0.12s, 0.08±0.06s under regadenoson hyperemia (p<0.001), respectively 17,8mmHg (SD=12,4), 19,3mmHg (SD=18,3) and 21,9mmHg (SD=19,4) under hyperemia (p<0.001), however underlying mechanisms involving microcirculatory dysfunction in hypertrophic ventricle are still not clear.

Conclusions: The real-time, direct analysis of flow velocity profile and computation of severity of aortic stenosis and of left ventricle hypertrophy gives new insight in pathophysiology of heart muscle microcirculation dysfunction in aortic stenosis.

P4429 | BEDSIDE
Complex relation between post-ischemic arterial vasodilation and shear rate pattern during flow-mediated vasodilation: insight from a novel open ultrasound platform

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Background: Flow mediated vasodilation (FMD) is widely used to assess endothelial dysfunction in the clinical setting. However, the lack of a direct estimate of wall shear rate (WSR), i.e. the putative stimulus to the nitric oxide release and vessel dilation during post-ischemic hyperemia, limits the informative value of the technique. Aim of the study was to explore the relations between WSR and diameter changes during FMD test in normal subjects.

Material and methods: 18 healthy subjects (5 men) volunteered for the study with age range 26±12 years, BMI range 21±5 kg/m2. FMD was performed at the non dominant brachial artery level according to current guidelines by a novel ultrasound device with a radiofrequency data port and high spatial and temporal resolution, which allows direct simultaneous recording of blood flow velocity profile, WSR and vessel diameter.

Results: After the occluding cuff release, systolic WSR rapidly increased from 12±5±5 to 519±195 s⁻¹, and time to peak for WSR was 12.2±2.9 s (all values represent an average between near and far wall measurements). Average FMD was 6±2.8%, with a time to peak for FMD of 18±7 s and maximal FMD was significantly related to the area under the curve (AUC) of WSR (r=0.48; p<0.04), but not to the WSR peak value (r=0.27; p=0.28).

Discussion: CFR values adjacent to the near and far arterial wall were strongly related each other at baseline stage (r=0.87; p<0.0001), while their association became weaker in post-ischemic hyperemia (r=0.48; p<0.04), in keeping with a shift of flow velocity profile from a parabolic to a skewed one. In 9 subjects the WSR post-ischemic raise was characterized by a biphasic pattern (Group A), described by two distinct slopes of WSR against time, while the remaining subjects exhibited a single slope (Group B). Compared to Group B, Group A showed significantly higher AUC for post-ischemic WSR (19968±7989 vs 12465±6454, p<0.05), a steeper early increase of WSR during reflow (first slope: 71.3±21.8 vs 49.8±24.51 s⁻¹, p<0.05), a prolonged time to peak increase (130.1±69.9 vs 35.6±6.0, p<0.05), and a trend to higher FMD values (6.3±3.3 vs 5.6±4.4%, p=0.16).

Conclusion: The XINSORB scaffold can effectively suppress the neointima hyperplasia as measured by OCT findings over time. The real-time, direct analysis of flow velocity profile and computation of shear rate pattern during flow-mediated vasodilation, limits the informative value of the technique. A biphasic pattern of early hyperemic response during post-ischemic phase supports the hypothesis of multiple local mechanisms operating in some individuals which increase the strength of shear stimulus upon the arterial wall resulting in higher vasoconstriction.
peripapillary in the long-term follow-up. At 36 months, few struts are recognizable and most of them show a dissolved black box appearance.

**Acknowledgement/Funding:** National Natural Science Foundation of China (No.81370323 and 81521001) and the Doctoral Program of High Education of China (No.20130071120065)

**P4431 | BEDSIDE**

The ratio of coronary arterial lumen volume to left ventricle mass identifies patients with nonobstructive coronary artery disease having vessel-specific ischemia measured by fractional flow reserve

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**Background/Introduction:** The mechanism for positive fractional flow reserve (FFR) values in vessels with no focal lesions ≥50% diameter stenosis is not known. We hypothesize that in humans with suspected coronary artery disease (CAD), the ratio of coronary arterial lumen volume to myocardial mass (V/M) varies among subjects and that low values of V/M are indicative of a patient phenotype predisposed to ischemia, independent of the presence of obstructive CAD.

**Purpose:** To assess whether vessels with low FFR in the absence of focal stenosis ≥50% are more prevalent in patients with low V/M.

**Methods:** In the “HeartFlow analysis of coronary blood flow using CT angiography: NeXt sTeps” (NXT) trial (NCT01757678), V/M was computed in 254 patients suspected of having CAD who underwent clinically indicated coronary CTA, QCA and FFR studies. Nitroglycerin was administered in all patients prior to CT, QCA and FFR acquisition. The total arterial lumen volume was calculated as the sum of volumes of the patient-specific anatomical model derived from CTA and a morphometric model of the smaller arteries and arterioles downstream of the image-based model generated using branching laws. The total arterial lumen volume was divided by the left ventricular mass, also calculated from the image data. Vessel-specific ischemia was defined by FFR <0.80.

**Results:** The mean value of V/M was 75.6±42.9 mm³/g and the median value was 65.3 mm³/g. Quartiles of V/M ratio were defined as Q1: <45 mm³/g; Q2: 45–65 mm³/g; Q3: 65–94 mm³/g; Q4: >94 mm³/g. A total of 384 vessels had QCA stenosis ≤50% and measured FFR. The frequency of measured FFR values <0.8 with QCA diameter stenosis ≤50% was 29%, 16%, 3% and 1% for V/M quartiles 1–4, respectively and 11% overall (figure a, b – results for QCA diameter stenosis ≤50%).

**Conclusion:** Among patients without angiographically significant epicardial stenosis (DS≤50%), there is a large variation in the ratio between total coronary vascular volume and the perfused myocardial mass (V/M ratio). Patients with a small V/M ratio are at increased risk of ischemia in the absence of obstructive CAD. V/M is a novel metric derived from coronary CT angiography that may indicate balance or imbalance between the supply capacity of the coronary arterial tree and the demand for blood from the myocardium. Whether low V/M is due to diffuse atherosclerosis or other mechanisms is currently unknown.

**Acknowledgement/Funding:** HeartFlow, Inc.

**VULNERABLE PLAQUE**

**P4432 | BEDSIDE**

Microvascular obstruction at cardiac magnetic resonance is a powerful predictor of adverse events after primary PCI for STEMI

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**Objectives:** To assess the prognostic impact of microvascular obstruction (MVO) at cardiac magnetic resonance (CMR) in patients with ST-elevation myocardial infarction (STEMI) recanalized by percutaneous coronary intervention (PCI).

**Methods:** We enrolled 86 consecutive STEMI patients within 12 hours of symptom onset who underwent primary PCI. Angiographic no reflow (nRFR) was defined as TIMI flow grade ≤3. Patients underwent standard CMR between 2 and 5 days after STEMI. MVO was defined as the hypo-enhanced core within hyper-enhanced areas (LGE) on T1 IR sequences acquired 15 mins after injection of 0.15 mmol/kg of Gadobutrol. Infarct size was calculated as LGE volume % of LV mass (LGE%). The primary study endpoint was a composite of death, non-fatal myocardial infarction, unplanned revascularization, target lesion revascularization (TLR). Secondary outcomes were the single endpoints.

**Results:** Thirty-two patients (37%) had evidence of nRFR whilst 56 (63%) had MVO at CMR. Among patients with nRFR, only one did not have MVO whilst of the 57 patients with MVO, 26 had nRFR and 31 did not.

Patients with MVO had higher hsTnT peak (2203±2285 vs 8205±6722 ng/ml; p<0.0001) and larger LGE% (20.9±11.2% vs 33.4±10.6%; p<0.001). Mean clinical follow-up was 457±275 days. The primary study endpoint occurred in 23 patients (40%) with MVO and in only 2 patients (7%) without MVO (p<0.001).

Clinically-driven TLR rate was significantly higher in patients with compared to those without MVO (0% vs 25%, p=0.007). After Cox regression analysis adjusted for cardiovascular risk factors, age and sex, MVO was the only independent predictor (p<0.0001) of the primary study endpoint, whereas LGE% was not (p=0.23).

**Conclusion:** Our data suggest that MVO at CMR is highly effective and superior to angiography for prognostic stratification of STEMI patients. The main novel finding of our study is the significantly higher incidence of TLR in patients with MVO. Moreover, MVO is a more robust independent predictor of adverse outcome than infarct size.

**P4433 | BEDSIDE**

Progression of atherosclerotic plaques adjacent to the edges of drug-eluting stent: a 3-time optical coherence tomography and intravascular ultrasound study

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**Background:** The direct evidence of impact of drug-eluting stent (DES) on the progression of adjacent coronary artery atherosclerotic plaque by serial optical coherence tomography (OCT) and intravascular ultrasound (IVUS) imaging.

**Objectives:** To systematically assess how the DES affects the progression of adjacent coronary artery atherosclerotic plaque by serial optical coherence tomography (OCT) and intravascular ultrasound (IVUS) imaging.

**Methods:** A total of 54 lipid-rich plaques with mild stenosis, proximal or distal to stent edge were identified in 44 patients who underwent OCT and IVUS follow-up.
up at 6 months and 12 months after drug eluting stent implantation. Fibrous cap thickness (FCT) was assessed by OCT. Plaque volume (PV) and percent plaque volume (PPV) were assessed by IVUS. Plaque progression was assessed by calculating the changes in FCT, PV, and PPV at follow up from the baseline. The relationship of plaque position and stents were evaluated according to the distance of the plaque to the stents.

Results: Compared with the plaque located <10mm away from the stent edge, plaques located within 5mm from the stents edge showed significant change in FCT at 6 months (94.5±98.2 μm vs 43.8±41.4 μm, p=0.03) as well as 12 months (132±102.6 μm vs 73±49.6 μm, p=0.02) after stenting. Whereas IVUS demonstrated greater regression in the plaque located >10mm away from the stents characterized by significant reduction in PV (−0.6±12.2 mm³ vs −8.2±7.5 mm³, p=0.02) and PPV (1.2±4.5% vs 2.3±1.7%, p=0.007) at 6 months. There were no significant differences observed in FCT 6 months: 83.9±98.2 μm vs 70.7±108.5 μm, p=0.58; 12 months: 117±281.3 μm vs 149±7123.1 μm, p=0.45) by OCT, and PV (6 months: −3.0±12.4 mm³ vs 2.3±1.17 mm³, p=0.29; 12 months: −7.6±18.5 mm³ vs −1.7±10.4 mm³, p=0.03) and PPV (6 months: 0.6±1.4% vs 1.9±0.5%, p=0.48; 12 months: 0.5±3.3% vs 1.6±4.8%, p=0.46) by IVUS between the plaques located within 5mm proximal and distal to the edges of stents.

Conclusions: The plaques adjacent to the stent edge showed greater progression as compared with the distant plaques, indicating the adverse effect of DES on plaque progression.

Acknowledgement/Funding: National Natural Science Foundation of China (grant contract number: 81200076)

P4434 | BEDSIDE

Relation of new morphological features of culprit coronary plaques, as determined by VH-IVUS and a new computational method, with troponin-I elevation after PCI

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Background: Mild Troponin-I elevation is often observed after stent implantation due to mechanical deformation of the atherosclerotic plaque. The presence of necrotic core within the plaque has been reported as risk factor, since mechanical compression forces during implantation may predispose to plaque rupture and distal embolization. Due to the limitations of currently available techniques, the association of plaque morphology with Troponin-I elevation after stent implantation is unclarified.

Aim: We used a new computational method for post-processing of virtual histology – intravascular ultrasound images (VH-IVUS) in order to detect plaque characteristics that might be related with Troponin-I elevation.

Methods: Eighteen consecutive patients (12 males, age: 63.8±9.1 yrs) undergoing PCI and VH-IVUS (20MHz) were examined. Second generation drug-eluting stents were deployed at 28 culprit lesions at 16 atm. Troponin-I levels were measured at baseline and 6 months after PCI. OCT -FORMIDABLE registry (grant contract number: 81200076).

Results: Characterized by a greater percentage of necrotic core within the plaque, by using a new computational method (VH-IVUS Image analysis. Additional indices of each component's distribution and heterogeneity (dispersity) within the plaque, by using a new computational method (VH-IVUS Image analysis. For each pair of images the percent and the area of calcium, necrotic core, fibrous and fibro-fatty tissue within the plaque were determined by VH analysis. Additional indices of each component's distribution and heterogeneity (dispersity) within the plaque, by using a new computational method (VH-IVUS Image analysis.

Conclusion: The OCT analysis can be a valuable tool for the prediction of plaque rupture after PCI, and it might help to identify patients with an increased risk of ACS.

P4435 | BEDSIDE

While optical coherence tomography (OCT) in acute coronary syndrome (ACS) is useful, the OCT-FORMIDABLE registry

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Background: Plaque features assessed by Optical Coherence Tomography (OCT) in Acute Coronary Syndromes (ACS) are peculiar, but the relation with clinical characteristics of patients with this disease is still unknown. Aim of this study was to evaluate the correlation between clinical features and culprit plaques characteristics.

Methods and results: The OCT-FORMIDABLE registry enrolled retrospectively all consecutive patients who performed OCT on culprit plaque in patients with ACS in 9 centres. The primary endpoint was the correlation of unstable plaques – UP (defined as at least one between plaque rupture, necrotic core with macrophage infiltration, thin cap fibro-atheroma and thrombus) at OCT with main clinical features.

The study included 285 patients of which 79.6% were male and with a mean age of 60.4±12.8 years. Hypertension was present in 57.5%, hyperlipemia in 51.9%, diabetes mellitus in 15.8% of which 14.4% were insulin-dependent (IDDM), and 61.4% of patients were smokers. 52.6% were already treated with statins, 40.7% with ACE-inhibitors or ARBs, 42.8% with beta-blockers and 50.2% with aspirin. At OCT analysis culprit plaque rupture (PR) was present in 65.3% of cases, thin cap fibro-atheroma (TCFA) in 61.1%, and 33.8% presented necrotic core with macrophage infiltrations (NCM). 12.3% of the patients experienced MACEs during the follow-up (11.7±13.7 months).

At the univariate analysis unstable plaques were significantly correlated with age (p=0.006), hypertension (p=0.001), IDDM (p=0.006) and previous statin therapy (p=0.036), the last being in accordance to the presence of lipid components in the plaque (p=0.028). The features of the plaque identified as markers of instability were also related to a higher rate of ACS during the follow-up (p=0.031).

At the multivariate analysis only IDDM was independently related to UP (HR 9.1, IC 1.2–68.9, p=0.032), while previous statin therapy was near to significance to be protective (HR 0.513, IC 0.247–1.068, p=0.074).

Multivariate analysis

<table>
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<th>Variable</th>
<th>HR</th>
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<tr>
<td>Unstable plaque – female gender</td>
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<tr>
<td>Unstable plaque – hyperlipemia</td>
<td>0.866</td>
<td>0.943</td>
</tr>
<tr>
<td>Unstable plaque – diabetes mellitus</td>
<td>0.675</td>
<td>0.831</td>
</tr>
<tr>
<td>Unstable plaque – insulin-dependent DM</td>
<td>0.032</td>
<td>9.122</td>
</tr>
<tr>
<td>Unstable plaque – previous statin therapy</td>
<td>0.074</td>
<td>0.513</td>
</tr>
</tbody>
</table>

Figure 3.1: Plaque markers of instability

A. Plaque rupture – PR; B. Thin cap fibroatheroma – TCFA; C. Necrotic core with macrophage infiltration – NCM

Conclusion: IDDM is independently related to the presence of an unstable plaque and OCT analysis in ACS. Previous statin therapy may have an impact on the prevention of these plaque features.
P4437 | BEDSIDE
Promoted plaque neovascularization in diabetic patients with peripheral arterial disease detected by contrast-enhanced intravascular ultrasound
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Background: Neovascularization in atherosclerotic plaque is associated with plaque vulnerability. Prior studies have confirmed that the density of neovascularization is more increased in vulnerable plaques compared to stable plaques. Quantification of neovascularization using intravascular imaging may be useful to find vulnerable plaque.

Purpose: The aim of this study is to image and quantify peripheral artery neovascularization using contrast-enhanced intravascular ultrasound (IVUS), and to compare the results between diabetic and non-diabetic patients.

Methods: Contrast-enhanced IVUS was performed in 14 (6 diabetic, 8 non-diabetic) patients with peripheral arterial disease who underwent endovascular treatments for stenotic lesions in the common/external iliac or superficial femoral artery. Intra-arterial perfusion with microbubble contrast agent was performed at the target lesion. IVUS images were recorded before, during, and after microbubble injection. The pixel-wise differences were calculated by subtracting the gray scales before microbubble injection from those after. Neovascularization area was defined by >40 difference in gray scale, ranging from 0 to 255.

Results: Between diabetic patients and non-diabetic patients, there was no significant difference in patient characteristics, except for the presence of diabetes. Among the two groups, the percentage of neovascularization area divided by total plaque area in diabetic patients was significantly greater than in non-diabetic patients (Figure).

Conclusions: Neovascularization was more promoted in diabetic patients compared to non-diabetic patients. Contrast-enhanced IVUS may be useful to evaluate plaque vulnerability in peripheral arterial disease.

P4438 | BEDSIDE
Clinical outcomes and insights from optical coherence tomography of paclitaxel-coated balloon inflation for the treatment of stent fracture

Background: The efficacy of paclitaxel-coated balloon (PCB) for in-stent restenosis (ISR) with stent fracture (SF) has not been clarified.

Methods: From April 2014 to March 2015, SF cases treated with PCB in our center were retrospectively enrolled for this study. SF was defined as partial or complete separation of stent struts detected with plain fluoroscopy. Angiographic follow-up with OCT was planned at least once within 1 year after the procedure.

Results: During study period, 338 ISR cases were treated with PCB in our center. Of these, 25 cases were diagnosed as SF and enrolled for this study. All of them were successfully treated with PCB without adding metal stents implantation and underwent pre- and post-procedural OCT pull-back. In 18 cases, multiple stents (<2) had already been implanted at SF site. 20 cases were diagnosed as first-time SF at this time. The types of fractured stents were as follows: bare metal stent, 12.5% (n=3); 1st generation drug-eluting stent (DES), 20.0% (n=5); 2nd generation DES, 66.0% (n=17). Pre-dilatation with scoring balloon (n=19) or noncompliant balloon (n=6) at relatively high pressure (17.8±4.9atm) were performed for all cases before PCB inflation. PCBs (diameter, 3.0±0.5mm; length, 24±6.3mm) were successfully released. Post-procedural OCT findings were as follows: minimal lumen diameter (MLD), 1.32±0.37mm; minimal lumen area (MLA), 1.71±0.97mm²; minimal stent diameter (MSD), 2.42±0.42mm; minimal stent area (MSA), 5.45±1.81mm², respectively. Post-procedural OCT showed that MLD, MLA, MSA, and MSA were 2.16±0.50mm, 4.44±1.82mm², 3.15±2.13mm, and 7.90±2.61mm², respectively. The acute gain was 2.67±1.62mm². During follow-up days (296 days, IQR: 240–403), the rate of target lesion and target vessel revision were 12.0% (n=3) and 20.0% (n=5), respectively. There was no evidence of cardiac death, MI, or peripheral arterial disease, and stent thrombosis. Furthermore, follow-up OCT showed acceptable lumen late-loss (1.06±1.35mm²).

Conclusions: PCB might be potentially effective treatment for ISR with SF without using other metal cages.

P4439 | BEDSIDE
Impact of serum EPA/AA ratio on vulnerability of in-stent neoatherosclerosis: an optical coherence tomography study
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Background: In-stent neoatherosclerosis has been suggested to be a potential mechanism of late restenosis and stent thrombosis (ST). A low ratio of EPA/AA is associated with thin-cap fibroatheroma (TCFA) in native coronary artery according to Optical Coherence Tomography (OCT) study. But the association between EPA/AA ratio and neoatherosclerosis is uncertain.

Methods: We retrospectively evaluated 100 consecutive patients with in-stent restenosis (>75% angiographic stenosis) after drug-eluting stents implantation using OCT. Patients with hemodialysis, CKD, inadequate OCT image acquisition, and who underwent pre-dilation were excluded. Finally, 63 patients were enrolled. Patients were divided into 2 groups according to median value of EPA/AA ratio: low group (n=31, EPA/AA=0.53) or high group (n=32, EPA/AA=0.53). OCT images were evaluated both qualitatively and quantitatively: frequency of TCFA like neoinitima, vasa-vasorum, intimal rupture, thrombus, and macrophage infiltration, lipid plaque length and angle, and thickness of fibrous cap. And we defined the presence of TCFA or thrombus or intimal rupture as vulnerable neoinitima.

Results: There were no statistically significant differences in patient characteristics. OCT findings, including the presence of TCFA like neoinitima (38.7 vs. 9.4%, P=0.008), vasa-vasorum (32.3 vs. 9.4%, P=0.032), and Vulnerable neoinitima (48.4 vs. 18.8%, P=0.017) were more frequently observed in the low EPA/AA group. This group also showed thinner fibrous cap and wider lipid arc than the high EPA/AA group (78.6±36.0 vs. 128.±61.0 mm, P=0.002 for were inflamed and (236±98.1 vs. 172±45.4 mm, P=0.004 for maximal lipid thickening, respectively). In multivariate analysis, low EPA/AA ratio was selected as a factor for the presence of vulnerable neointima (Oddsratio 3.79, 95% CI 1.21–11.9, p=0.022).

Conclusion: Low serum EPA/AA ratio was independently associated with the vulnerability of in-stent neoatherosclerosis.
P4440 | BEDSIDE
Mechanisms of late lumen enlargement in coronary arteries after drug-coated balloon angioplasty - serial volumetric intravascular ultrasound analysis

Background: Previously, late negative remodeling of the vessel wall was demonstrated as a main cause of restenosis after coronary plain old balloon angioplasty. Instead, a recent clinical study, using quantitative angiography, has shown drug-coated balloon (DCB) angioplasty for denovo native coronary arteries without stenting induces late lumen enlargement in 70% of study patients (Clin Cardiol 2015;104:217). However, the underlying mechanism of this finding remains unknown.

Purpose: We report the use of volumetric intravascular ultrasound (IVUS) analysis to assess serial changes after DCB angioplasty.

Methods: Serial (pre-, post-intervention and 6-month follow-up) volumetric IVUS was used to study 40 denovo native coronary lesions after DCB angioplasty without stenting. Volumetric analysis was performed for vessel, lumen and plaque (vessel minus lumen). Each volume was divided by measurement length to adjust for different lesion length (volume index [VI]), expressed as mm³/mm.

Results: Late lumen enlargement occurred significantly: lumen VI increased from 6.63±3.76 mm³/mm after intervention to 10.67±4.33 mm³/mm at follow-up (p<0.0001). From post-intervention to follow-up, plaque VI decreased significantly (from 9.15±4.92 to 8.23±4.31 mm³/mm, p<0.05) and vessel VI enlarged significantly (from 17.78±8.20 to 18.90±4.42 mm³/mm, p<0.05). At follow-up, 45% of the increase in lumen VI was due to a decrease in plaque; 55% was due to an increase in vessel VI. The ∆Lumen VI correlated strongly with the ∆Vessel VI (r=0.60, p<0.001), but not with the ∆Plaque VI. A total of 83% (33 lesions) showed an increase in vessel VI whereas 17% (7 lesions) had a minor decrease in vessel VI.

Volumetric IVUS Analysis

<table>
<thead>
<tr>
<th></th>
<th>Pre</th>
<th>Fin</th>
<th>FU</th>
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<tbody>
<tr>
<td>Vessel VI (mm³)</td>
<td>17.18±7.45</td>
<td>17.78±2.80</td>
<td>18.90±4.42</td>
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<tr>
<td>Plaque VI (mm³)</td>
<td>11.40±5.90</td>
<td>10.95±4.92</td>
<td>8.23±4.31</td>
</tr>
<tr>
<td>Lumen VI (mm³)</td>
<td>5.78±2.55</td>
<td>6.83±3.76</td>
<td>10.67±4.33</td>
</tr>
</tbody>
</table>

Acute and Late Lumen Dynamics

<table>
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<th></th>
<th>Acute (Fin - Pre)</th>
<th>Late (Fin - FU)</th>
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<tbody>
<tr>
<td>∆Vessel VI (mm³)</td>
<td>+0.60±1.23</td>
<td>-1.12±3.16</td>
</tr>
<tr>
<td>∆Plaque VI (mm³)</td>
<td>-2.25±2.01</td>
<td>-0.92±2.60</td>
</tr>
<tr>
<td>∆Lumen VI (mm³)</td>
<td>+2.85±2.23</td>
<td>+2.04±2.37</td>
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</tbody>
</table>

*p<0.05; ∆= difference

Conclusions: DCB angioplasty positively effects to reduce neointimal hyperplasia and even to enlarge vessel wall during late follow-up. The late lumen enlargement pattern appears to be determined primarily by the positive remodeling of the vessel wall.

P4441 | BEDSIDE
Effects of low-dose vs. moderate-dose pitavastatin in coronary neointimal hyperplasia at 12 months follow-up in type 2 diabetic patients: optical coherence tomography analysis
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Background: Current guidelines recommend the use of high-dose statins for diabetic patients; however, moderate-dose or low-dose statins are not infrequently used after coronary stenting in Asia.

Purpose: We compared the effects of moderate-dose versus low-dose pitavastatin in coronary neointimal volume with optical coherence tomography in diabetic patients at 12 month's follow-up.

Methods: A total of 74 diabetic patients with significant coronary artery stenosis were randomized to low-dose (1mg [n=37]) or moderate-dose pitavastatin (4mg [n=37]) after everolimus-eluting stent implantation. The primary endpoint was to compare neointimal volume at 12 months follow-up. Secondary endpoints were to compare changes in brachial artery flow-mediated dilation (baFMD) and inflammatory markers such as IL-6, TNF-alpha, high-sensitive C-reactive protein, adiponectin, sICAM-1, and sVCAM-1 between the 2 groups.

Results: Neointimal volume was significantly lower in the moderate-dose group (11.31±5.38mm³ vs. 19.02±13.34mm³, p<0.001) with significant decrease in mean neointimal thickness of covered struts (0.06±0.04mm vs. 0.11±0.08mm, p<0.001) during the follow-up. Improvement in baFMD was significantly greater in the moderate-dose group than the low-dose group at 12-month (0.53±0.18mm vs. 0.30±0.15mm, p=0.005, respectively). Decreases in the levels of inflammatory markers such as IL-6 and TNF-alpha were significantly greater in the moderate-dose group than the low-dose group during the follow-up.

Conclusions: Moderate-dose pitavastatin significantly reduced neointimal volume when compared to low-dose pitavastatin with significant improvement in baFMD during the 12-month follow-up.

P4442 | BEDSIDE
Long-term follow-up of patients with left main stent patency assessed with multislice computed tomography
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1 University Hospital of Bellvitge, Cardiology, Barcelona, Spain; 2 University Hospital of Bellvitge, Radiology, Barcelona, Spain

Background: Multislice CT (MSCT) has demonstrated in previous studies to be a reliable imaging tool to assess stent patency in patients with left main coronary artery (LMCA) stenting. However limited data are available regarding the long-term outcomes of patients with left main stent patency assessed with MSCT.

Purpose: The aim of this study was to evaluate long-term outcomes of patients with LMCA stenting assessed by MSCT, focusing in those in which stent patency was non-invasively confirmed.

Methods: We prospectively included patients with LMCA disease who underwent LMCA percutaneous coronary intervention (PCI) in our center and in whom follow-up MSCT was scheduled at 9–12 months. All patients were regularly followed in outpatient clinic. Patients with atrial fibrillation, impaired renal function (creatinine clearance <60ml/min) or complex PCI bifurcation technique (more than 1 stent) were excluded.

Results: We included 116 patients. Nine (8%) of them had impaired image quality due to heavy calcification or motion artifacts and were excluded from the follow-up. Clinical follow-up was performed in 107 patients with a medium follow-up of 36 (19–81) months. Mean age was 66±11 years, 87% male, 74% hypertensive and 26% diabetic. Medium syntax score was 19 (13–26). Stent patency was identified by MSCT in 100 patients (93.5%). At long-term follow-up, the overall incidence of MACE (cardiovascular death and target lesion revascularization) in those patients with MSCT confirmed stent patency was 4%. There were three patients with cardiovascular death and one patient with target lesion revascularization.

Conclusions: Patients with LMCA PCI with MSCT confirmed stent patency have an excellent long term prognosis, with a low rate of cardiac mortality or target lesion revascularization. Follow-up MSCT appears to be a useful clinical imaging tool in patients with LMCA disease percutaneously treated.

P4443 | BEDSIDE
Plasma endocan levels in patients with isolated coronary artery ectasia
T. Turan1, A.R. Aykaz1, A.C. Aykan1, S. Kul1, O.F. Cirakoglu1, A.O. Aslan1, I. Gu2, U. Ucar1, S. Demir1, S. Celik1, A. Abi Ewir Cardiovascular and Thoracic Surgery Hospital, Cardiology, Trabzon, Turkey; 2 Sifa University, Cardiology, Izmir, Turkey; 3 Karadeniz Technical University (KTU), Nutrition and Dietetics, Trabzon, Turkey

Background: Endocan is a soluble proteoglycan, secreted by human vascular endothelial cells. Endocan is a marker for vascular pathologies and an important modulator of angiogenesis, strongly associated with inflammation, vascular endothelial dysfunction and atherosclerosis. The relationship between coronary artery ectasia (CAE) and endocan has not been evaluated. We aimed to investigate this association.

Methods: Fifty-four patients with isolated CAE without coronary stenosis and 30 control subjects with normal coronary angiogram were included in this study. Endocan plasma concentrations were measured by using an enzyme-linked immunosorbent assay (ELISA).

Results: Patients with isolated CAE had significantly higher levels of endocan compared with the control subjects (18.9±7.3 vs 15.6±3.6 ng/mL, p<0.007). There was a significant correlation between endocan levels and severity of isolated CAE according to the Marks classification (r=0.59, p<0.001).

Figure 1
Table 1. Clinical, laboratory and angiographic characteristics of the study population

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<th>Non-ME</th>
<th>P value</th>
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<tbody>
<tr>
<td>Age (years)</td>
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<tr>
<td>Male gender, n (%)</td>
<td>36 (66.7%)</td>
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<tr>
<td>Hypertension, n (%)</td>
<td>27 (50%)</td>
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<td>Smokers, n (%)</td>
<td>21 (38.9%)</td>
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</tbody>
</table>

Conclusion: There were no changes in age, gender and body weight as well as procedure time and fluoroscopy time (6.8±6.1 min vs. 6.9±6.3 min). Interestingly, the proportion of uncovered struts, struts being both malapposed and uncovered at 12-month was found to be substantially higher in patients having MEs; 2.0% (1.0–6.0%) versus 0.0% (0.0–0.3%), p<0.001, and the proportion of struts being both malapposed and uncovered at 12-month was found to be substantially higher in patients having MEs; 10.9% (5.3–13.3%) versus 2.5% (0.0–7.4%), p<0.001. Also, the 12-month percentage of malapposed struts, and the proportion of struts being both malapposed and uncovered, and positive vascular remodeling was evaluated. OCT-detected MEs were defined as outward bulges of the vessel wall with a minimal evagination depth of 10% of the nominal stent diameter present in ≥3 consecutive analyzed frames. IVUS-detected external elastic membrane (EEM) estimates were normalized for the individual stent size by dividing the absolute volume with the length of the implanted stent.

Results: In total, 18 N-BES (23.1%) treated NSTEMI patients exhibiting OCT- detectable MEs at 12-month follow-up. There were no significant differences in neither baseline nor lesion/procedure characteristics between ME-patients (n=18, 23.1%) and non-ME-patients (n=60, 76.9%). The proportion of uncovered struts at 12-month follow-up was significantly higher in ME-patients as compared to non-ME-patients; 10.9% (3.2–14.8%) versus 2.4% (0.3–7.1%), p<0.002. Also, the 12-month percentage of malapposed struts, and the proportion of struts being both malapposed and uncovered at 12-month was found to be substantially higher in patients having ME; 2.0% (1.0–6.0%) versus 0.0% (0.0–0.0%), p<0.001, and 0.9% (0.0–3.1%) versus 0.0% (0.0–0.0%), p<0.001, respectively. Furthermore, proportional change in normalized EEM was significantly larger in ME-patients; 10.7±12.5% versus -1.0±6.6%, p<0.004.

Conclusions: MEs are relatively frequent morphological findings following N-BES-implantation in the clinical setting of a NSTEMI. MEs co-exist with other signs of impaired arterial healing, and are correlated to positive vascular remodeling.

Acknowledgement/Funding: The Danish Heart Foundation
P4447 | BEDSIDE
Prevalence and prediction of high-sensitivity troponin-I elevation after diagnostic coronary angiography
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Background: An increased level of serum cardiac troponin-I is a specific biomarker for myocardial necrosis, which has been reported to have powerful predictive value for adverse outcomes. We aimed to investigate high-sensitivity troponin-I (hs-cTnI) levels to determine myocardial necrosis following diagnostic catheterization (CAG) and to evaluate the prevalence and predictors of the changes in hs-cTnI levels after CAG.

Methods: A prospective cohort study was carried out between Jan 1 2013 and Dec 31 2015 in 560 patients, consisting of 428 males and 132 females (age; 67.9), who underwent CAG using 5F system in a tertiary hospital. Blood samples were collected before and 12–18 hours after CAG procedure to determine pre-CAG hs-cTnI and post-CAG hs-cTnI levels, respectively. Procedure-related myocardial necrosis was defined as the hs-cTnI change (ΔcTnI) calculated by post-CAG hs-cTnI minus pre-CAG hs-cTnI values. Association of clinical and procedural factors with ΔcTnI was assessed by univariate and multivariate generalized linear regression analysis.

Results: Median pre-hs-cTnI and post-hs-cTnI values were 5 ng/l (IQR: 3–11) and 19 ng/l (IQR: 8–53), respectively. Of all, 231 (41.3%) patients showed post-CAG hs-cTnI levels more than the cut point of the 99th percentile of a healthy reference population, as recommended by the manufacturer (the sex-specific cut point for female and male was 34 ng/l and 34 ng/l for male, respectively), whereas 65 (11.6%) patients had pre-CAG hs-cTnI levels more than these cut point values. No major complications were observed in catheterization laboratory during the procedures. Mean and median ΔcTnI were 54.8 ng/l and 10 ng/l, respectively. In univariate analysis, aortic stenosis, dialysis, estimated glomerular filtration rate, NT-proBNP, pre-CAG hs-cTnI, ejection fraction, left ventricular mass, aspirin use, procedure time, right heart catheterization (RHC) and brachial artery approach were significantly associated with ΔcTnI (all; P<0.05). Adverse COT or FFR examinations were not correlated with ΔcTnI. Multivariate analysis, aspirin use (coefficient; -50.016 [95% CI -94.023 to -6.008], p=0.026), RHC (coefficient; -92.526 [95% CI -169.289 to -15.764], p=0.018), brachial artery approach (coefficient; 62.329 [95% CI 6.304 to 116.154], p=0.029) and procedure time (coefficient; 6.836 [95% CI 4.692 to 9.881], p<0.001) remained independent predictors of greater ΔcTnI.

Conclusion: CAG-related myocardial necrosis was not uncommon, and was associated with aspirin use, RHC, brachial artery approach and procedural time. Further study is warranted to investigate prognostic implication of CAG-related myocardial necrosis.

P4448 | BEDSIDE
Non-culprit artery-related infarct: relationship with infarct size and clinical outcomes: the CIRCUS MRI sub-study
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Background: Non-culprit related infarcts are rare in anterior STEMI but tend to be associated with larger myocardial damage and worse functional and clinical outcomes at one-year.

Methods: A prospective single-blind study was performed between Jan 1 2013 and Dec 31 2015 in 560 patients, consisting of 428 males and 132 females (age; 67.9), who underwent CAG using 5F system in a tertiary hospital. Blood samples were collected before and 12–18 hours after CAG procedure to determine pre-CAG hs-cTnI and post-CAG hs-cTnI levels, respectively. Procedure-related myocardial necrosis was defined as the hs-cTnI change (ΔcTnI) calculated by post-CAG hs-cTnI minus pre-CAG hs-cTnI values. Association of clinical and procedural factors with ΔcTnI was assessed by univariate and multivariate generalized linear regression analysis.

Results: Median pre-hs-cTnI and post-hs-cTnI values were 5 ng/l (IQR: 3–11) and 19 ng/l (IQR: 8–53), respectively. Of all, 231 (41.3%) patients showed post-CAG hs-cTnI levels more than the cut point of the 99th percentile of a healthy reference population, as recommended by the manufacturer (the sex-specific cut point for female and male was 34 ng/l and 34 ng/l for male, respectively), whereas 65 (11.6%) patients had pre-CAG hs-cTnI levels more than these cut point values. No major complications were observed in catheterization laboratory during the procedures. Mean and median ΔcTnI were 54.8 ng/l and 10 ng/l, respectively. In univariate analysis, aortic stenosis, dialysis, estimated glomerular filtration rate, NT-proBNP, pre-CAG hs-cTnI, ejection fraction, left ventricular mass, aspirin use, procedure time, right heart catheterization (RHC) and brachial artery approach were significantly associated with ΔcTnI (all; P<0.05). Adverse COT or FFR examinations were not correlated with ΔcTnI. Multivariate analysis, aspirin use (coefficient; -50.016 [95% CI -94.023 to -6.008], p=0.026), RHC (coefficient; -92.526 [95% CI -169.289 to -15.764], p=0.018), brachial artery approach (coefficient; 62.329 [95% CI 6.304 to 116.154], p=0.029) and procedure time (coefficient; 6.836 [95% CI 4.692 to 9.881], p<0.001) remained independent predictors of greater ΔcTnI.

Conclusion: CAG-related myocardial necrosis was not uncommon, and was associated with aspirin use, RHC, brachial artery approach and procedural time. Further study is warranted to investigate prognostic implication of CAG-related myocardial necrosis.

P4449 | BEDSIDE
Impact of plaque morphology as assessed by optical coherence tomography on procedural outcomes in patients with acute coronary syndrome undergoing percutaneous coronary intervention
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Background: Plaque rupture (PR) as assessed by optical coherence tomography (OCT) is the most frequent plaque morphology responsible for acute coronary syndrome and is associated with worse prognosis at 3 years as compared to patients (pts) with intact fibrous cap (IFC). Studies focused on the impact of plaque morphology on procedural outcome of percutaneous coronary intervention (PCI) are lacking. We aimed to compare outcomes in pts with non-ST elevation myocardial infarction (NSTEMI) undergoing OCT evaluation pre- and post-PCI, according to plaque morphology (PR vs IFC).

Methods: Prospective study including consecutive NSTEMI pts undergoing PCI of the culprit lesion less than 72 hours after symptom onset. Plaque morphology was evaluated pre-PCI, and result of stenting post-PCI, both by OCT. PR was defined as the presence of fibrous cap disruption, while IFC was defined as the presence of an intact thrombus overlying an intact plaque or luminal irregularity without thrombus.

Results: We included 70 pts aged 60±11.3 years. Thirty-one (44%) pts had a PR as a culprit lesion morphology, and 39 (56%) had IFC. Clinical and angiographic findings (quantitative coronary angiography and TIMI thrombus score) were similar in both groups. OCT pre-PCI showed no significant difference between groups in the nature of the plaque (fibrous vs lipid-rich), the presence of calcified nodules, plaque neovascularisation or necrotic core, and fibrous cap thickness. There was no significant difference in the rate of thrombus presence (69% in the PR group vs 81% in the IFC group, p=0.17), but the volume of thrombus was significantly greater in the PR group (3.5±4.1 vs 1.4±7.2±4.6, p=0.022).

Consequently, there was a significantly higher rate of peri-procedural type IVa MI in the PR group (61% vs 32% in the IFC group, p=0.032). MBG was significantly higher in the PR group 1 was 40% vs 80% in group 2, P=0.032. MBG was significantly higher in the PR group (61% vs 32% in the IFC group, p=0.032).

Conclusion: Plaque morphology by OCT has an impact on procedural outcomes in NSTEMI pts undergoing PCI. In our series, PR was associated with a higher thrombus volume, leading to more peri-procedural MI, whereas IFC was associated with suboptimal results of stenting.

P4450 | BEDSIDE
Efficacy and safety of distal intracoronary drug delivery in treatment of no-reflow phenomenon
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Objectives: We investigated whether local injection of verapamil and/or adrenaline in the distal coronary bed is more effective than their intracoronary (IC) injection through the guiding catheter in the treatment of no-reflow phenomenon following percutaneous coronary intervention (PCI).

Background: The distal IC route of drug delivery allows high concentrations of the drugs to be achieved and allows longer residence time of the drugs in the coronary microcirculation.

Methods: A total of 40 patients with no-reflow following PCI were randomized into two groups. Group 1 received IC adrenaline and/or verapamil through a well-cannulated guiding catheter while group 2 received the above mentioned drugs through a selective microcatheter or Clearway® catheter. The primary end points were the achievement of TIMI III flow with at least MBG II or III. Secondary end points were the occurrence of hypotension, arrhythmias and MACES during hospital stay.

Results: After drug injection, the percentage of patients achieving TIMI III in group 1 was 40% vs 80% in group 2, P=0.032. MBG was significantly higher.
in group 2 where 15% achieved MBG II and 65% MBG III vs 10% and 25% respectively in group 1, P=0.033. Primary end point was achieved in only 35% of patients in group 1 and in 80% of patients in group 2 (odds ratio, 7.43; 95% confidence interval 1.78 to 31.04, P <0.01). Secondary end points weren't different between both groups however, there was a trend towards less mortality in group 2 (11.1% vs 5.0%, P=0.15).

Conclusions: Distal delivery of adrenaline and/or verapamil in the coronary microcirculation is a safe and effective method for the treatment of no-reflow phenomenon complicating PCI compared to their delivery through the guiding catheter.

P4451 | BENCH
Vascular biofunctionalization to support endothelial regeneration: development of crGD-generated crosslinking 2-component hydrogels for endovascular trans-catheter application
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Background: Drug-eluting stents with polymer coatings have been developed for a prolonged delivery of anti-inflammatory drugs but entail the risk of a foreign vessel body response; drug-eluting balloons avoid a permanent foreign-body stimulus by constraining the drug delivery to the time of intervention. Research on endoluminal paves strategies has aimed at providing a local therapeutic platform for temporary lesion-direction and multi-targeted therapy.


Methods: Hydrogel systems consist of six armed star shaped polymers and a backbone of statistically copolymerized ethylene or propylene oxide (ratio 4:1; sp(EO-stat-PO)). The formulation of the gelating solution is tailored to generate a stable hydrogel film; therefore, HCO2 and diacrylate are assayed for gelation speeds. Biocompatibility is assessed by testing of adhesive capacity of human endothelial cells (EC), EPC and smooth muscle cells (SMC). Seeking for induction of specific adhesion of EPC, the peptide sequence H-Gly-Pen-Gly-Ary-Gly-Asp-Ser-Pro-Cys-Ala-OH (cRGD) is immobilized in the hydrogel through Michael Addition reaction. Applicability of the hydrogel system using a specific balloon catheter that allows for delivery of fluids through inbound side holes is tested in a silicone tubing and in domestic pig post-mortem coronary arteries.

Results: cRGD was immobilized in the hydrogel at an initial molar ratio of 1 peptide per 2 sp(EO-stat-PO) molecules; with decreasing cRGD concentration, adhesion testing yielded a concentration-dependent more-to-similar EPC adhesion (cRGD concentration: 0.1M, 0.05M, 0.01M, 0.01M) resulted in full but delayed polymerization at 0.1M (-2 minutes), 0.05M (molarity: hydrogel/diacrylate 1:1.5; 1:10; 1:20) resulted in rapid and full gelation at 60 seconds (1:1 molarity). Thus, the formulation of the gelating solution was tailored for gelation at the target site. 400 µl of the 2-component hydrogel were successfully applied in simulated use in silicone tubings and pig coronary arteries and rapidly gelated at the inner wall of the tubing or the coronary artery to form a complete uniform endoluminal thin layer.

Conclusion: A novel 2-component in-situ cross-linking crGD-functionalized hydrogel system was evidenced to in-situ gelate after application through a specific balloon catheter and might serve as a future therapeutic platform for broadbased endovascular therapeutic approaches aimed at biomaneulating disease as well as post-interventional atherosclerotic lesions.

MECHANISM OF ARRHYTHMIA IN ATRIAL FIBRILLATION.
NEW DATA ON REMODELLING BIOMARKERS AND ANTI-ARRHYTHMIC DRUGS

P4452 | BENCH
Increased arrhythmia stability is associated with risk-factor specific structural remodelling in a porcine model of arterial hypertension and atrial fibrillation
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Introduction: Arterial hypertension (HT) is found in 60–80% of atrial fibrillation (AF) patients, is a predictor of new-onset AF and contributes to AF progression via unknown mechanisms. We established a large animal model of rapid atrial pacing (RAP) induced AF combined with DOCA (desoxycorticosterone acetate) induced HT to investigate how HT affects the progression of AF.

Methods: 17 landrace pigs were implanted with custom made, telemetrically controllable pacemakers to induce AF. DOCA pellets were subcutaneously implanted in a subgroup of 9 animals (HT group). The other 8 animals served as controls (RAP). Pacemakers were activated at a rate of 600/min two weeks prior to the final experiment which included echocardiography, hemodynamic measurements, atrial invasive electrophysiologic studies, high density endo- and epicardial multielectrode mapping as well as histological analysis

Results: Both groups had comparable body weight, cardiac output, pulmonary arterial pressure, left ventricular end diastolic pressure and left atrial pressure. Animals in the RAP+HT group had significant arterial hypertension (mean aortic pressure 109.9 (100-137) vs. 82.8 (79.96) mmHg, p <0.05), concentric left ventricular hypertrophy, atrial dilatation and increased left (33.5±8.4 vs. 24.9±6.5 g, p<0.05) and right (23.7±2.9 vs. 19.4±3.1 g, p<0.05) atrial weights. AF duration was significantly higher in RAP+HT animals, while left and right AERPs were unaltered. Epicardial multielectrode mapping showed increased conduction velocities on both atrial free walls. Enhanced conduction velocity during closed 3D electroatomic mapping of the whole atria in DOCA+HT animals could be confirmed for the left, but not for the right atrium.

Increased AF stability was not associated with increased AF complexity in both atria; mean AF cycle length, waves per cycle length, number of epicardial breakthroughs and mean conduction velocity during atrial fibrillation were unaltered. In animals in the RAP+HT group, histological evaluation showed bialtral cardiomyocyte hypertrophy (area LA: 243.7±41.8 vs. 174.4±30.0 mm², p<0.01; RA: 271.6 (232.3±262) vs. 186.8 (169.2±204) mm²), p<0.01 as well as increased interstitial fibrosis (LA: 14.0±2.2 vs. 8.5±1.6%, p<0.01; RA: 14.4±3.4 vs. 8.3±1.5%, p<0.01) while distribution of Connexin 43 remained unchanged.

Conclusion: In this model of secondary hypertension, higher AF stability after 15 weeks of rapid atrial pacing is mainly driven by atrial remodeling and may be associated with atrial conduction velocities.

Acknowledgement/Funding: EUTRAF
induced AF were examined in open-chest experiments in anaesthetized pig subjected to 7 days AT-P as well as sham operated control pigs. In both sets of experiments AP14145 was given as bolus injections of 5 mg/kg, 8 mg/kg, and 8 mg/kg with 30 minutes intervals. Results: The time for the development of vernakalant-resistant AF was 17±6.5±2 days in AT-P. In B/P pigs, AP14145 converted non-vernakalant-resistant AF to sinus rhythm. 4 pigs converted after the low dose, 3 pigs after the middle dose and 1 pig after the maximal dose. Reinduction attempts (3xburst pacing) failed in all pigs after conversion with AP14145. In open-chest experiments, vernakalant and AP14145 significantly prolonged atrial ERP by 68±31 ms and 107±10 ms, respectively in the AT-P and P groups and by 49±32 ms and 100±19 ms in the control pigs and significantly reduced AF-duration without affecting the ventricular ERP or blood pressure in pigs subjected to 7 days AT-P. Conclusions: AP14145 is safe and feasible, and its induction of AF was longer than that of vernakalant in the open-chest experiment.

Conclusion: SK current inhibition was effective even after some remodeling when vernakalant was no longer effective. This implies that SK inhibition may have advantages over current treatments and is therefore a promising concept for further development for treatment of AF.

Acknowledgement/Funding: Wellcome Trust.

P4454 / BENCH
Inducibility of atrial fibrillation after epicardial injection of the new pharmaceutical composition containing botulinum toxin into epicardial fat pads
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Background: Prior clinical and animal studies suggest that botulinum toxin injection into the epicardial fat pads can suppress atrial fibrillation (AF) recurrences and inducibility. However, currently known botulinum toxin compositions do not have a prolonged action, nor increase the therapeutic efﬁcacy of botulinum toxin and are not intended to treat cardiac arrhythmias.

Objective: The aim of the present study was to assess the efficacy and safety of the new pharmaceutical composition containing botulinum toxin and mucopolysaccharide injection into epicardial fat pads for prevention of AF.

Methods: Twenty-four dogs were separated into 3 groups: epicardial approach for the new pharmaceutical composition containing botulinum toxin and mucopolysaccharide (chitosan; WOC2014184746 A1) injection into 3 main epicardial fat pads, epicardial approach for placebo (normal saline) injection (control 1; n=8) and epicardial approach for pure botulinum toxin injection (control 2; n=8).

Results: 3 epicardial injections (50 unit of botulinum toxin per 1 mL at each) were administrated into 3 main left atrial autonomic nervous system projection of each animal. Injections of all forms botulinum toxin demonstrated dramatic prolongation of ERP in all PV-atrial junctions and vagal stimulation shortened ERP was less pronounced. Suppression of AF inducibility was observed at day 7 after all forms botulinum toxin group injections. The reduction of AF inducibility after pure botulinum toxin injection was: at 7 day - 57% (p<0.001 vs placebo); at 1 month - 38% (p<0.001 vs placebo); at 3 months - 23% (p=0.003 vs baseline). Composition containing botulinum toxin and mucopolysaccharide showed the lowest AF inducibility and prolonged effect: at 7 day - 86% (p<0.05 vs pure form); at 14 day - 75% (p<0.05 vs pure form); at 1 month - 71% (p<0.05 vs pure form) and 3 months - 60% (p<0.05 vs baseline). Composition containing botulinum toxin and mucopolysaccharide injection into epicardial fat pads was feasible and safe, increased and prolonged effect of complete abolishment of cardiac vagal responses and significant AF suppression.

Conclusion: Composition containing botulinum toxin and mucopolysaccharide injection into epicardial fat pads can suppress atrial fibrillation and inducibility after 7 days following injection.

P4455 / BEDSIDE
Can we predict the effect of antiarrhythmic pharmacotherapy in atrial fibrillation and metabolic syndrome patients: focus on gecalis-3
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Introduction: Metabolic syndrome (MetS) is an important risk factor of non-valvular atrial fibrillation (AF). Purpose: To evaluate the role of profibrogenic factor gecalis-3 (GAL3) in the prediction of AF and effectiveness of antiarrhythmic pharmacotherapy in patients with MetS. Methods: 576 AF patients hospitalized in cardiology department (2013–2014 years) were examined. 82,2% (n=473) were non-valvular AF patients. 180 patients with paroxysmal AF were examined. 327 patients with 3 or more components of MetS (IDF, 2005) and 259 patients with paroxysmal AF: paroxysmal (58%) and persistent (42%) were included. Control groups: 50 patients with MetS without AF and 50 healthy persons without cardiovascular diseases. Groups did not differ by age, eGFR (p>0.05). Medical history, anthropometry, echocardiography, serum GAL3 (Enzyme immunoassay) were estimated. Antiarrhythmics amiodarone (32%), beta-blockers (42%), sotalol (12%), propafenone (14%) were applied during 16.7±6.9 months. Antiarrhythmic effect of pharmacotherapy was established if no episodes of AF were registered after follow-up.

Results: GAL3 in MetS and AF patients was higher than in healthy control (720.2 [441.4;1360.2] and 320.3 [280.3;1420.3] pg/ml; p<0.001), and it was higher than in MetS without AF (440.4 [420.1;1220.3] pg/ml; p<0.001). Serum GAL3 in patients with persistent AF was higher than in patients with paroxysmal AF (1020.2 [520.2;1540.1] pg/ml vs 540.1 [410.1;1310.1] pg/ml; p<0.001). In patients with paroxysmal AF, the degree of tissue fibrosis was higher in patients with 1–2 paroxysms per year (1310.1 [920.1;4210.1] and 530.4 [410.1;720.1] pg/ml; p<0.001). Multivariate logistic regression analysis indicated that the GAL3 - independent risk factor of AF in patients with MetS (OR=1.27, 95% CI 1.02–1.56, p=0.024). GAL3 in patients with recurrent paroxysms of AF and without the effect of antiarrhythmic therapy was higher than in patients without recurrent paroxysms of AF irrespective of antiarrhythmic drug (1310.2 [750.4;2492.4] and 502.2 [410.1;720.2] pg/ml; p=0.001). The multivariate regression analysis demonstrated that high level of GAL3 is an independent predictor of non-effective antiarrhythmic pharmacotherapy of AF (OR=2.38, 95% CI 1.12–5.04, p=0.024). The risk of non-effective antiarrhythmic therapy was in 3.6 fold higher (RR=3.6; 95% CI 1.6–7.9, p=0.002) in AF and MetS patients with serum GAL3 above 770.0 pg/ml (cut-off point on ROC-curve) during follow-up period.

Conclusion: Marker of fibrosis - gecalis-3 in patients with metabolic syndrome and atrial fibrillation was higher than in metabolic syndrome patients without arrhythmias and much more higher than in healthy persons. We propose that high level of gecalis-3 predicts low effectiveness of antiarrhythmic pharmacotherapy in AF and may be an additional indicator for radiofrequency ablation.
pendent prognostic factor for atrialfibrin recurrence in patients with atrial fibrilla-
(af) treated with electrical cardioversion and antiarrhythmic drugs.

Purpose: To understand the mechanisms at the bases of this correlation, we
studied miRNAs regulating apelin expression in patients with atrial fibrillation.

Methods: We recruited 68 patients with AF: 38 present a persistent AF and un-
derwent external electrical cardioversion. Quantitative Real-time PCR was per-
formed, with LNA probes and SYBR master mix, for has-miR-30b-5p, has-miR-
30c-5p, has-miR-155-5p, has-miR-142-3p, has-miR-143-3p and has-miR-124-3p

Results: In the entire population of patients with AF we found high expres-
sions of has-miR-124-3p (0.29- fold), has-miR-130c-5p (0.15-fold), has-miR-155-
5p (0.29- fold), has-miR-142-3p (0.63-fold), has-miR-143-3p (0.13-fold) and has-
miR-124-3p (1.2-fold) as compared to controls. Statistically significant difference
for the miR-30b-5p was also found, comparing the values of relative quantifica-
tion among patients with AF recurrence after external electrical cardioversion and
patients who maintained sinus rhythm.

Conclusion: Our studies confirm the hypothesis that apelin and apelinergic sys-
tem plays a role in the pathophysiology of AF. The future determination of cut-off
values for miRNAs involved in the regulation of apelin could allow the creation of
an effective prognostic score that can be useful to determine which therapeutic
strategy to adopt in each patient according to his chances of maintaining the pace
before cardioversion external power supply.

P4458 | BENCH
Platelet hypo-responsiveness to nitric oxide in new onset atrial fibrillation has a physiological, as opposed to pathological, basis

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Introduction: New onset atrial fibrillation (AF) is a period of elevated throm-
boembolic risk with respect to chronic AF. The physiological bases of this risk are
uncertain and as yet, there are no specific therapeutic recommendations for this
population of patients. Recently, we observed that patients presenting with
new onset AF displayed impaired platelet inhibition (of aggregation) in response to
nitric oxide (NO). It has also been established that certain classes of drugs
(i.e. angiotensin-converting enzyme (ACE) inhibitors, statins) can improve NO re-
sponse in patients with cardiovascular disease.

Purpose: We therefore sought to determine whether differences in (1) risk factors
for impaired NO responses or, (2) differential rates of therapy with NO-potentiating
drugs (ACE inhibitors, statins) might account for the observed differences.

Methods: We compared new onset AF (n=27) and chronic AF (n=65) patients
regarding demographics, pharmacotherapy and platelet reactivity. Whole blood
impedance aggregometry was used to assess platelet reactivity (Figure), using
ADP to induce aggregation and the NO donor, sodium nitroprusside (SNP), to
induce inhibition. Potential interactions between pharmacotherapy and platelet
reactivity were evaluated by two-way ANOVA.

Results: No significant differences in clinical presentation (heart failure, hyperten-
sion, diabetes mellitus, gender) were observed between new onset and chronic AF,
except for age (66 [62, 76] years vs. 74 [68, 83] years, p < 0.01). Rates of phar-
macotherapy were also similar. ADP-induced aggregation did not vary according to
duration of AF, though platelet SNP response was significantly impaired (fig-
ure). Two-way ANOVA indicated no significant interactions between new onset
AF and ACE inhibitor (F1,68=1.467, p=0.229) or statin (F1,68=0.04, p=0.817)
threatories.

Conclusion: These results therefore suggest that impaired platelet NO response in
new onset AF has an intrinsic physiological basis, rather than reflecting initial
under-treatment of patients.

P4459 | BENCH
Linagliptin prevents atrial electrical remodeling by the decrease of Reactive Oxygen Species (ROS) of atrial tissue in canine model of atrial fibrillation

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Background: Dipeptidyl peptidase 4 (DPP4) inhibitor is a member of pro tease inhibitors and used clinically as antiadipic agent. They have been reported to
exhibit additional cardioprotective effects in some pathological conditions but their
effect in atrial remodeling, such as in construction of arrhythmogenic substrate of
atrial fibrillation (AF), remains unclear. In this study, the effect of linagliptin, a
DPP4 inhibitor, against the atrial electrical and structural remodeling and oxidative
stress was evaluated in the canine AF model.

Methods: Continuous rapid atrial pacing (400 bpm) was performed by im-
plantable device for 3 weeks to produce AF model 16 beagle dogs. The atrial
pacing lead was fixed against the right atrial appendage and connected to the
pacing device. Additional electrode wires were fixed against the epicardial sur-
faces of the both atria and they were used for the following electrophysiological
study. Linagliptin (9mg/day) was orally administered in 8/16 dogs and they were
defined as linagliptin group. The remaining 8/16 dogs without linagliptin were de-
efined as control group. In each dog, atrial effective refractory period (AERP), con-
duction velocity (CV), and AF inducibility was evaluated in every week during the
3 week protocol. At the end of the protocol, atrial tissues were sampled for the
histological examination using Hematoxylin and Eosin (HE) and Azan staining. To
evaluate the the production of superoxide, dihydroxyethidium (DHE) staining
was also performed.

Results: During the 3 week pacing, the gradual AERP shortening and CV de-
crease as well as the increase of AF inducibility were documented in the control
group. In the linagliptin group, the CV decrease was suppressed in comparison with
the control (p < 0.05) although the AERP shortening was not affected. The AF
inducibility was gradually increased in the control group, but it was suppressed in
the linagliptin group (p < 0.05). The control group exhibited histological changes
characterized by irregularity of myocytes and interstitial fibrosis. In contrast in the
linagliptin group, the tissue fibrosis was suppressed in comparison with the con-
trol. The DHE staining also exhibited the suppression of ROS production in the
linagliptin group, although it was enhanced in the control group.

Conclusions: Linagliptin suppressed AF inducibility and CV decrease during the
3 week atrial pacing. This effect was considered to be correlated with suppression
of tissue fibrosis and hyper-oxidative stress.
P4461 | BEDSIDE
Non-valvular atrial fibrillation recurrence after sinus rhythm restoring at 1-year follow-up: nonlinear association with rs10465885 polymorphism in connexin-40 gene and phenotypic parameters
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Purpose: To investigate the predictors of atrial fibrillation (AF) recurrence after sinus rhythm restoring (SRR) in patients (pts) with non-valvular AF at 1-year follow-up, and whether the single nucleotide polymorphism rs10465885 in connexin-40 gene (Cx40) is predictive for AF recurrence.

Methods: We enrolled 186 pts before the age of 65 years (mean age [M±SD] (55±10) years; males 123 [66.1%]) with non-valvular AF (paroxysmal – 86, persistent – 72, stable – 28 pts; first onset (FO) AF – 48 pts). Clinical, laboratory and electrocardiographic data were analyzed. SNP-Cx40 was genotyped by real-time polymerase chain reaction (T – reference, C – minor allele) in 112 pts. Genotype distribution of SNP-Cx40 was as follows: TT – 25.9% (n=29); CT – 49.1% (n=55); CC – 25.0% (n=28). SRR was performed in 112 cases (102 pts) with non-permanent AF: 30 – drug, 62 – electric cardioversion, 20 cases – radiofrequency ablation. At 1-year follow-up, AF recurrence occurred in 76 (69.1%) cases. We performed logistic regression and several machine learning algorithms to select and rank the predictors of AF recurrence.

Results: Genetic algorithm Input Selection revealed 16 parameters, associated with SRR: age, body mass index (BMI), glucose level, estimated glomerular filtration rate, red cell distribution width (RDW), total serum cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol (LDL), left atrial volume (LAV), left ventricular (LV) mass, left atrial appendage diameter, left atrial appendage volume (LAAV), presence of left atrial thrombus, presence of atrial septal defect, presence of permanent atrial fibrillation (AF). Among these, the most significant predictors of AF recurrence were clinical parameters: male sex, first onset AF, age, left atrial volume, LV mass, left atrial appendage diameter, duration, average AF event duration, FO AF, laboratory (fasting glucose level, total cholesterol, LDL, HDL, triglycerides), and rank the predictors of AF recurrence.

Conclusions: High Gal-3 serum values predict fibrillation on right atrial appendage. Moreover, NYHA scale and previous cardiac disease also were associated with the presence of fibrillation in patients undergoing surgery. This atrial fibrillation results the only independent predictor for AF postsurgical occurrence in our model.

Acknowledgement/Funding: RETIC, RD12/0042/0049; IMIB-ARRIAXA

P4462 | BENCH
Galentin 3 as marker of interstitial atrial remodeling involved in atrial fibrillation

Background: Changes in atrial function and structure are known as atrial remodeling and appears related to underlying conditions as hypertension, diabetes, ischemic heart disease as well as in atrial fibrillation (AF) development. Atrial fibrosis evaluated as tissue atrial fibrosis (TAF) and atrial fibrosis type (AF type) are considered to be important predictors of AF recurrence. Artificial Neural networks (ANN) of AF recurrence prediction were built. ANN’s analysis revealed, that area under curve (AUC) for multilayer perceptron (with 1 hidden layer), included all 16 variables (MLP16), was significantly higher than in linear ANN model (Lin16): 0.874 (95% confidence interval for AUC 0.798–0.929) vs. 0.678 (CI 0.583–0.763); p=0.037. In order to obtain the maximal reduction of predictors, we identified the sensitivity of the set of 5 variables, included in MLP model (MLPS): HF stage (ratio value [RV] 1.90), SNP-Cx40 (RV 1.69), LAD (RV 1.71), FO AF (RV 1.49) and AF type (RV 1.24). The AUC for MLPs (0.808, CI 0.723–0.876) was also higher than in Lin16 (p=0.046).

Conclusions: AF recurrence in pts with non-valvular AF after SRR at 1-year follow-up was non-linearly associated with SNP-Cx40 and certain phenotypic parameters, including HF stage, FO AF and LAD. The further search of the most important genotyping of fibrosis, and epigenetic predictors of AF recurrence at different time periods after SRR is of crucial importance.

P4463 | BEDSIDE
Galectin-3 predicts long-term procedure outcome in atrial fibrillation patients undergoing catheter ablation
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Background: Galectin-3 (Gal-3) is highly expressed in fibrotic tissues and upregulated in chronic inflammatory conditions. It is believed to play a crucial role in atrial tissue remodeling in patients with atrial fibrillation (AF).

Purpose: We evaluated if post-ablation change in Gal-3 level has any prognostic association with long-term ablation outcome.

Methods: One-hundred-forty-five patients (male 69%, non-PAF 41%) were included in this prospective study. Patients with chronic inflammatory conditions or taking anti-inflammatory drugs were excluded. Fasting blood samples were collected at baseline and 24-hours post-ablation. Patients were followed up for 15±4 months for AF recurrence by cardiology evaluation, EKG and 7-day Holter monitoring.

Results: Mean Gal-3 concentration was 4.3±1.6 ng/mL at baseline and 3.5±1.4 ng/mL at 24-hour post-ablation. At 15±4 month follow-up, 35 (32%) patients experienced recurrence. The change in Gal-3 level was observed to be -0.77±0.99 and -0.39±0.92 ng/mL in patients without and with recurrence respectively (p=0.037). After adjusting for sex, AF type, and LVEF in multivariable Cox model, elevated level of post-ablation Gal-3 was found to be an independent predictor of recurrence (hazard ratio 1.6 [95% CI 1.1 to 2.4] p=0.025).

Conclusion: Substantial reduction in post-ablation Galectin-3 level is significantly associated with recurrence of atrial fibrillation. Higher concentration of this biomarker likely indicates extensive substrate remodeling that leads to increase in the risk of arrhythmia recurrence.

P4464 | BEDSIDE
The impact of circulating microRNAs expression on the recurrence of atrial fibrillation after pulmonary vein isolation in patients with paroxysmal atrial fibrillation
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Background: Atrial fibrillation is the most common arrhythmia and has a significant genetic component. Recently, some reports showed functional role of small non-coding RNAs (microRNAs, miRs) in the pathophysiology of atrial fibrillation. Especially, it was reported that miR-21, 29a, 133a, 155 promote the structural and electrical remodeling in the left atrium (LA).

Purpose: We evaluated if post-ablation change in Gal-3 level has any prognostic association with long-term ablation outcome in patients with atrial fibrillation (AF).

Methods: Between April 2013 and January 2015, consecutive 109 patients with paroxysmal atrial fibrillation who underwent catheter ablation at Yamagata University Hospital were considered for the study. After exclude defeciveness of the data and blood sampling, we enrolled 19 patients in the present study. Total RNA extracted with NucleoSpin (Macherey-Nagel GmbH & Co, Germany) according to the manufacturer's instruction. We performed qRT-PCR to confirm the expression of circulating miRs.

Results: All patients underwent successful pulmonary vein isolation, and there were no complications or deaths at 30 days post-procedure. The mean procedure time was 186±50 minutes and radiation exposure level was 385±259 mGy. The mean patient age was 58±13 years, and the majority was male (58%). There were no patients who had a history of congestive heart failure, stroke, or recent ischemic attack. There were no recurrences after 3 months blank periods from procedure. There was no significant difference between patients with and without recurrence related to age, gender, body mass index, duration of atrial fibrillation history, LA diameter and ejection fraction estimated by transthoracic echocardiography.
Mechanism of arrhythmia in atrial fibrillation. New data on remodelling biomarkers and anti-arrhythmic drugs

P4466 | BENCH
VAMP2 was involved in the translocation of atrial SK2 channels to plasma membrane in atrial fibrillation

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Background: Small conductance Ca2+−activated potassium channel type 2 (SK2 channels) were specifically expressed in atrial tissues compared with ventricle, which may attribute to atrial arrhythmia, such as atrial fibrillation (AF). Previous researches showed that SK2 currents in patients with chronic AF were increased, while, the encoded mRNA and protein of SK2 channels were decreased. However, the underlying mechanism kept unknown. Synaptobrevin 2 (VAMP2), a key protein, plays a key role in vesicle fusion, which may contribute to the trafficking of ion channels protein.

Purpose: Here, we aim to investigate the role of VAMP2 on the translocation of SK2 channels and explore the underlying mechanism of the inconsistent change of SK2 channels protein in AF.

Method: Human atrial tissues, cultured newborn rat cardiomyocytes (NRCMs) and HEK293 cells were used in this study. The mRNA and protein levels of SK2 and VAMP2 were detected with Real-time PCR and Western blotting. The SK2 currents were recorded with patch-clamp technique. The trafficking of SK2 channel protein was investigated with confocal microscopy, flow cytometry and total internal reflection fluorescence (TIRF).

Results: The mRNA and protein levels of VAMP2 were increased in patients with chronic AF (P < 0.05 or P < 0.01, nAF=19, nSR=17). In HEK293 cells, VAMP2 increased the SK2 currents under whole-cell configuration (P < 0.01 at Vm=−120 mV, n=10). VAMP2 can co-localate with SK2 channels in cardiomyocytes and in expressing HEK293 cells. In HEK293 cells, VAMP2 increased the expression of SK2 and accelerated the trafficking of SK2 channels protein to cell membrane. VAMP2 also stabilised SK2 channels protein in cell membrane with inhibiting the internalization of SK2 channels protein.

Conclusions: VAMP2 was up-regulated in chronic AF. VAMP2 contributed to the translocation of SK2 channels protein to membrane through increasing the expression, accelerating the cell membrane trafficking of SK2 channels protein with high-stability and stabilizing the expression of SK2 channels in membrane interaction with SK2 channels, which may involved in the translocation of atrial SK2 channels in AF.

Acknowledgement/Funding: This work was supported by National Natural Science Foundation of China (No: 31300948)

P4467 | BENCH
Integral clusters of patients with non-valvular atrial fibrillation, based on rs10465885 polymorphism in connexin-40 gene and phenotype: the risk of arrhythmia recurrence after sinus rhythm restoring

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Purpose: To study the risk of atrial fibrillation (AF) recurrence after sinus rhythm restoring (SRR) in different integral clusters (IC) of patients (pts) with non-valvular AF, based on the single nucleotide polymorphism rs10465885 in connexin-40 gene (SNP-Cx40) and some phenotypic parameters.

Results: Of 186 pts before the age of 65 years mean age [±SD] (55±10) years; males [123 (66,1%)], with non-valvular AF (paroxysmal – 86, persistent – 72, stable – 28 pts; mean age of AF onset: 49±10 years) were enrolled. We analyzed clinical and echocardiographic data. Real-time polymerase chain reaction was used to genotype SNP-Cx40 (T–C; reference – T – minor allele) in 112 pts. Genotype distribution of SNP-Cx40 was as follows: TT – 25.9% (n=29); CT – 49.1% (n=55); CC – 25.0% (n=28). SRR was performed in 121 cases (104 pts) with non-permanent AF: 31 – drug (DC), 64 – electric cardioversion (EC), 26 cases – radiofrequency ablation (RA). During the follow-up period (median – 18 months) the AF recurrence was registered in 83 cases (68.6%); DC – 22 (71%), EC – 48 (75%), RA – 13 (50%). Artificial neural network genetic algorithm was performed to reveal the phenotype parameters, associated with SNP-Cx40. The risk of AF recurrence (hazard ratio [HR]) after SRR was estimated by Cox proportional hazards model.

Conclusion: Genetic Algorithm Input Selection revealed 5 parameters, associated with SNP-Cx40: clinical (age AF onset, heart failure [HF] status) and echo (left ventricular posterior wall thickness [LVM], LV mid-wall fractional shortening (MFSW) and LV myocardial mass, indexed by height2.7 [MM2/7]). According to these parameters the sample of 104 pts was stratified into 4 phenotypic clusters (PC): PC1 (n=43), PC2 (n=24), PC3 (n=18) and PC4 (n=19), PC1, comparing with combined (PC2+PC4), was characterized by higher proportion of CC genotype (39% vs. 20%; P=0.026), earlier AF onset [Me (IQR) 40 (35–51) vs. 51 (45–56) years, respectively; P=0.001], higher proportion of HF absence (51% vs. 2%; P=0.001), lower PWT (1.0 (0.9–1.1) vs. 1.2 (1.1–1.3) sm; P=0.001), better LV MFSW (15.5 (14.5–17.3) vs. 13.2 (12.2–14.7)%; P=0.001) and lower MM2/7 (40.4 (35.4–47.1) vs. 56.0 (48.6–66.0) g/2.7; P<0.001). According to genotype PC1 is similar the sample of 121 SRR cases was stratified into 4 IC: IC1 (PC1/T/T; n=32); IC2 (PC1/C/C; n=25); IC3 (PC2–4/T/T; n=50); IC4 (PC2–4/T/T; n=14; reference). The HR of AF recurrence was as follows: 2.73 (95% confidence interval [CI] 1.15–4.66; P=0.023) in IC2; 2.34 (95% CI 1.04–5.25; P=0.040) in IC3; 1.85 (95% CI 0.78–4.39; P=0.167) in IC4.

Conclusion: Among pts with non-valvular AF before the age of 65 years, there was an identified IC, characterized by the earlier AF onset, the absence of HF and less substantial LV remodeling/dysfunction, and associated with higher proportion of SNP-Cx40 CC. The risk of non-valvular AF recurrence after SRR is increased in pts with rs10465885 CC genotype, and without overt phenotypic predictors.

P4468 | BENCH
Right atrial electrophysiological properties determine cardioversion success by vernakalant in the goat

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Background: Vernakalant is an effective drug to cardiovert recent onset AF but the effect is lost in patients with longer AF durations. So far, clinical investigations only identified gender as predictor of sinus rhythm restoration. The purpose of this study is to determine the electrophysiological properties that predict cardioversion.

Methods: In one group of goats AF was induced for 3 weeks (n=8) and in a second group of goats AF was induced for 22 weeks (n=8). In an open chest experiment, the left (LA) and right RA atrium was simultaneously mapped, with
two 249-electrode grids. After baseline AF-recordings vernakalant was infused (0.13 mg/kg/min) and AF-recordings were repeated. Goats were assigned to a cardioversion group (CardV) if AF terminated or to a persistent group (Pers) in case of failure. AF cycle length (AFLC), conduction velocity (CV), fibrillation waves properties (activation of wave-time) and rotors (phase analysis) were analyzed in 60-second files.

Results: In 9 goats AF terminated during vernakalant infusion and 7 remained in persistent AF. At Baseline AFLC gradients were present in all goats with shorter AFLCs in the RA. Pers had a larger LA-RA gradient than CardV (43±10 ms and 29±15 ms, respectively (p=0.056)). In the LA at baseline no differences between the CardV and Pers groups were present for AFLC, CV, waves properties or rotors. In contrast, in the RA a shorter AFLC and more transient rotors were present in Pers combined with a trend towards more waves and breakthroughs. In both Pers and CardV the effect of vernakalant was a prolongation of the AFLC, slowing of CV and a reduction number of waves, breakthroughs and rotors. Despite these effects the RA of Pers goats remained fastest with most complex conduction patterns.

Conclusion: Right but not left atrial electrophysiological properties determine the success of cardioversion by vernakalant in goats with persistent AF.

Acknowledgement/Funding: This research was performed within the framework of C3M, the Center for Translational Molecular Medicine, Project COHIFAR (grant 01C-203-001).

P4469 | BENCH

Galectin-3 in the human atria and serum of patients with atrial fibrillation does not reflect progression of the fibrotic substrate


Purpose: We investigated the relation between atrial fibrosis and Galectin-3 concentration in patients with atrial fibrillation (AF) and may reflect atrial fibrotic remodeling. Therefore, Galectin-3 is suggested as a biomarker for AF progression.

Background: Galectin-3 (Gal-3) is a soluble lectin that is expressed in a variety of tissues and appears to be an important mediator of cardiac fibrosis, particularly in heart failure. Gal-3 levels are associated with increased risk of developing atrial fibrillation (AF) and may reflect atrial fibrotic remodeling. Therefore, Gal-3 is suggested as a biomarker for AF progression.

Methods: The left atrial appendages (LAA) and serum were collected from consecutive patients undergoing thoracic surgical pulmonary vein isolation (TPVI) for treatment of AF. In addition, serum was collected 6 months after TPVI. Gal-3 concentrations in tissue and serum were measured with ELISA and normalized for total protein concentration. Picrosirius red staining was performed for quantification of interstitial fibrosis. Spearman rank test was used to analyse correlations. Clinical parameters associated with AF recurrence were studied using a linear regression model.

Results: Ninety-eight patients (76% male, mean age 60±9 years) underwent TPVI for paroxysmal (PAF, n=44) or persistent AF (PeAF, n=54). The percentage of left atrial fibrosis was 7.5±3.3 in PAF and 8.0±4.1 (p=0.6) in PeAF, and did not correspond to local Gal-3 expression (93.7±28.2 ug/l and 92.0±28.4 ug/l respectively, p=0.8). Serum Gal-3 levels were not significantly different in PAF and PeAF (14.2±4.1 and 14.1±3.6 ug/l, p=0.97) and did not correlate with tissue Gal-3 (r=0.3, actual atrial fibrosis (p=0.2) or left atrial volume index (p=0.9). Serum Gal-3 correlated with hypertension after multivariate analysis (p=0.03). Patients with and without AF recurrence one year after procedure had similar Gal-3 levels at baseline (14.4±3.2 ug/l and 13.9±2.8 ug/l respectively, p=0.5) and serum Gal-3 did not significantly change after the procedure, independent of outcome (recurrence p=0.1 and no recurrence p=0.6).

Conclusion: Atrial fibrosis does not correspond to circulating Galectin-3 in patients with AF and neither correlates with local Galectin-3 expression in atrial tissue. Our data suggest that changes in Gal-3 in GAEC may reflect remote processes and are not mechanistically related per se to AF progression. This may limit the clinical applicability of circulating Galectin-3 as a biomarker for progression of the fibrotic substrate of AF.

Acknowledgement/Funding: Grant from Aticure Inc and is supported by a personal VIDI grant of NOW/ZonMW 016.146.310.

P4470 | BENCH

Ivabradine reduces heart rate safely without increasing atrial fibrillation inducibility, irrespective of underlying vagal activity, in dogs

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Background: Ivabradine (IVA), a pure bradycardic agent, has been shown to improve outcomes of patients with heart failure. However, an increase in atrial fibrillation (AF) risk associated with IVA treatment has been reported, which has not been thoroughly investigated. Bradycardia when coupled with shortening of atrial effective refractory period (ERP) can enhance AF inducibility as observed in the activation of vagal neural system.

Purpose: We sought to experimentally investigate the effects of IVA treatment on AF inducibility under various vagal activity.

Methods: In 10 anesthetized closed-chest dogs, electrodes were attached to bilateral cervical vagal nerves for vagal stimulation (VS, 20Hz, 5V). Action potential duration at 90% repolarization (APD90) and ERP were determined at the right atrial endocardium by programmed stimulation. AF induction was attempted by 3-second bursts (20Hz, 3V) of right atrial pacing, which was repeated 8 times to determine AF induction rate (AFIR). Heart rate (HR), APD90, ERP and AFIR were obtained under baseline, VS, injection of IVA (0.5 mg/kg) (n=6, IVA group) or saline (n=4, control group), and then IVA+VS or saline+VS. A two-way analysis of variance for repeated measures with Bonferroni’s post hoc test was used for the intra and inter-group comparisons.

Results: In IVA group, HR in VS and IVA were similarly and significantly lower than HR in baseline, while HR in IVA-VS was significantly lower than HR in VS (Figure A). There were no significant differences in trends of APD90 (Figure B), ERP (Figure C) and AFIR (Figure D) between IVA and control groups. Whether IVA or saline was injected or not, VS significantly reduced APD90 and ERP, and increased AFIR similarly in both groups. Interestingly, though bradydcardic effects were comparable between IVA and VS (Figure A), AFIR in IVA was significantly lower than AFIR in VS (Figure D).

Conclusions: Despite its intense bradydcardic effect, IVA does not increase AF inducibility under various vagal activity.

Acknowledgement/Funding: Supported by Japan Society for the Promotion of Science, and by Japan Agency for Medical Research and development.
index to body surface area (LAdim/BSA) and left atrial volume index to body surface area (LAvol/BSA) were estimated with two dimensional echocardiography. Baseline demographic and clinical characteristic were assessed as well as the duration from the first presentation of AF.

Results: The duration of AF in subjects with chronic AF was range from 1−17 years and in subjects with paroxysmal AF from 0−17 years. Subjects with chronic AF compared to subjects with paroxysmal AF were older (p<0.02), had impaired LVEF (p<0.001) increased LAdim/BSA (p<0.001), increased LAvol/BSA (p<0.001), increased LVmass/BSA (p=0.06) and impaired creatinine clearance (p<0.05). Atrial fibrillation in chronic AF had impaired FMD compared to subjects with paroxysmal AF (4.79±1.03% vs. 7.02±1.24% p<0.001). Importantly, subjects with chronic AF had impaired FMD compared to subjects with paroxysmal AF (4.79±1.03% vs. 7.02±1.24% p<0.03). Interestingly, stratified analysis revealed that only in subjects with chronic AF, the duration of AF was inversely associated with FMD (r=-0.45, p=0.006). A linear regression model revealed that duration of chronic AF was inversely associated with FMD (β=-0.058, p<0.001) and longer duration of AF [5 (2–13) vs. 1 (0–2), p<0.001].

Conclusions: Endothelial function is impaired in subjects with AF and it further deteriorates over time in subjects with chronic AF. These findings highlight the detrimental effects of AF on vascular endothelium.

P4472 | BEDSIDE
Is conduction block during sinus rhythm associated with development of post-operative atrial fibrillation?

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Purpose: Conduction block (CB) is associated with initiation and persistence of atrial fibrillation (AF). It is unknown if and in what extent CB is present in electrocardiographic (ECG) tracings during sinus rhythm (SR). Aims of the study were to quantify the amount and spatial distribution of CB measured at a high-resolution scale at the entire epicardial surface of the atria and to test the correlation between CB and development of early post-operative AF (PoAF).

Methods: High-resolution (128/192 electrodes; inter-electrode distances 2.0mm) intra-operative epicardial mapping of the right atrium (RA), Bachmann’s Bundle, pulmonary vein area and left atrium during SR was performed in 209 patients (175 male, age 66±9.6years) with coronary artery disease. The area underneath the mapping array was divided into 1cm² quadrants. Differences in activation time between neighboring electrodes were calculated in areas of ≥2-electrodes. The maximum activation time difference between two adjacent electrodes was calculated to identify conduction delay (CD, ≥7 ms) and CB (≥11 ms). Prevalence and amount of CD and CB were quantified per quadrant. PoAF was documented by electroanatomical (EA) mapping.

Results: Recordings were derived from a total of 390,379 sites, resulting in 1,868,285 electrodes per patient. Areas of CD/CB were present in all patients and at respectively 2,273 (34%) and 1,470 (22%) quadrants. Median prevalence of CB and CD was 1.3 (0.1–3.4)% and 11.3 (0.1–31.5)% cm². CD and CB mainly occurred at quadrants confined to the superior intercaval area of the RA. Sixty-three patients (30%) developed PoAF. There was no significant correlation between CB and PoAF (r=-0.075, p=0.56). For CD the correlation was also absent (r=-0.083, p=0.48).

Conclusion: Quantification of the amount and spatial distribution of CD and CB per cm² during SR demonstrated a wide intra- and inter-individual variability. The prevalences of CD/CB were very low, however a predilection site at the superior RA could be identified. CD/CB was not associated with development of PoAF. Our dataset generates a detailed reference dataset for future research on the arrhythmogenic substrate of AF.

P4473 | BEDSIDE
Cardioprotective effects of Melatonin in patients undergoing cardiac surgery

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Cardiac surgery and cardiopulmonary bypass (CPB) play a key role in the induction of oxidative stress and myocardial injury. ROS may lead to electroanatomical remodeling and increase the vulnerability to cardiac arrhythmias. A few randomized controlled trials have demonstrated a small beneficial effect pre-treating patients undergoing cardiac surgery with statins, which are known to have anti-ROS properties. Other trials have also explored compounds with similar mechanistic effects. The problem is that most antioxidants used to date, fail to reach optimal concentrations inside the cells, making them ineffective. Melatonin (N-acetyl-5-methoxytryptamine) has been shown to be a powerful scavenger of ROS and is regarded as the most potent endogenous antioxidant. In fact, melatonin (M) is more effective than other antioxidants in removing free radicals and activating the antioxidant transcription factor NRF-2, and has both lipophilic and hydrophilic properties contributing to its more consistent penetration through cellular membranes. We have previously shown that M prevents pressure overload hypertrophy and pressure in animals. This time we decided to test the hypothesis that Melatonin will prevent cardiac arrhythmias in patients undergoing cardiac surgery.

Methods: In this randomized, double blind, placebo controlled pilot study, (DREAM study) 20 patients were randomized to receive high dose M, 40 mg at night or placebo (P) starting 2 days before the surgery through post-op day 3. Left atrial appendage (LAA) was removed at the end of surgery before decanulation for ROS determination by TBARS (ELISA), and the antioxidant transcription factor NRF-2 (qPCR). The primary endpoint was incidence of post op atrial fibrillation (AF). The secondary endpoint was post op complications specified as ventricular arrhythmias (VF/VT), hypotension requiring vasopressors, coagulopathy, death, renal or liver failure, or death. Patients were followed from pre-op day until discharged from hospital.

Results: 10 patients received Melatonin and 10 placebo. There was no difference in the incidence of AF (3 in each group). Among patients receiving P, 4 had post op complications (3 with VF/VT, 2 with hypotension, one with coagulopathy), whereas none in the M group did (p=0.001). Patients receiving M were also discharged earlier from the hospital, and had better post op renal function (p<0.05). The antioxidant transcription factor NRF-2 (mRNA) was also higher in LAA from patients receiving M (P<0.005; M versus P).

Conclusion: Melatonin seems to be cardioprotective in patients undergoing cardiac surgery, let least in part through a ROS scavenging mechanism and also by an effect mediated by the antioxidant transcription factor NRF-2.

P4474 | BEDSIDE
The relationship of focal fibrosis, according to MRI, to myocardioocytes receptors cardiomyocytes and ventricular arrhythmias in patients with dilated cardiomyopathy

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Cardiac MRI late gadolinium enhancement (LGE) phenomenon is known to be associated with increased risk of ventricular arrhythmias in patients with ischemic and dilated cardiomyopathy (DCM). DCM could be a consequence of the ongoing myocardial inflammation which is associated with activation of autoimmune mechanisms. Elevated concentration of autoantibodies to cardiomyocytes structures including β1adrenoreceptor and M2-muscarinic receptor are usually observed in pts with DCM. At the same time autoantibodies to beta-1-adrenergic receptor (β1-Abbs) and M2 muscarinic receptor (M2-Abbs) are known to cause arrhythmias and be an independent predictor of sudden cardiac death. The aim of the study was to reveal the relationship between these independent ventricular arrhythmias risk factor.

Materials and methods: 64 patients (pts, mean age 42±12.9 years, 43 male) with clinical symptoms of heart failure (II−IV functional class NYHA) and instrumental signs of dilated cardiomyopathy (DCM) (left ventricular ejection fraction 33±9.4%, and diastolic diameter 6.7±0.8 cm) underwent cardiac MRI with assessment of myocardial edema (ME) early (EGE) and late gadolinium enhancement (LGE) with quantification of LGE and gray zones volume. In serum of all the pts the level of β1-Abbs and M2-Abbs was estimated by ELISA.

Results: MRI revealed various localized LGE zones in 44 (68.8%) pts. LGE-positive DCM pts were characterized by frequent ventricular premature beats (1,350 in 5 thousand per 24 hours) and episodes of sustained ventricular tachycardia (VT) (p<0.027). LGE phenomenon was associated with ME or EGE in such pts. 71.8% DCM pts were IgG β1-Abbs-positive, 37.5% DCM pts were M2-Abbs-positive. The level of IgG β1-Abbs was significantly higher in LGE-positive pts (1.35 [0.82; 2.2] vs 0.79 [0.55; 0.95]). Moreover the level of β1-Abbs correlated with total LGE volume and gray zone volume (r=0.62, p=0.66 respectively; p<0.05) and was directly associated with number of non-sustained ventricular tachycardia (VT), total amount of VPC (r=0.61, 0.55 respectively; p<0.05).

Conclusion: LGE persistence with borderline gray zone according MRI together with increased level of β1-Abbs is closely associated with ventricular arrhythmias in DCM pts. These factors may be used as additional markers in the stratification of ventricular arrhythmias in DCM pts.

P4475 | BEDSIDE
Variation in atrial excitation during sinus rhythm unmasked by high resolution epicardial mapping

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Introduction: Excitation of the atria is determined by membrane properties, tissue structure and wavefront geometry. We investigated the individual variation in excitation of the right atrium (RA), Bachman’s bundle (BB), the pulmonary vein (PV) and the left atrium (LA) with the atrial appendage (LAA) as a reference to quantify the amount and spatial distribution of CB measured at a high-resolution scale at the entire epicardial surface of the RA and LA was performed.
in 381 patients (289 male (76%), age 67±10 years) with ischemic and/or valvular heart disease (IHD/VD) undergoing cardiothoracic surgery. The atria were divided in the superior intercaval, inferior intercaval, supraventricular and interventricular region of the RA (SIC, IIC, SL, LI), BB, LAVG and PVA. SR propagation maps of the atrial surface were reviewed to analyze interindividual variations in activation patterns and the incidence and spatial distribution of EBs.

**Results:** Earliest activation occurred in the RA in all patients (SIC N=237, 92%), BB was activated by either 1 wavefront from right to left (N=167, 64%) or by multiple wavefronts (N=92, 36%). The LAVG was activated via 1) BB (N=111, 43%), 2) PVA (N=73%), or 3) BB and PVA (N=141, 54%). EBs were found in RA (N=92, 45%), LA (N=86, 42%) and BB (N=27, 13%) with a significantly higher incidence in IHD patients (N=111, 48%), compared to VD or VD and IHD patients (N=12, 15%) and N=13, 20%, respectively.

**Conclusion:** There is a wide variation in excitation of the atrial epicardial surface during SR. Interalateral conduction occurred first via BB in most patients, although interatral conduction via the interatrial septum was also observed. EBs emerged scattered throughout the atrium without any clear predilection sites and were more frequently observed in IHD patients.

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**P4476 | BEDSIDE**

**The morphological substrate of left bundle branch block**

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The morphological substrate of left bundle branch block is a question of a particular importance in the era of cardiac resynchronization therapy (CRT). The presence of fibrotic scar in interventricular septum might determine the LBBB formation and but its persistence decreases the CRT response. The meaning of focal and interstitial fibrosis in the population of LBBB patients was not defined yet. The aim of the study was to determine the role of fibrosis in LBBB development in patients with dilated cardiomyopathy as well as in pts with structurally normal heart.

**Materials and methods:** 15 pts with DCM and LBBB (group 1, mean age 47±17.1 years, 7 male, QRS duration 174±24 ms), 16 DCM pts without LBBB (group 2, mean age 35±11.3 years, 6 male, QRS duration 80±12.1 ms) and 15 pts with LBBB and structurally normal heart (group 3, mean age 38±16.5 years, 6 male, QRS duration 158±11.1 ms) were included in the study. In all of them cardiac MRI with quantification of LGE volume was performed. Serum of all pts underwent endomyocardial biopsy (EMB) with quantitative assessment of inflammatory cells infiltration, percentage of interstitial fibrosis and semiquantitative analyses of cardiomyocyte hypertrophy.

**Results:** Cardiac MRI revealed LGE lesions in 46.7% group 1 pts. The localization of LGE zones was various: only in 3 cases they were located in interventricular septum and according to EMB corresponded to local fibrosis resulted from resolved inflammation (Figure 1). The comparison of interstitial fibrosis between EMB samples of group 1 and 2 pts demonstrated no difference (28±1.12±8.2% of total EMB sample square vs. 22±7.07±7.3%, p=0.35). Group 1 pts were characterized by increased grade of cardiomyocytes' hypertrophy (2.0±0.7 vs 1.5±0.7, p=0.046) while group 2 pts were younger (35.4±11.3 vs 47.7±7.1, p=0.005) and revealed more CD3+ cells in EMB samples (6.0 [1.5; 8.5] vs 11.0 [4.0; 17.0], 1 mm², p=0.04). TGF-ß1 serum level in both DCM groups was not related to volume of fibrosis estimated by quantification of LGE zones. TGF-ß1 level was significantly more likely elevated in group 3 pts than in DCM pts (73.3% vs 13.3% in group 1 and 12.5% in group 3), its concentration in group 3 was 21545 [17928; 37489] ng/ml. Cardiac MRI revealed no LGE lesions in these pts.

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**Conclusion:** There is a wide variation in excitation of the atrial epicardial surface during SR. Interalateral conduction occurred first via BB in most patients, although interatral conduction via the interatrial septum was also observed. EBs emerged scattered throughout the atrium without any clear predilection sites and were more frequently observed in IHD patients.

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**P4477 | BEDSIDE**

**Left atrial activation changes and asymmetric anatomical remodelling in patients with atrial fibrillation: results of a prospective study using pulsed-wave tissue Doppler imaging**

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**Introduction:** Atrial fibrillation (AF) progression is associated with asymmetric left atrial (LA) dilatation. Slower or asynchronous conduction contributes to AF perpetuation, but its relation with LA remodelling is not well studied. Based on our previous results, we used pulsed-wave tissue Doppler (PW-TDI) to examine the relation between specific activation patterns and LA symmetry changes.

**Methods:** AF patients (n=75, 55% male) referred for AF ablation and 70 matched patients without AF (controls) were examined prospectively by PW-TDI in sinus rhythm. The time intervals from the onset of P-wave to A at 4 mitral annulus sites (septal, lateral, anterior, posterior) were measured. Patients were grouped to an upward (U: activation is earlier posterior and delayed anterior) and a Non-U pattern (reverse or similar activation times). CT-data were used for reconstruction of the LA volume (LAV) in AF patients. A cutting plane, between the pulmonary veins and the appendage and parallel to the posterior wall, divided LAV into anterior (LAA) and posterior-LA parts. The ratio LAA/LAV was defined as asymmetry index (ASI).

**Results:** The upward LA activation was more common in AF patients than in normal controls (88% vs 21%, p<0.001). AF patients with upward LA activation (n=55) showed a significantly higher ASI (65±6 vs 61±3%, p=0.014), age (61±11 vs 51±11 years, p=0.014) and a tendency for a higher E/A ratio (1.3±0.4 vs. 1.0±0.3, p=0.08), without further differences in other LA or clinical characteristics. Multivariate logistic regression revealed that an advanced age (OR 1.1 per year, CI 1.007–1.199, p=0.034) and a higher E/A ratio (OR 1.41, CI 1.013–1.961, p=0.049) were independent predictors of an upward LA activation.

**Conclusion:** A delayed activation at anterior mitral annulus in PW-TDI (U-pattern) is frequently seen in AF patients and is associated with increased LA asymmetry (mostly anterior dilatation). Advanced age and higher E/A ratio (i.e. diastolic dysfunction) are associated with this pathologic LA activation. A U-pattern may be useful to detect patients prone to AF or facilitate early interventions prior to further anatomical remodelling.

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**P4478 | BEDSIDE**

**Conventional versus 3D-echocardiography to predict arrhythmia recurrence after atrial fibrillation ablation**

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**Introduction:** Arrhythmia recurrence after ablation (AF) ablation is high and requires repeat interventions in a substantial number of patients. In this context, we assessed the value of conventional and 3D-echocardiographic parameters to predict AF recurrence.

**Method:** Consecutive patients undergoing AF ablation were included at a tertiary cardiology center. An echocardiogram was obtained prior to the ablation procedure and analyzed offline in a standardized manner, including 3D volumetry and LA sphericity determination. The primary endpoint, AF recurrence (~30sec) between 3 and 12 months after AF ablation, was independently adjudicated.

**Results:** We included 276 patients (74% male, mean age 60±10 years). Paroxys-
The association between gamma-glutamyl transpeptidase level and the risk of atrial fibrillation: a nationwide population-based study

**Abstract**

A total of 9,046 patients (mean 72.1±12.1 years; 49.4% male) were screened, including 973 (10.8%) who underwent repeated screening. Newly identified AF was found in 7.8% of screened individuals, including 2.9% of those with a history of stroke and 10% were taking oral anticoagulants (OAC) for indications other than AF.

**Methods**

Consecutive LAAO procedures from 38 German centers were prospectively included in the LAARGE registry between 07/14 and 12/15. Indications, procedural features, antithrombotic therapies were collected and analysed. We compared the results between elderly and younger patients.

**Results**

A total of 636 patients were enrolled into LAARGE, 400 (63%) were > 75 years and 236 (37%) < 75 years. Results are shown in the table.

**Conclusions**

Interventional left atrial appendage occlusion (LAAO) is considered an alternative to oral anticoagulation therapy (OAC) for stroke prevention in patients without non-valvular atrial fibrillation. Little is known about differences in indications, procedural success rates and safety of LAAO between elderly and younger patients in clinical practice.
Conclusion: In clinical practice about 2/3 of LAAO procedures are performed in the elderly (≥75 yrs). Overall success rate is high and complications rates are low, without any differences between elderly and younger patients. Follow-up results will determine the efficacy of LAAO for stroke prevention.

Acknowledgement/Funding: Stiftung Institut für Herzinfarktforschung

P4482 | BEDSIDE
Left atrial appendage closure using a novel occluder system with an active fixation mechanism

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Introduction: In patients (pts) with non-valvular atrial fibrillation sharing increased thromboembolic and bleeding risk left atrial appendage (LAA) closure is an established treatment option. The used device is provided with an active system of interlocking anchors engaging the surrounding tissue after deployment inside the landing zone.

Purpose: We aimed to investigate efficacy, procedural safety and short term outcome of this novel LAA occlusion device.

Methods: In all pts a transesophageal echo (TEE) was performed during the procedure to rule out LA thrombus, measure LAA extensions (landing zone, depth) and guide single transseptal puncture. LAA anatomy was visualized using angiograms in RAO 30/20 caudal and RAO 30/15 cranial. Device size (22 mm, 27 mm, 32 mm) was selected according to the manufacturer’s recommendation. The device implantation consisted of two sequential steps. Step 1: device positioning, step 2: device fixation. Before release, correct device position was evaluated combining TEE, angiograms and tug testing. All pts were scheduled for follow up TEE 6 weeks after device implantation.

Results: A total of 35 pts (75±10 years, 20 males, CHA2DS2-VASC: 4±2, HAS-BLED: 3±1, BMI 28±5) between October 2013 and November 2015 were included. Acute implantation success was obtained in 34/35 (97%) pts. Mean procedure and fluoroscopy times were 54±18 min and 5±4 min, respectively. Acute procedural complication was observed in 1/35 (3%, dislodgment n=1) pts. No stroke/TIA or acute cardiac tamponade were observed. However, after implantation delayed pericardial effusion required drainage in 3 pts. All pts were prescribed dual platelet inhibition (ASA 100 mg + clopidogrel 75 mg) for 6 weeks. In 29/35 (83%) pts follow up TEE excluded device related thrombus (0/27/0%, respectively), whereas residual peri-device flow (<5 mm) was observed in 5/27 (19%) pts. During short term follow up (30 days) one patient died and no stroke occurred.

Conclusion: LAA closure using a sequential active anchoring mechanism appears to be feasible. However, long term outcome and safety need to be assessed in a larger patient cohort.

P4483 | BEDSIDE
Comparison of Amplatzer and Watchman device for percutaneous left atrial appendage closure: a meta-analysis

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Introduction: Atrial fibrillation (AF) is responsible for 15% of all strokes, mainly ischemic stroke, and one study found another ischemic stroke at 3 months, all in the Amplatzer group. No additional stroke was detected in 7 studies with at least 12 (range: 12-24) months follow up.

Results: A total of 35 pts (75±10 years, 20 males, CHA2DS2-VASC: 4±2, HAS-BLED: 3±1, BMI 28±5) between October 2013 and November 2015 were included. Acute implantation success was obtained in 34/35 (97%) pts. Mean procedure and fluoroscopy times were 54±18 min and 5±4 min, respectively. Acute procedural complication was observed in 1/35 (3%, dislodgment n=1) pts. No stroke/TIA or acute cardiac tamponade were observed. However, after implantation delayed pericardial effusion required drainage in 3 pts. All pts were prescribed dual platelet inhibition (ASA 100 mg + clopidogrel 75 mg) for 6 weeks. In 29/35 (83%) pts follow up TEE excluded device related thrombus (0/27/0%, respectively), whereas residual peri-device flow (<5 mm) was observed in 5/27 (19%) pts. During short term follow up (30 days) one patient died and no stroke occurred.

Conclusion: LAA closure using a sequential active anchoring mechanism appears to be feasible. However, long term outcome and safety need to be assessed in a larger patient cohort.

P4484 | BEDSIDE
Impact of left atrial low-voltage area on thromboembolic risk in patients with atrial fibrillation

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Background: Atrial fibrillation (AF) is associated with an increased risk of thromboembolism. The CHA2DS2-VASc score, including clinical parameters and comorbidities, is recommended for thromboembolic risk stratification in AF patients.

Purpose: The purpose of this study was to test the hypothesis if left atrial low voltage area (LVA) is associated with silent cerebral ischemia (SCI) detected by magnetic resonance imaging (MRI) and the previous history of stroke in patients with AF.

Methods: Two-hundred patients (8±10.5 years, 75 women (37.5%)) with symptomatic paroxysmal (n=88, 44%) or persistent AF undergoing AF ablation were prospectively enrolled. Left atria LVA (a voltage cutoff <0.5mV) was estimated by intra-procedural bipolar voltage mapping (>300 points per patient) during sinus rhythm and expressed in a ratio of LVA to total atrial surface area (%). Cerebral delayed enhancement MRI was performed 1 to 2 days after the index procedure to rule out pre-existing SCI. SCI were defined as focal, sharply demarcated, regularly or irregularly shaped areas that are hyperintense on T2-weighted fluid-attenuated inversion recovery (FLAIR) images or isointense on T1-weighted images.

Results: Overall 2017 patients (8.5%) had previous history of stroke. Pre-existing SCI were detected in 135 patients (67.5%). The mean CHA2DS2-VASc score was 2±3.1. Patients with previous stroke (4±0.1±5 vs. 1±1±3, p<0.0001) had a significantly higher CHA2DS2-VASc score. Left atrial LVA was significantly larger in patients with previous stroke (12.5±8.5% vs. 33.4±5.4%, p<0.0001) as well as SCI (5.8±6.9% vs. 0±8.1±1%, p<0.0001).

Conclusions: Left atrial remodeling, estimated by left atrial LVA, shows significant association with cerebral thromboembolism in patients with AF. Thus, atrial substrate may be utilized as an index for thromboembolic risk evaluation and to guide individual anticoagulation therapy.

P4485 | BEDSIDE
MDCT is comparable to TEE in the exclusion of LA/LAA thrombus: a retrospective analysis of 764 patients with atrial fibrillation/flutter

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Background: Multi-detector computed tomography (MDCT) is commonly performed prior to atrial catheter ablation (CA) or left atrial appendage occlusion (LAAO) to visualize the anatomy of left atrial (LA)/left atrial appendage (LAA), as well as transesophageal echocardiography (TEE) to exclude or evaluate LA/LAA thrombus. The final conclusion on whether MDCT alone is sufficient to correctly
The safety, durability and efficacy of concomitant device-enabled LAA occlusion during elective open heart surgery in regard to stroke reduction.

Methods: A total of 291 AtriClip devices were deployed epicardially on 291 consecutive patients comprising of forty patients from a first-in-man device trial and 251 patients from a consecutive institutional registry. The primary efficacy end-point for stroke reduction was defined as the occurrence of ischemic or hemorrhagic neurological events during FU (Stroke). The primary safety endpoint was any device related event (periprocedurally, in-hospital, FU). Secondary endpoints included overall mortality and durability as assessed by CT. A composite end-point including death for cardiovascular cause or of unknown cause, systemic embolism and hemorrhagic or ischemic stroke was created. To assess the efficacy after epicardial LAA occlusion, time intervals for each patient on or off anticoagulation or antiplatelet therapy were determined. Individual risks for stroke (computed/calculated stroke risk) according to the obtained time interval and the CHA2DS2-VASc-Score were calculated.

Results: The AtriClip device was successfully implanted in all patients and overall mean follow-up (FU) was 36.1±23.1 months (median FU 31 months; range: 0.7–97.1 months). Early and late mortality was 5.5% and was 17.9% with none for device related issues and no device-related complications were detected throughout the entire study indicating a favorable safety profile. Long-term computed-tomography in selected patients (5.1–8.1 years post implant) displayed complete LAA occlusion without any signs of residual reperfusion or substantial LAA-stump secondary displacement. No LAA thrombus was detected. Interestingly, in 177 patients with AF in whom oral anticoagulation is deemed unsuit-

Conclusion: Although the specificity and positive predictive value of MDCT were relatively low, its excellent performance in sensitivity and negative predictive value made it a satisfactory alternative to TEE in the exclusion of LA/LAA thrombus.

P4487 | BEDSIDE

Epicardial left atrial appendage occlusion provides first evidence on stroke reduction in patients with atrial fibrillation undergoing cardiac surgery

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Background: Epicardial left atrial appendage occlusion (LAAO) is increasingly performed during elective open heart surgery in regard to stroke reduction.

Methods: Patients who underwent both MDCT and TEE prior to CA/LAAO at a University Hospital between May 2010 and September 2015 were included. Demographic data were obtained and CHA2DS2-VASc score was calculated accordingly. Two cardiologists blinded to clinical data made the imaging diagnosis independently. Two scoring systems were made to quantitatively analyze the imaging results of MDCT and TEE.

Results: A total of 764 patients (mean age 55±11 years; male 72.3%) were included. Eight patients with thrombus (1.05%, 75% male) were detected by TEE, all being also confirmed by MDCT. Twenty patients had spontaneous echo contrast (SEC, 2.62%, 70% male), of whom 4 patients were shown with thrombus at the same time. With TEE as the reference standard, the sensitivity, specificity, the positive predictive value and negative predictive value of MDCT in the detection of thrombosis were 100%, 95.77%, 20%, and 100% respectively.

Conclusion: The high specificity and high negative predictive value of MDCT makes it a valuable imaging modality for the complete exclusion of LA thrombus. These results are in agreement with previous data with its intuitive simplicity and lower cost of implementation.

P4488 | BEDSIDE

Long-term follow-up of thorascopic pulmonary vein isolation in patients with advanced paroxysmal and persistent atrial fibrillation


Background: Electrophysiological guided, thorascoscopic pulmonary vein isolation (TPVI) is employed to treat patients with advanced symptomatic atrial fibrillation (AF), refractory to anti-arrhythmic drugs (AAD) and usually with severely enlarged left atria or long AF duration. Data on long term outcome of TPVI is lacking.

Purpose: We aimed to investigate the single procedure efficacy of TPVI at five year follow-up in patients with paroxysmal or persistent AF.

Methods: Patients were followed up prospectively for two years in our outpatient clinic with ECG and 24-hour Holter every three months. Subsequently, we invited all patients for a follow-up visit after five years. Additionally, medical charts, ECGs and Holters from referring hospitals, obtained during the entire follow-up, were reviewed and used for analysis. Clinical parameters associated with AF recurrence were studied using a multivariable Cox regression model to calculate hazard ratios (HR) with corresponding 95% confidence intervals (CI).

Results: Sixty-six consecutive patients (49 men, mean age 57±8 years, mean left atrial volume index 36±12 m³/m² underwent TPVI for paroxysmal (n=33) or persistent AF (n=33) between 2008 and 2010. Twenty-nine patients (44%) had a previous catheter ablation. Fifty-eight patients (88%) were followed up after a median of 66 (58–83) months. At 5 years, 48 patients (83%) had sinus rhythm on ECG and 20 (34%) used AAD. Of all patients (n=66), 22 (67%) with paroxysmal and 11 (33%) with persistent AF were free of any AF (Figure). Freedom of AF recurrence after 1, 2, 3, 4 and 5 years was 73%, 61%, 52%, 52% and 49% respectively. Seventy-six percent of first recurrences occurred within the first 2 years.

Figure 1. Kaplan-Meier

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years. Type of AF (HR 2.28, 95% CI 1.09–4.74) and a history of catheter ablation (HR 1.44, 95% CI 1.02–2.05) were independent predictors of AF recurrence. **Conclusion:** Thoracicoperative pulmonary vein isolation is successful for the treat-
ment of advanced AF at long term follow-up. At five years, 83% of patients was in
sinus rhythm and 66% off antithrombotic drugs after a single procedure.

**Acknowledgement/Funding:** Grant from AtriCure Inc and is supported by a per-
sonal VDI grant of NOW/ZonMW 016.146.310

**P4489 | BEDSIDE**

Feasibility and effectiveness of combined AF ablation and left atrial
appendage closure for stroke prevention: data from a large
prospective multicentre registry

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**Background:** Catheter ablation (CA) is an effective treatment in symptomatic, drug-refractory atrial fibrillation (AF). Long-term freedom from AF and conse-
quently the potential for stroke reduction remains unpredictable. Continuation of oral anticoagulation (OAC) is therefore recommended in patients with high risk of cerebrovascular accidents. Percutaneous Left Atrial Appendage occlusion (LAOO) has emerged as an effective and relatively safe mechanical alternative for stroke prevention in AF patients.

**Purpose:** To evaluate the long-term clinical results of combined CA and LAAO in one single procedure in patients with AF in a large-scaled, multicentre, "real-world" cohort.

**Methods:** Five centres with a high level of experience in both catheter ablation as well as device implantation participated in this study. The prospective databases of these centres of patients with non-valvular AF that underwent combined CA and LAAO procedure were pooled. Catheter ablation could be performed with any available ablation technique according to local standards. LAAO was performed with the Watchman device. Trans-esophageal echocardiography (TEE) was used both during and 6 weeks after the procedure to evaluate device position and LAA sealing.

**Results:** From February 2009 to November 2015, 350 patients with AF (203 (58%) male, age 63.1±8.2 years: CHADS2 2.0 (1.0–3.0), CHA2DS2-VASC 3.0 (2.0–4.0), HASBLED 3.0 (2.0–3.0), 56% paroxysmal AF) were included. Indica-
tions for LAAO included previous stroke (35%), history of bleeding (26%), poor anticoagulation control (8%) and physician/patient preference (27%). After PVI, complete LAA occlusion was achieved in 100% of patients, with a median number of 1 (1.0–1.0) device used. Total procedure time was 153 minutes with 26 min-
utes fluoroscopy time. Per-procedural complications up to 30 days included mi-
nor groin hematoma (4.4%) and pericardial effusion (1.5%) and one minor stroke (0.3%), but no death. After 6 weeks, successful sealing of the LAA was shown
in 99% of patients. After a median follow-up of 28 (18–37) months, 46% of pa-
tients were in sinus rhythm and 66% off antithrombotic drugs after a single procedure.

**Conclusion:** Although PVI crosses esophageal contact area, LAAO isolation is important for the better clinical outcome in catheter ablation with linear ablation strategy for the patients with PeAF.

**P4490 | BEDSIDE**

Durability of left atrial linear ablation and clinical outcome after catheter ablation for persistent atrial fibrillation

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**Background:** It is not clear whether bidirectional block (BBB) of linear ablations
reduces AF recurrence after RFCA. We hypothesized that BBB of LAAO has peripheral predictive value for AF recurrence after RFCA.

**Methods:** Among 1793 consecutive patients in Yonsei AF ablation Cohort, we included 398 patients with PeAF (75.6% male, 59.6±10.3years old) who under-
went catheter ablation therapy protocol of Dallas lesion set: CPVI, cavoatrial isthmus ablation (CTI), roof line (RL), posterior inferior line (PIL), and anterior line (AL).

**Results:** BBB rates of de novo ablation lines were 100% in CPVI, 100% in CTI, 84.7% in RL, 44.7% in PIL, and 63.6% in AL during the study period (2006–2013). Among 75 patients who underwent repeat procedures (23.0±16.1 months after de novo procedure), maintenance rate of LAPW isolation was 75% (18/24), and BBB maintenance rates for CTI, RL, and AL were 94.2% (49/52), 75% (33/44), and 72.4% (21/29), respectively.

**Conclusions:** Over time the risk of recurrent atrial fibrillation has decreased fol-
lowing first-time ablation. Simultaneous there has been a decrease in atrial fibril-
lation duration, prior use of antithrombotic drugs and use of DC cardioversion

**P4491 | BEDSIDE**

Temporal changes in recurrence rates of atrial fibrillation after ablation

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**Background:** Ablation is an accepted strategy in rhythm control management of
patients with atrial fibrillation. Ablation techniques have improved over time, which could lead to better outcomes following ablation.

**Purpose:** The risk of recurrent atrial fibrillation following ablation was compared between two 2-year periods.

**Methods:** Through Danish nationwide registers, all patients with first-time atrial fibrillation ablation, between 2006 and 2013 were identified. Recurrent atrial fibril-
lation after ablation was identified after a 60 days blanking period with one year follow-up. Recurrent atrial fibrillation was defined as a composite of admission with atrial fibrillation, cardioversion, second ablation, or claimed prescription of an antithrombotic drug.

**Results:** A total of 4,123 patient’s undergoing first-time ablation were included. During 2 years of follow-up, recurrent atrial fibrillation was defined as a composite of admission with atrial fibrillation, cardioversion, second ablation, or claimed prescription of an antithrombotic drug.

**Results:** Among 75 patients who underwent repeat procedures (23.0±16.1 months after de novo procedure), maintenance rate of LAPW isolation was 75% (18/24), and BBB maintenance rates for CTI, RL, and AL were 94.2% (49/52), 75% (33/44), and 72.4% (21/29), respectively.

**Conclusions:** Over time the risk of recurrent atrial fibrillation has decreased fol-
lowing first-time ablation. Simultaneous there has been a decrease in atrial fibril-
lation duration, prior use of antithrombotic drugs and use of DC cardioversion

**Figure 1**
**P4494 | BEDSIDE**

**Incidence and predictors of serious pericardial effusion during and immediately after catheter ablation for atrial fibrillation**


**Purpose:** To investigate clinical factors associated with serious pericardial effusion (PE) during and immediately after atrial fibrillation (AF) catheter ablation using a multivariate logistic model.

**Methods:** A total of 330 consecutive patients with AF (age 63.2±10.2 years, 252 male, 206 paroxysmal AF) who underwent PVI were enrolled. ETAF was defined as patients who underwent invasive treatment (69/328, 2.1%, p<.005). Univariate analysis showed that PE occurred more frequently when a CARTO mapping system was not used (2.0%) than when used (0.7%, p<.001). Univariate analysis revealed that PE that needed invasive treatment occurred more frequently when a CARTO mapping system was not used (2.0%) than when used (0.7%, p<.001). We also used multivariate logistic model to identify factors associated with ETAF. The Cox proportional hazards model was used to identify factors associated with ETAF. We also used multivariate Cox proportional hazard model and Kaplan-Meier curve to determine whether ETAF was associated with late recurrence of AF in patients with AF who underwent pulmonary vein isolation (PVI).

**Results:** Early observation of transient atrial fibrillation after pulmonary vein isolation is associated with increased late recurrence of atrial fibrillation during the long-term period

H. Koke, T. Fujino, R. Nakaniishi, M. Shinohara, I. Watanabe, H. Yuzawa, T. Suzuki, S. Fukunaga, K. Kobayashi, T. Ikeda. Toho University, Department of Cardiovascular Medicine, Tokyo, Japan

**Purpose:** To investigate clinical factors associated with ETAF and assess whether ETAF predicts late recurrence of AF in patients with AF who underwent pulmonary vein isolation (PVI).

**Methods:** A total of 330 consecutive patients with AF (age 63.2±10.2 years, 252 male, 206 paroxysmal AF) who underwent PVI were enrolled. ETAF was defined as patients who underwent invasive treatment (69/328, 2.1%, p<.005). Univariate analysis showed that PE occurred more frequently when a CARTO mapping system was not used (2.0%) than when used (0.7%, p<.001). We also used multivariate logistic model to identify factors associated with ETAF. The Cox proportional hazards model was used to identify factors associated with ETAF. We also used multivariate Cox proportional hazard model and Kaplan-Meier curve to determine whether ETAF was associated with late recurrence of AF in patients with AF who underwent pulmonary vein isolation (PVI).

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non-paroxysmal AF revealed that ETAF (HR, 3.99; 95% CI 2.56–6.21; p = 0.001) and AF originating from the non-PV foci (HR, 2.12; 95% CI 1.37–3.26; p < 0.001) were significant factors associated with late recurrence of AF beyond the blanking period. Kaplan-Meier showed ETAF was associated with increase in risk of late recurrence of AF (Figure).

Conclusion: AF originating from the non-PV foci and age are associated with the incidence of ETAF in patients who underwent PVI for AF. Besides, ETAF predicts their long-term recurrence.

P4496 | BEDSIDE
Is the “blanking period” truly blank? early recurrence of arrhythmia during the blanking period highly associated with recurrence on long-term follow up

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Introduction: Pulmonary vein isolation (PVI) is effective for management of atrial fibrillation. The current guidelines allows for a 3 months blanking period following ablation during which recurrent atrial arrhythmias are not considered as failure.

Purpose: Our aim is to evaluate the prognostic value of early recurrent atrial arrhythmia during each of the 3 months of the blanking period.

Methods: We reviewed data of 325 patients who underwent PVI between Jan 2011 and July 2012. The procedure included isolation of all pulmonary veins and left atrial substrate as needed. The incidence of recurrent arrhythmia, defined as any documented atrial arrhythmia lasting more than 30 seconds, during each of the 1st month, 2nd month, and 3rd month following PVI was analyzed as a predictor of long-term success after the 3 months blanking period.

Results: Our study included 325 patients: mean age 61.5±10.7, 79 (24%) females, mean BMI 30.6±2.4, median AF duration of 4 years (Q1-Q3: 2.9), 148 (46%) persistent AF, CHA2DS2VASc score ≥ 1 (Q1-Q3: 1.3), mean EF of 54.4±9.3, mean left atrium diameter of 4.3±0.7 cm.

On long-term follow of 605 days (Q1-Q3: 213, 1188), 166 (51%) patients had recurrent atrial arrhythmia (45% in patients with paroxysmal AF and 59% in those with persistent AF). The majority of patients who had recurrence during the blanking period, also had recurrent atrial arrhythmia on long-term follow up. 108 (76%) of the 143 patients who had recurrence in first month, 72 (81%) of the 89 patients in the second month, and 63 (97%) patients of the 65 who had recurrence in the third month of the blanking period developed late recurrence. In total 123 (74%) of the 166 who had any recurrence during the blanking period had recurrence on long-term follow-up.

Conclusion: Recurrent arrhythmia during the 3 months blanking period following PVI is highly associated with late recurrent atrial arrhythmia on long-term follow up. The later the recurrence during the blanking period, especially during the 3rd month, the higher the likelihood of long-term recurrence.

P4497 | BEDSIDE
Quickly and efficiently mapping by novel online phase mapping system complemented by in silico prediction of excitation is very useful for confirming the effectiveness of non-PAF ablation (ExTRa Mapping Project)

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Background: Modulation of atrial fibrillation (AF) driver (or perpetuator) has been proposed as one of the potentially effective ablation strategies for non-paroxysmal AF (non-PAF). However, existing clinically-available phase mapping systems employed in such driver-targeted ablation usually require enormous offline analyses and take more than hours to visualize the complex wave dynamics. Moreover, some of recent studies concerned about the accuracy of the existing phase mapping systems because of their low mapping resolution (1–3 signals/cm²).

Purposes: To develop a clinically-available higher-resolution phase mapping system with online fully-automatic visualization, and to confirm the usefulness of the remapping of complex wave dynamics just before and just after the non-PAF ablation.

Methods: We developed an online real-time phase mapping system called “Ex-TRa Mapping” to quickly visualize the complex wave dynamics during non-PAF. Higher resolution (~8 signals/cm²) phase map movies (2.5 cm in diameter) were automatically created within 5 sec (ultra-rapidly) by spatiotemporal interpolation based on 41 intra-atrial bipolar signals recorded by a 20-pole spiral-shaped ring catheter (Figure, left) and by in silico (computer simulation) rapid prediction of spatiotemporal atrial excitations (Figure, bottom). The accuracy of the phase mapping system was satisfactorily confirmed by using in silico non-PAF model.

Then we applied the novel phase mapping system to 15 non-PAF patients scheduled to undergo ablation in our hospital.

Results: (1) Employing the novel mapping system just before the non-PAF ablation, we found no region of stationary rotors but regions of multiple wavelets (25±11%) (Figure, top right panel), meandering rotors (12±8%), and passive activation (63±27%). (2) After ablation targeting the non-passive activation region where multiple wavelets and/or meandering rotors were frequently observed, the post-ablation remapping by the novel mapping system clearly showed that the wave dynamics in most cases changed into passive activation and/or more organized non-passive activation (Figure, top right). Furthermore, the ratio of the non-passive activation period to the total recording period (non-passive ratio) within the ablated region was significantly decreased from 65±12% to 36±20% (p<0.01). (3) The remapped data also visually showed that the additional ablation to the region where the non-passive ratio was not decreased by the prior ablation was effective for the organization of non-PAF wave dynamics. (4) The decrease in the non-passive ratio by ablation usually resulted in spontaneous non-PAF termination or loss of AF inducibility after electrical cardioversion.

Conclusion: Complex non-PAF activations were quickly visualized by our online mapping system. The quickly remapping by our online mapping system for confirming acute effectiveness of the ablation could open a new avenue for non-PAF ablation.

P4498 | BEDSIDE
What is the makers of Holter-ECG which predict the outcome of catheter ablation for atrial fibrillation?

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Background: Atrial fibrillation (AF) is the most frequent tachyarrhythmia and contributor of ischemic strokes. Nowadays radio frequency catheter ablation (RFCA) based on circumflex pulmonary vein isolation become a effective strategy of the rhythm control, however, the refractoriness of AF is the serious concern, which happen in about 30% of patients. Although 24 hours consecutive Holter-ECG is the most popular tool for AF detection after RFCA, it is difficult to detect AF directly. We investigated whether parameters of Holter-ECG except AF could predict AF-recurrence during the early follow-up period.

Method: We studied 219 continuous patients retrospectively who underwent RFCA as the first session in our institute from 2013 to 2014. Holter-ECG was examined in 104 patients of them (34 females, age: 67±9±5, 30 patients with non-paroxysmal AF, CHADS2 score: 1.26±1.0) who were followed up without hemodialysis, structural heart disease, prior heart surgery, left atrial diameter (LAD) above 50 mm, symptomatic bradycardymhy, and arrhythmia devices (implanted cardiac defibrillators and pacemakers). All patients were followed up at least 1 year in our institute. The clinical data, echocardiographic data including left ventricular ejection fraction (LVEF) were evaluated in 1 and 3 months after RFCA. Holter-ECG was examined around 3 months after RFCA. Parameters of Holter-ECG included heart rates (minimum, average, and maximum), the total number of paroxysmal atrial contractions (PACs), and the frequency of multiple PAC runs or of pauses over 2.0 seconds. The multiple PAC run was defined as more than 3 consecutive narrow QRS couplets. The number of pauses were counted in sinus rhythm, and the pauses in AF were excluded. Antiarrhythmic drugs including amiodarone or beta blockers were administrated after RFCA, if necessary. The recurrence of AF was defined as ECG-based detection after the blanking period (3 months) after RFCA.
Result: All patients underwent RFCAs without major complication and examined 24 hours consecutive Holter-ECGs without cessation. AF was recurrent in 32 patients (30.7%), which was associated with the frequency of pause (p=0.004) and multiple PAC runs (p=0.017), and LVEF (p=0.039). There were no relationships between the AF recurrence and the other Holter-ECG variables. The number of talking analysis and functional reentries with PACs (N=14) was 32 (21%) and 39 (31%) patients, respectively, though there were also no influence of these drugs on AF recurrence or Holter-ECG variables. On multivariate analysis, the number of multiple PAC runs was an independent predictive factor (p=0.001, OR 10.4 for 10 times of PAC runs, 95% CI: 0.09 to 0.012, and P=0.020).

Conclusion: The multiple PAC runs had the predictive value independently as AF-recurrence in the early stage after CA. In these patients, more detail examination tool like multiple days consecutive recorders should be effective for the detection of AF-recurrences.

MECHANISM OF ARRHYTHMIA

P4499 | BENCH
Microscopic analysis of anatomical and functional reentrant mechanisms in human cardiac cell cultures
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Introduction: Limited knowledge of the mechanisms of perpetuation of fibrillation is hampering the development of effective anti-arrhythmic treatments. The goal of the present study is to link the mechanism of reentry during fibrillation (e.g. microanatomical vs. functional reentries) with its response to verapamil.

Methods: Cells of human cardiac myocytes differentiated from pluripotent stem cells were analyzed with a novel microscopic optical mapping system. During fibrillation the dominant reentry was identified (i.e. anatomical vs. functional reentry) and characterized in terms of its dominant frequency (DF). The pharmacological response to verapamil administration of each type of reentry was analyzed.

Results: In all analyzed cell cultures, a reentry was identified as the mechanism of maintenance of the arrhythmia. Microscopic analysis of the reentries allowed their classification into (1) micro-anatomical (46%, N=12) or functional reentries (54%, N=14). Isochronal maps of a representative example of each group are shown in the figure. Anatomical reentries presented lower DFs than functional reentries (i.e. 1.08±0.19 vs. 2.96±0.24 Hz, p<0.01). Interestingly, the administration of verapamil produced opposite effects in each group: whereas DF increased in 15±3.4% for anatomical reentries, it decreased in 11±3.6±8% for functional reentry (p<0.01).

Conclusions: Microscopic mapping of reentries allows the identification of the mechanism of perpetuation mechanisms which has been demonstrated to be linked with different pharmacological response.

P4500 | BENCH
Mutation- and age-dependent presentation of HCN4 syndrome comprising sinus node dysfunction, atrial fibrillation, noncompaction cardiomyopathy, mitral valve defects and ascending aortic dilation
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Background/Introduction: Mutations in the HCN4 pacemaker channel are linked to a novel electrical and structural cardiac syndrome comprising a broad clinical spectrum of sinus node dysfunction, atrial fibrillation (AF), noncompaction cardiomyopathy (NCCM) and defects of the mitral valve (MVD). Recently ascending aortic dilation (AAD) has been identified as a part of the syndrome complex in several families. However, clinical severity and penetrance of these symptoms vary among HCN4 mutation carriers.

Purpose: We set out to elucidate determinants underlying the differences in the clinical spectrum among patients carrying distinct HCN4 mutations.

Methods: Five unrelated German families harboring by 4 different HCN4 mutations were systematically examined (n=19 HCN4 mutation carriers). Clinical assessment comprised medical history, physical examination, 12-lead electrocardiogram, Holter ECG-monitoring, exercise testing and multimodal imaging (echo-cardiography and/or cardiac magnetic resonance imaging). Clinical data were related to biophysical properties of mutated channels, studied by patch-clamp recordings.

Results: Sinus bradycardia was a common characteristic among all HCN4 mutation carriers investigated in this study. The extent of heart rate decrease was related to the electrophysiological effect of the underlying mutation. “Loss-of-function” mutations located in the channel pore domain showed the most pronounced current reduction and the most severe bradycardia phenotype. By contrast, structural alterations were not uniformly present in patients carrying HCN4 mutations. NCCM, MVD and AAD were strongly associated with specific mutations and showed high penetrance in these families. Early onset of bradycardia, NCCM, and MVD in young mutation carriers reflects congenital manifestation of these symptoms independent of patient age. AAD and AF, however, were more frequently seen in older subjects, indicating additional acquired modifiers with respect to the underlying pathogenesis.

Conclusion: “HCN4 Syndrome” is characterized by a phenotypic spectrum that is determined by patient age and by functional properties of the underlying HCN4 mutations. Genotype-phenotype correlations provide insights into HCN4-associated cardiac pathophysiology and support mechanism-based patient care.

P4501 | BENCH
Characterization of the novel mutant A78T-HERG from a long QT syndrome type 2 patient: instability of the mutant protein and stabilization by heat shock factor-1
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Background: The human ether-a-go-go-related gene (HERG) encodes the alpha subunit of the potassium current IKr. Its mutations destabilize the HERG protein and cause long QT syndrome type 2 (LQT2). We studied the stability of a novel mutant A78T-HERG carrying the missense mutation in its intracellular loop and examine the effects of heat shock and heat shock factor (HSF) family on its stability.

Aims and methods: The aims of this study were to analyze the properties of A78T-HERG protein and investigate whether HSF family can improve the stability of A78T-HERG protein or not. To analyze the protein expression patterns of the wild-type HERG (WT-HERG) channel and the A78T-HERG channel proteins, we conducted transfection of the WT flag-tagged-herg gene and the mutant flag-tagged herg gene into HEK293 cells and western-blotting for evaluation of the HERG protein expression levels and the ubiquitination levels. Immunostaining of the gene-transfected cells was also performed to evaluate the cellular localizations of the HERG proteins. We conducted patch-clamp of the cells transfected with WT and A78T genes for the measurement of Ikr. HEK293 cells were co-transfected with A78T mutant gene and either HSF-1, HSF-2, and HSF-4 to investigate whether these HSF family can improve the stability of A78T-HERG protein.

Results: In transfected HEK293 cells, the level of the mature form of A78T-HERG at 155kDa was remarkably lower than that of WT-HERG associated with significant decreases in its ubiquitination. There were no changes in the levels in immature form at 135kDa. A78T-HERG was predominantly localized in the cytosol, whereas WT-HERG was predominantly localized on the plasma membrane. This localization was also supported by the small amplitude of Ikr through A78T-HERG associated with small tail currents. Heat shock for 1 hour significantly increased the mature form of A78T-HERG accompanied with increase of amplitude of Ikr. It has been also tested whether HSF family could stabilize A78T-HERG. HSF-1 but not HSF-2 and HSF-4 increased the mature form of the A78T-HERG proteins, indicating their stabilization.

Conclusions: A78T-HERG showed the impairment of trafficking to plasma membrane, and was degraded by the ubiquitin-proteasome pathway. HSF-1 significantly increased the mature form of A78T-HERG, and HSF-1 might be a potential target in the treatment of LQT2 resulting from A78T-HERG mutation.

P4502 | BENCH
Reactive oxygen species inhibit inward rectifying K current by redox-activated protein kinase A
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Rationale: Reactive oxygen species (ROS) have been shown to inhibit inward rectifying K current (IKr), which may contribute to delayed depolarization and focal arrhythmias. Interestingly, a novel PKA activation pathway by oxidation of cysteine 17/38 of regulatory subunit I (RI) has recently been described.

Objective: We tested the hypothesis that ROS inhibit IKr by redox-activation of PKA.

Methods and results: IKr was measured in mouse ventricular myocytes (whole-cell patch clamp). Analysis of current-voltage relation (I-V, fig.) showed that exposure to H2O2 (200 μM) significantly reduced IKr amplitude (ANOVA, p<0.05).
vs. vehicle), which was completely abolished in the presence of the selective PKA inhibitor Rp-8-Br-cAMPS (10 μmol/L, † -p < 0.05 vs. H2O2). In parallel experiments, myocytes were isolated from homozygous knock-in mice with R1106Q mutations in KCNT1 17 to serine mutation (KI), which are devoid of oxidation-dependent PKA activation. Compared to WT, the basal IK1 amplitude was smaller in KI due to a significantly reduced expression of Kir2.1 (fig. 1B). Surprisingly, exposure of KI myocytes to H2O2 resulted in a significant increase in IK1 amplitude (fig. 1), which was not influenced by the presence of Rp-8-Br-cAMPS but could be blocked by selective inhibition of Ca/CaM-dependent protein kinase II (CaMKII) using autocamidt 2-related autoinhibitory peptide (AIP, 1 μmol/L, †). ROS regulate IK1 by PKA and CaMKII. In WT, ROS-dependent activation of PKA seems to be the major pathway of IK1 inhibition, which may contribute to action potential prolongation and arrhythmias. In contrast, if oxidative PKA activation was abolished (KI), ROS increase IK1 by activation of CaMKII. The relevance of the latter pathway remains unclear.

Acknowledgement/Funding: The work was funded by the DZHK (Deutsches Zentrum für Herz-Kreislauf- Forschung – German Centre for Cardiovascular Research)

Figure

Conclusion: ROS regulate IK1 by PKA and CaMKII. In WT, ROS-dependent activation of PKA seems to be the major pathway of IK1 inhibition, which may contribute to action potential prolongation and arrhythmias. In contrast, if oxidative PKA activation was abolished (KI), ROS increase IK1 by activation of CaMKII. The relevance of the latter pathway remains unclear.

Acknowledgement/Funding: The work was funded by the DZHK (Deutsches Zentrum für Herz-Kreislauf- Forschung – German Centre for Cardiovascular Research)

P4503 | BENCH
Cyclopamine A: a novel cardiac marker in arrhythmogenic cardiomyopathy
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Background: Arrhythmogenic Cardiomyopathy (ACM) is an inherited desmosomal disease characterized by fibro-fatty replacement of functional myocardial tissue, inflammation and oxidative stress. The fibro-fatty replacement, predominantly located in the ventricles, exacerbates ventricular arrhythmias, causes abnormal ventricular function and increases the risk of sudden cardiac death. Cyclopamine A (CyPA) is an ubiquitous immunomodulator involved in the development of several cardiovascular diseases. CyPA has been recently described as a new adipokine in addition to play a key role in cardiac fibrosis, inflammation and oxidative stress responses.

Purpose: The aim of the present study is to investigate the involvement of CyPA in ACM.

Methods: CyPA expression was measured by immunostaining of right ventricular tissue sections obtained from explanted hearts of 4 ACM patients and 4 healthy controls. CyPA expression was measured by immunostaining of right ventricular tissue sections obtained from explanted hearts of 4 ACM patients and 4 healthy controls.

Results: CyPA protein expression was significantly higher in right ventricular tissue of ACM patients vs. healthy controls (Figure 1; P < 0.005). CyPA localization was predominantly in the peri-adipocyte area of ACM patients vs. healthy controls. Interestingly, CyPA expression strongly correlates with fatty tissue substitution (Pearson's correlation test r = 0.87, P < 0.011). In addition, a correlation trend was found between CyPA expression and tissue fibrosis (Pearson's correlation test r = 0.653, P = 0.079). Surprisingly, plasma levels of CyPA were not statistically different between ACM patients and healthy controls (t-test P = 0.239).

Conclusion: In patients CHD and RA volume overload, electrophysiology was found diffusely throughout the atria; conduction disorders were predominantly located at BB. Consequently, the arrhythmogenic substrate involved in the pathogenesis of atrial tachyarrhythmias may not only be confined to the RA.

P4504 | BEDSIDE
Predication sites for electrophysiology during sinus rhythm in patients with congenital heart disease associated with right atrial stretch

Introduction: Congenital heart diseases (CHD) can be associated with right atrial (RA) volume overload. The resulting atrial stretch causes intra-atrial conduction abnormalities which may be involved in the pathophysiology of atrial tachyarrhythmias.

Objectives: We examined whether there are preferential sites of electrophysiology during sinus rhythm (SR) in patients with CHD and RA volume overload.

Methods: Intra-operative, high-resolution (inter-electrode distances 2mm) epicardial mapping studies of the RA, Bachmann's Bundle (BB), left atrioventricular groove (LAVG) and pulmonary vein area (PVA) during SR were performed in 12 CHD patients with RA volume overload. Three patients had paroxysmal atrial fibrillation. Unipolar voltages, conduction delay (CD) and conduction block (CB) were quantified per 1 cm² quadrants. Data are expressed as mean; median (P0; P100).

Results: Unipolar signals were recorded from 22,965 sites (1,914±329/patient). Median atrial voltage was 2.5; 2.5 (1.4–3.5) mV/cm²; there were no differences between unipolar voltages/cm² of the RA, BB, LAVG and PVA (P = 0.461). Voltages ≥ 0.5mV were measured in 6 (50%) patients at 12 (2.9%) quadrants, mainly at the superior RA (N=5; 2.5%) and at BB (N=4; 8.3%, P = 0.105). Median amount of CD and CB were respectively 1.6; 1.3 (0.9–2.9)%; and 1.6; 1.3 (0.7–3.5%). CD and CB occurred most frequently at BB (CD: 52%; CB: 41%). The amount of CD and CB was highest at BB (CD: 2.4%/cm², P = 0.027; CB: 3.2%/cm², P = 0.004).

Conclusion: Unipolar voltages and conduction abnormalities in patients with CHD and RA volume overload were predominantly located at BB. Intra-atrial conduction abnormalities may include a possible perpetuation of atrial fibrillation. Unipolar signals were recorded from 22,965 sites (1,914±329/patient). Median atrial voltage was 2.5; 2.5 (1.4–3.5) mV/cm²; there were no differences between unipolar voltages/cm² of the RA, BB, LAVG and PVA (P = 0.461). Voltages ≥ 0.5mV were measured in 6 (50%) patients at 12 (2.9%) quadrants, mainly at the superior RA (N=5; 2.5%) and at BB (N=4; 8.3%, P = 0.105). Median amount of CD and CB were respectively 1.6; 1.3 (0.9–2.9)%; and 1.6; 1.3 (0.7–3.5%). CD and CB occurred most frequently at BB (CD: 52%; CB: 41%). The amount of CD and CB was highest at BB (CD: 2.4%/cm², P = 0.027; CB: 3.2%/cm², P = 0.004).

P4505 | BENCH
The Brs-associated KCNT1 mutation R1106Q changes calcixin 2A1 effect toward PMCA
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Background: The KCNT1 gene (also known as SLACK, SLO2.2, and KCa4.1) encodes a sodium-activated potassium (KNa) channel. KCNT1 mutations have been reported to link with Brugada syndrome (BrS) a rare cardiac channelopathy associated with sudden cardiac death (SCD). In the nervous system, a recent study has shown that in addition to regulating ion flux, KCNT1 has a non-conducting function involved in developmental signaling pathways. However, the physiology and mechanism of KCNT1 R1106Q in cardiac remains unknown.

Purpose: Because cardiac electrical activities are highly dependent on proper regulation of Ca²⁺ currents, we investigated whether KCNT1, as a putative K²⁺ channel, also regulates cellular Ca²⁺ homeostasis. The aim of the present study is to understand how KCNT1 mutation is related to Brugada syndrome by determining the functional consequences of this mutation and the mechanism.

Figure

Conclusion: In patients CHD and RA volume overload, electrophysiology was found diffusely throughout the atria; conduction disorders were predominantly located at BB. Consequently, the arrhythmogenic substrate involved in the pathogenesis of atrial tachyarrhythmias may not only be confined to the RA.

P4505 | BENCH
The Brs-associated KCNT1 mutation R1106Q changes calcixin 2A1 effect toward PMCA
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Background: The KCNT1 gene (also known as SLACK, SLO2.2, and KCa4.1) encodes a sodium-activated potassium (KNa) channel. KCNT1 mutations have been reported to link with Brugada syndrome (BrS) a rare cardiac channelopathy associated with sudden cardiac death (SCD). In the nervous system, a recent study has shown that in addition to regulating ion flux, KCNT1 has a non-conducting function involved in developmental signaling pathways. However, the physiology and mechanism of KCNT1 R1106Q in cardiac remains unknown.

Purpose: Because cardiac electrical activities are highly dependent on proper regulation of Ca²⁺ currents, we investigated whether KCNT1, as a putative K²⁺ channel, also regulates cellular Ca²⁺ homeostasis. The aim of the present study is to understand how KCNT1 mutation is related to Brugada syndrome by determining the functional consequences of this mutation and the mechanism.

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Methods: KCNT1 wild-type (WT) and mutant R1106Q tagged with IRES-GFP were expressed in HEK293T cells for 24hrs. These cells were then loaded with the Ca²⁺ indicator Fura-2 and imaged by fluorescent microscopy. Images were taken every 6 seconds for 1 minute, to record baseline cytosolic [Ca²⁺]. Then image every 6 seconds for 9 minutes after adding thapsigargin (SERCA inhibitor) and EGTA (Ca²⁺ chelator). The drugs will immediately release Ca²⁺ from the endoplasmic reticulum (ER) to induce a sharp increase of [Ca²⁺] in the cytosol. Ca²⁺ will later be pumped through the plasma membrane out of the cell, mainly by PMCA and NCX.

Results: By performing disease-targeted multi-gene sequencing, one KCNT1 mutation site R1106Q were identified in patients with the Brugada syndrome. Also, bioinformatics algorithms predicted severe functional interusions in this mutation loci. And we found that in fura2 calcium image, HEK293T overexpressed with the KCNT1 WT and the R1106Q mutant show significant difference at the calcium extrusion rate which is determined by PMCA after adding caloxin 2A1 (PMCA inhibitor) (before adding caloxin 2A1: WT 0.027±0.0022 A.U., N=8 vs MT 0.026±0.0023 A.U., N=11, P=0.6442; after adding: WT 0.023±0.0014 A.U., N=9 vs MT 0.029±0.0008 A.U., N=12, P<0.0006) This finding indicates that KCNT1 mutant R1106Q may have an enhancement effect on PMCA, caused PMCA can't be inhibited by caloxin 2A1.

Conclusions: Together with our bioinformatics and Ca²⁺ imaging data, we hypothesize that KCNT1 may have a significant role in cardiac Ca²⁺ homeostasis. Furthermore, the disruption of Ca²⁺ signaling by mutant KCNT1 may contribute to Brugada syndrome. To verify such speculation, further experiments still need to be conducted.

P4507 | BENCH
Regional ventricular wall stretch is weakly related to arrhythmia triggers but strongly associated with vulnerability to ventricular fibrillation following acute coronary occlusion in vivo

Background: Myocardial stretch induces electrophysiological changes and arrhythmogenesis. Studies in different experimental models have suggested that regional left ventricular (LV) wall stretch may increase the risk of spontaneous ventricular fibrillation (VF) following coronary occlusion, yet its association with ventricular ectopy has been inconsistent among studies and its potential arrhythmogenicity in different stages of the cardiac cycle has not been systematically evaluated.

Purpose: We assessed the association between diastolic or systolic regional LV distension and the incidence of ventricular premature beats (VPBs) and VF following coronary occlusion in a large database of in vivo experiments in untreated pigs.

Methods: In 91 thiopental-anesthetized, open-chest pigs of either sex (36±6 kg) not receiving other medications, the mid left anterior descending artery was ligated for 40–50 min. End-diastolic segment length (EDL, expressed as % of baseline value) and systolic bulging (maximum systolic length–EDL) of 100 EDLs were measured 15 min after coronary occlusion by ultrasonic crystals (all animals had valid measurements). The incidence of VPBs and VF was assessed.

Results: Fifteen minutes after coronary occlusion, EDL increased to 112.7±5.6% of the pre-occlusion value (P<0.001) and systolic bulging averaged 3.4±2.2%. The number of VPBs averaged 52 (IQR, 16–110), 2 (0–7) in phase Ia, 11 (3–34) in phase Ib, and 2 (0–7) in phase Ic, the first episode appearing 24±6 (16 to 39) min after coronary occlusion. The increase in EDL was strongly associated with VF occurrence (11.5±5.7 and 111.4±13.1% in animals with and without VF, respectively, P<0.001) and with VF number (P=0.003) but was not related to VPB number (square-root transformed), either overall (r=0.028, P=0.801) or in phases Ia or Ib. Systolic bulging was related neither with VF occurrence (3.1±2.2 and 3.5±2.2%, respectively, P=0.561) nor with VPB number (r=0.095; P=0.397, also consistently in phases Ia and Ib). The increase in EDL remained a strong predictor of VF after adjusting for the size of the ischemic area and K⁺ levels (odds ratio for 1% increase: 1.17, 95% CI 1.06–1.29, P<0.001).

Conclusions: Diastolic regional LV wall distension strongly and independently predicts VF occurrence following coronary occlusion in vivo, whereas neither diastolic nor systolic distension are associated with ventricular ectopy. The results suggest that stretch is arrhythmogenic during acute ischemia mainly by increasing the vulnerability to malignant arrhythmias.

Acknowledgement/Funding: Funded by the Spanish Ministry of Economy and Competitiveness (ISCIII-P12/01844)

P4508 | BENCH
Melatonin receptor activations protects against low potassium induced ventricular fibrillation: role of connexin-43
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Introduction: Hypokalemia, a common electrolyte abnormality in clinical practice, enhances the propensity for ventricular fibrillation (VF). Melatonin up-regulates the gap junction channels protein, connexin-43 (Cx43), rendering the heart more resistant to electrical induced VF. We hypothesized that melatonin may protect against low potassium induced VF in part by affecting Cx43 through the activation of its membrane receptors.

Methods: Isolated rat hearts underwent 10 min of Krebs-Henseleit perfusion (4.5 mEq/L K⁺) followed by K⁺-deficient (1 mEq/L) perfusion in the presence of 100 μM melatonin, a melatonin receptor blocker (luzindole 5 μM), luzindole + melatonin or the vehicle of the drugs. Low K⁺ perfusion was maintained 25 min unless VF occurred earlier. Two min VF was followed by normokalemic perfusion aimed to restore sinus rhythm. The incidence of arrhythmias and heart function were registered and analyzed using Biolab® software. Ventricular tissue analysis was performed for Cx43 expression and distribution.

Results: Melatonin was the only treatment that reduced the incidence of low K⁺-induced VF from 100% (vehicle 15/15; luzindole+melatonin 10/10; and luzindole 8/8) to 69% (9/13) (P=0.0349 vs vehicle by Fisher test) and delayed the occurrence of VF to 12 min (9–25 IQR) from 7 min (5–12 IQR) in vehicle group (P=0.041). Luzindole and luzindole+melatonin developed VF at a median of 5 min (4–11 IQR) and 8 min (6–14 IQR), respectively, resulted in a faster recovery of sinus rhythm restitution (P=0.047). Melatonin, luzindole or luzindole+melatonin did not affect heart rate, PR and QT intervals as well as the incidence of transient arrhythmias. The levels of total Cx43 was not changed by any treatment, however, melatonin prevented dephosphorylation and abnormal topology (lateralization) of Cx43.

Conclusions: Our results suggest that acute treatment with melatonin protects...
against low potassium induced VF in part due to the prevention of abnormal expression and distribution of myocardial CaV4.3 mediated by melatonin receptors activation.

P4500 | BENCH
Direct thrombin inhibitors prevent atrial remodeling and arrhythmia susceptibility independently of their anticoagulant properties in a rat model of heart failure
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During atrial fibrillation (AF) and atrial dilatation, thrombin accumulates in the atrial chambers favoring the formation of thrombus and explaining the high risk of stroke in these setting. In addition to its role in coagulation cascade, thrombin has pleiotropic effects notably by binding to protease-activated receptor-1 (PAR-1). Here we test the hypothesis that thrombin contributes to the atrial remodeling associated with heart failure (HF). HF was induced by realizing an extensive myo-cardial infarction in rats. Animals were treated immediately or one month post-MI with either vehicle control, 25 mg/kg/day dabigatran or 6 mg/kg/day of another direct thrombin inhibitors (DTI), S35972. Two months treatment with DTIs reduced both left atria dilatation and the duration of burst pacing-induced AF whereas treatments had no effect on ventricle dilatation and systolic dysfunction (n=10 rats). PAR-1 antagonist (n=10) had similar effect than DTI on atrial dilatation and AF susceptibility whereas the vitamin K antagonist, Warfarin (n=6), had no effect on atrial remodeling. DTIs suppressed the expression of myocardial hypertrophic markers such as brain natriuretic peptide and β-myosin heavy chain. In a atrial explant culture model, 10 nM thrombin upregulated hypertrophic markers through PAR-1 and the Rho/Rho kinase pathway suppressed using the ROCK inhibitor Y27632 (n=12). The phosphorylation of the signal transducer and activator of transcription 3 (Stat3) downstream effector of RhoA (n=6). In conclusion, thrombin is a potent hypertrophic factor of the atrial myocardium and that DTIs and PAR1 inhibitor could prevent the atrial remodeling and AF substrate formation.

P4501 | BENCH
Mesenchymal transformation of the epicardium contributes to the accumulation of epicardial adipose tissue in the atria
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Background: The abundance of the epicardial adipose tissue (EAT) is associated with a high risk and severity of atrial fibrillation. However, the origin of EAT of the atrial myocardium and factors regulating its local development are still unknown.
Methods: Surgical specimen of human right atrial specimens were used for histological and biochemical studies (n=60), as well as for harvesting epicardial progenitors derived cells (EPDCs) (n=20) which were then maintained in culture conditions. EPDCs were characterized using flow cytometry, proteomic and genic expression assays. In order to determine the cellular origin of atrial adipose tissue, we studied adult epicardial cell fate using a Wt1-CreERT2-Rosa-tdt+/+ lineage tracing mouse model (n=7). Mouse atrial tissue sections were studied by histological and immunostaining assays. Similar to human aEPDCs, cells were harvested from Wt1-Cre-Rosa-tdt+/+ atrial tissue and studied in cell culture.
Results: In the sub- and epicardial layer of atrial section, cells were positives for epicardial progenitor marker Wilm's tumor-1 (Wt1) and pre-adipocyte marker pre-adipocyte factor 1 (Pref-1) suggesting that EPDCs could engage in the adipogenic fate. This hypothesis was tested in vitro, using human and mouse aEPDCs obtained from atrial samples; atrial epicardial cells underwent an epithelio-to-mesenchymal transition (EMT) and acquired mesenchymal phenotypes (aEPDCs), and could subsequently differentiate into osteocyte or chondrocyte. When cultured using an adipogenic medium, around 40% of aEPDCs showed lipid droplets stained with oil red and expressed mature adipogenic markers perilipin, PPARγ and CEBPα. These results were supported by the formation of lipid droplet-en-tomato- adipocytes observed in murine aEPDC cultures induced by adipogenic medium. To follow the fate of Wt1+ epicardium in vivo, we used a lineage tracing Wt1-CreERT2-Rosa-tdt+/+ mouse model. We found that a number of adipocytes that compose the atrial EAT derived from aEPDCs through EMT process.
Conclusion: Atrial EAT derives, at least in part, from an EMT process of progenitors present in the epicardium of adult human and mouse atria. Factors regulating this process will be discussed.

P4512 | BEDSIDE
Secretoneurin, a novel endogenous CaMKII inhibitor, inhibits Ca2+−dependent arrhythmogenesis
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Background: Secretoneurin (SN) is increased in heart failure patients and patients with ventricular arrhythmia-induced cardiac arrest, and are predictive of clinical outcomes. SN has been shown to alter Ca2+ homeostasis in cardiac tissue. Secretoneurin (SN) levels are increased in heart failure patients and patients with ventricular arrhythmia-induced cardiac arrest, and are predictive of clinical outcomes. SN has been shown to alter Ca2+ homeostasis in cardiac tissue. In Langendorff-perfused mouse hearts, SN reduced Ca2+ sparks reactivity, and reduced CaMKII activation.
Methods and results: In Langendorff-perfused mouse hearts, SN reduced Ca2+ sparks reactivity, and inhibited CaMKII activity. In line with CaMKII and RyR inhibition, SN treatment decreased the frequency and dimensions of Ca2+ sparks in cardiomyocytes improved by adrenergic medium. In vivo, treatment with Ca2+ sparks in cardiomyocytes improved by adrenergic medium. In vivo, treatment with CaMKII and RyR inhibition, SN treatment decreased the frequency and dimensions of Ca2+ sparks in cardiomyocytes improved by adrenergic medium. In vivo, treatment with Ca2+ sparks in cardiomyocytes improved by adrenergic medium. In vivo, treatment with Ca2+ sparks in cardiomyocytes improved by adrenergic medium.
which corresponded to a lower incidence of delayed after-depolarizations and fewer spontaneous action potentials in patch-clamped cardiomyocytes. Furthermore, SN treatment reduced the incidence of early after-depolarizations induced by isoproterenol; an effect paralleled by reduced magnitude of L-type Ca²⁺ current.

**Conclusions:** SN treatment reduces CaMKII activity, which inhibits arrhythmogenesis by 1) reducing RyR activity, Ca²⁺ waves, and delayed after-depolarizations, and 2) inhibiting L-type Ca²⁺ current and early after-depolarizations. These findings suggest that increased SN levels are protective in patients with ventricular arrhythmia, and that further elevating SN levels may be therapeutic.

**P4513 | BEDSIDE**

**Supraventricular conduction disorders and atrial fibro-fatty infiltration**

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**Aim:** Fibro-fatty infiltration is widely considered as a leading cause of heterogeneous conduction in experimental studies, further responsible atrial fibrillation (AF). Cardiac low voltage zone (LVZ) is a well-established surrogate of fibro-fatty infiltration by experimental studies and human studies using surgically removed cardiac tissue. The aim of this study was to evaluate the potential role of fibro-fatty infiltration to clinical supraventricular conduction disorders in a large cohort. We explored the link between impaired conduction properties and fibrosis extent in atria, and further correlated clinical appearances.

**Subjects:** A total of 139 patients (65% male, 74±10 years) with ischemic heart disease were included, comprising 26 with atrioventricular conduction block (AVB) (n=26) and 113 with atrial fibrillation (AF) (n=113). Patients with atrial fibrillation were also divided in to 9 equally sized blocks. The median value within each block and the area and localization of low voltage zone (LVZ, bipolar amplitude <0.5 mV) was stored and used for further analysis.

**Results:** The existence of LVZ in patients with sick-sinus syndrome (SSS) (n=22) was significantly greater than those without SSS (n=114 vs. n=8, p=0.005). The area of LVZ in patients with SSS was also significantly greater than those without SSS (SSS 14±19.3 vs. 4.9±12.4 cm², p=0.001). Further, the existence of LVZ in patients with atrioventricular conduction block (AVB) (n=26) was significantly greater than those without AVB (n=16 vs. n=10, p=0.004). The area of LVZ in patients with AVB was also significantly greater than those without AVB (11.8±24.2 vs. 4.9±12.0 cm², p=0.021). The existence of LVZ in patients with persistent AF was significantly greater than those with paroxysmal AF (n=135 vs. n=57, p<0.0001). The area of LVZ in patients with persistent AF was also significantly greater than those with paroxysmal AF (9.0±16.4 vs. 2.1±7.8 cm², p<0.001).

**Conclusions:** We reported that existence of LVZ in human heart, indicating fibro-fatty infiltration, highly relates to the supraventricular conduction disorders. This suggests a novel concept that supraventricular conduction disorders, including SSS, AVB and AF, should be treated as a grouped-disease with a common cause.

**P4515 | BEDSIDE**

**Brugada syndrome - Late potentials detection by signal-averaged electrocardiography pre- and post-flecainide provocative test**


**Background:** Risk stratification of ventricular arrhythmias is crucial in the management of patients with Brugada syndrome (BS). However, there is no validated method for prognostic stratification of patients with asymptomatic BS, who represent the majority of patients. Late potentials (LP), detected by signal-averaged electrocardiography (SA-ECG) are associated with myocardial regions with delayed depolarization and abnormalities in electric conduction. Several studies demonstrated a higher prevalence of LP detected by SA-ECG in patients with BS and their presence was a strong prognostic predictor.

**Purpose:** To evaluate the presence of LP detected by SA-ECG and describe its modification after flecainide provocative test (FT) in patients with BS.

**Methods:** Single-center prospective study of consecutive patients with type 2 Brugada pattern (BP) and positive FT [2 mg/kg (maximum 150mg) infusion for 10 minutes] defined as inducible type 1 BP. Patients underwent LP detection by SA-ECG pre- and post-FT, with measurement of filtered QRS duration (IQRS), root-mean-square voltage of the terminal 40 ms of the QRS (RMS40) and low-amplitude (below 40μV) signal duration (LAS40). LP were positive if at least two of the following criteria were met: IQRS ≥ 114 ms, RMS40 <20 μV and LAS40 >38 ms. Statistical analysis was performed using the Mann-Whitney test, Pearson and Spearman correlations.

**Results:** We studied 15 patients with type 2 BP and positive FT (68.8% male, 45±14 years). Seven patients (43.8%) had evidence of LP pre-FT. The different components of LP changed significantly after flecainide infusion, with decreased duration of IQRS in 12 ms, LAS40 in 6 ms and reduction of RMS40 in 6 μV. Post-FT, 13 patients (81.2%) had evidence of LP. IQRS was higher post-FT in patients with longer IQRS at baseline (R: 0.64; p=0.018; Rho: 0.504; p=0.056), but had higher variation in patients with baseline shorter IQRS (Rho: 0.55; p=0.032). Similarly, RMS40 was higher post-FT in patients with longer RMS40 at baseline (Rho 0.61, p=0.016) and the magnitude of variation correlated inversely with the initial value (Rho -0.6; p=0.016). Finally, LAS40 was higher post-FT in patients with larger LAS40 at baseline (R: 0.53; p=0.043; Rho: 0.53; p=0.04), although there was no correlation between the magnitude of variation and the initial values.

**Conclusion:** In patients with type 2 Brugada pattern and positive flecainide provocative test (inducible type 1 BP) the presence of late potentials and the magnitude of their variation after flecainide infusion may be strong prognostic predictors.

**P4516 | BEDSIDE**

**Left atrial bipolar voltage map in a large AF-cohort: a prospective, retrospective study and its fundamental findings**

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**Aim:** Fibro-fatty infiltration is widely considered as a leading cause of heterogeneous conduction in experimental studies, further responsible atrial fibrillation (AF). Cardiac low voltage zone (LVZ) is a well-established surrogate of fibro-fatty infiltration.
by experimental studies and human studies using surgically removed cardiac tissues. However, lack of detailed data in human could systematically establish baseline values and fundamental characteristics of distribution in a large cohort. We built a large database of patients with AF aiming to establish the fundamental characteristics of impaired myocardium in patients with AF, indicating fibrosis extent and fatty infiltration in atria, and further to correlate to clinical appearances. Subjects: Consecutive 539 patients (309 male (57.3%), age 65±10 years) with highly symptomatic AF (paroxysmal: n=292; persistent: n=247), who underwent a bipolar voltage map (BVM) guided AF ablation, were enrolled into the current study.

Methods: A detailed LA-BVM was carried out for each patient using 3D mapping system during procedure. LA was divided into 5 zones, i.e. septum (S), anterior (AW), posterior (PW), inferior (IW) and lateral (LW) walls, except LA appendage (LAA). Each zone was further divided into 9 equally sized blocks. The median value within each block and the area and localization of LVZ (bipolar amplitude <0.5 mV) was stored and used for further analysis.

Results: Median area of LA-surface, including LAA, are 103.6 cm² (percentiles 5–95% 70.9–160.9 cm²), Median area of LVZ are 0 cm² (percentiles 5–95% 0.0–32.8 cm²). Median bipolar amplitude is 2.2 mV (percentiles 5–95% 1.0–4.2 mV) for the entire LA, 1.8 mV (0.4–4.4 mV) on AW, 1.7 mV (percentiles 5–95% 0.5–3.8 mV) on S, 2.4 mV (1.0–5.4 mV) on IW, 2.5 mV (1.1–5.3 mV) on PW, and 2.2 mV (0.6–5.5 mV) on PW, respectively. Median area of LVZ was 0 cm² for all walls (percentile 5–95%: AW: 0.0–12.7, S: 0.0–12.7, IW: 0.0–2.0, LW: 0.0–0.0, PW: 0.0–8.5, LAA: 0.0–0.0 cm²). The existence of LVZ on AW (n=113, 21%), S (n=109, 20.2%) and PW (n=75, 13.9%) are predominantly frequent than on IW (n=42, 7.8%), LW (n=25, 4.6%), and LAA (n=3, 0.6%) (p<0.001). The existence of AF with persistent atrial fibrillation was significantly greater than that with paroxysmal atrial fibrillation (n=135 vs. n=57, p<0.0001). The area of LVZ in patients with persistent AF was also significantly greater than those with paroxysmal AF (9.0±16.4 vs. 2.1±7.8 cm², p<0.001). For the entire LA, average bipolar amplitude in patients with persistent atrial fibrillation is significantly greater than in patients with persistent AF (2.7±1.0 vs. 2.0±0.9 mV, p<0.001).

Conclusions: We report that the baseline characteristics on bipolar voltage in human heart in large cohort patients with AF. Further, the area of LVZ in patients with persistent AF is predominantly greater than in patients with paroxysmal AF in line with previous histological studies. The most frequent localization of LVZ is anterior wall, septum and posterior wall.
model. Secondly, we determined whether anti-oxidative treatment could attenuate the arrhythmic effects induced hypotrophy via suppression of CaMKII activity. 

**Methods:** Angiotensin II (Ang II) or saline was administrated for 2 weeks via osmotic minipumps implanted subcutaneously in the midclavicular region. Hearts were perfused, mapped optically to analyze action potential durations (APD), and restitution kinetics, and tested for VF vulnerability. The intracellular calcium dynamics were measured in cardiomyocyte treated with Ang II (10 ng/ml) for 1 hour. 

**Results:** In Ang II rabbit groups, 2 (30%) rabbits died and had ventricular arrhythmias and hearts had enlarged left ventricle, longer ADP90, slower conduction velocity (CV: P<0.01 versus control) and higher numbers of transcripts for APD90 and CV (P<0.01). Programmed stimulation triggered VF in Ang II (n=5) and Ang II + saline (n=4), but not in control (n=0). Cardiomyocyte induced with Ang II showed increased spontaneous Ca²⁺ release (Ca²⁺ Wave Frequency: 1.0±0.0 vs. 5.1±0.5, p<0.001; Ca²⁺ Amplitude: 1.0±0.0 vs. 1.3±0.1, p<0.001) with control. CaMKII inhibitor reversed the change of Ca²⁺. 

**Conclusion:** Cardiac hypertrophy induced APD prolongation, EAD and ventricular arrhythmia. Anti-oxidative treatment might prevent the arrhythmogenic effects of hypotrophy by attenuating oxidative stress generation and CaMKII activation. The cardiac hypertrophy group had an increased incidence of arrhythmia caused by increased phosphorylation of Ca²⁺ handling proteins. These changes were partially reversed by antioxidants and CaMKII inhibition.

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**Table 1**

<table>
<thead>
<tr>
<th>General population (n=2,363)</th>
<th>Peri-event ECGs (n=34)</th>
<th>Remote ECGs (n=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short-coupled PVCs</td>
<td>0 (0)</td>
<td>25 (73.5%)*</td>
</tr>
<tr>
<td>Giant J wave (&gt;0.2mV &amp; &gt;80ms)</td>
<td>36 (1.7%)</td>
<td>18 (52.9%)*</td>
</tr>
<tr>
<td>Global J wave (&gt;3 regions)</td>
<td>11 (3.2%)</td>
<td>1 (6.2%)*</td>
</tr>
<tr>
<td>Horizontal/ascending ST segment</td>
<td>1514 (64.1%)</td>
<td>19 (55.9%)</td>
</tr>
<tr>
<td>Ascenting ST segment</td>
<td>849 (39.5%)</td>
<td>15 (44.1%)</td>
</tr>
</tbody>
</table>

*p value <0.05 vs. general population.

**Conclusion:** The ECG features of ER syndrome patients during peri-VF were highly specific for imminent VF episode. However, as the ECG features after the short window of peri-VF periods were indistinguishable from those of general population, application of the current risk stratification scheme in patients with suspected arrhythmic syncope or VF should be reevaluated.

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**P4523 | BENCH**

**Activation of the pattern recognition receptor AIM2 impairs reendothelialization and induced atherosclerotic plaques**

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**Background:** Previous studies have linked pattern recognition receptors (PRR) of the innate immune system to the chronic inflammatory process resulting in atherosclerosis. Acute and chronic cellular damage leads to the release of nucleic acids including DNA, which can be detected by endosomal or intracellular PRR. Absent in melanoma 2 (AIM2) is a PRR specialized in detecting specific DNA motifs and is expressed by vascular cells. We studied the biological effects of specific AIM2 activation in an in vitro setting and chronic vascular injury model. 

**Methods and results:** 12-week-old C57BL6 mice were subjected to a standard model of acute vascular injury by electric denudation of the left common carotid artery. For activation of AIM2, mice were injected with 50μg long double-stranded DNA (poly dA:dT). Reendothelialization was quantified 5 days after surgery. The specific PRR ligand or vehicle were injected intravenously every 4 hours starting two days prior to the carotid injury. Stimulation of AIM2 impaired reendothelialization of the common carotid artery compared to vehicle (poly dA:dT 42.1±48.9% versus 29.5±02.0%, p<0.05). The number of circulating endothelial microparticles was increased in AIM2-stimulated mice (0.259±0.05% versus vehicle 0.102±0.01%, p<0.05). The production of reactive oxygen species in the thoracic aorta was augmented in AIM2-stimulated mice (2393±416.1 RU/s versus

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**THE MULTIPLE CELLULAR FACETS OFATHEROSCLEROSIS I**

**P4522 | BEDSIDE**

**Early re polarization patterns in the coronary slow flow patients**

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**Background and introduction:** Although coronary slow flow (CSF) is a well known phenomenon but there are limited data about the clinical significance. Recently early re polarization syndrome (ER) has been considered as a risk factor for malignant arrhythmias.

**Purpose:** We sought to analyse J-point elevation in patient with CSF.

**Methods:** We have studied 115 patients with true CSF according to results of their diagnostic coronary angiography (TIMI frame count method) between the years 2010–2014 at two education institutions (33 Female, 82 Male patients; mean age: 51.9±11.5 years) were enrolled to study. Patients with normal coronary flow in the coronary angiography (13 Female, 32 Male; mean age: 50.8±11.7 years) were included as the control group. In all patients, we searched J-point elevation on the surface ECG). On the ECG the early re polarization (ER) was defined as “notching” or “slurring” of the terminal portion of QRS takeoff (J-point) that produces a positive hump known as J-wave (ST-segment elevation >0.1 mV within 100 ms after the J-point in at least two contiguous ECG leads).

**Results:** ERP was more commonly seen among patients with CSF than among control subjects (65% vs. 28%, p<0.001). The J-point elevation in the inferior leads (26% vs. 13%, p=0.002), in the D1 to AVL leads (22% vs. 15%, p<0.01), in the lateral leads (17% vs. 0%), (p<0.001) were significantly more common in CSF patients than control groups. Notching pattern was significantly different between groups (26.0% vs. 2.2%, p<0.0001), ST-segment concave/ascending (33.9% vs. 5.2%, p<0.006), horizontal/nonascendant pattern (14.7% vs 1.7%, p<0.054), horizontal/nonascendant ST-segment and notching pattern (15.6% vs. 2.2%, p<0.012) were more commonly seen among CSF patients than control subjects.

**Conclusions:** This study revealed for the first time that CSF phenomenon is associated with early re polarization J-wave and slurring patterns. Clinical significance need to be clarified.
989.8±155.3 RLU/s, p < 0.01). AIM2 activation nearly depleted the bone marrow of endothelial progenitor cells (EPC) (0.8±0.4% versus vehicle 3.7±0.52%, p < 0.001) while the number of circulating EPC remained unchanged. For investi-
gation of atherosclerotic plaque development 10-week-old C57BL6 ApoE−/− mice were fed a cholesterol-rich western diet for 8 weeks and were concomitantly in-
jected s.c. with either 50 μg poly dA:dT suspended in 200 μl PBS or vehicle ev-
eery other day for the final six weeks. The number of circulating endothelial mi-
croparticles was increased in poly dA:dT stimulated mice (0.067±0.017% versus vehicle 0.014±0.006%, p < 0.05) and the production of reactive oxygen species in
the thoracic aorta, as measured by L012-chlorominescence, was increased (395.7±37.72 RLU/s versus 269.8±33.83 RLU/s, p < 0.05). Histological analysis of atherosclerotic plaques in AIM2-treated mice of the aortic valve area shows augmented atherosclerotic plaque development.

Conclusion: Systemic stimulation of AIM2 in wild-type mice led to impaired reendothelialization, increased circulation of EMPs and elevated total ROS-
production. ApoE−/− mice showed an increased circulation of EMPs, elevated total ROS-production and above all augmented atherosclerotic plaque develop-
ment in chronic vascular injury. AIM2 might therefore play a role in vascular biology following acute and chronic vessel injury.

Acknowledgement/Funding: Else-Kröner-Fresenius-Stiftung (Bad Homburg,
Germany) and the medical faculty of the Rheinische Friedrich-Wilhelms Univer-
sität Bonn

P4524 | BENCH Hepcidin was produced from plaque macrophages and related to oxidative stress in endothelial cells
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Hepcidin has been demonstrated to be a key peptide in the regulation of iron homeostasis and chronic inflammation. Hepcidin binds to the iron transporter Fer-
ron-1 (FRTN) on the cell surface and inhibits FRTN internalization and iron acqui-
dition. As a result, the intracellular iron level is elevated. Previous study showed that the serum hepcidin and macrophage iron levels correlated with MCP-1 re-
lease and vascular damage in patients with metabolic syndrome. It is not deter-
mined whether hepcidin play an adverse role in coronary artery disease. Thus, we examined 1) the expression of hepcidin in the human blood and macrophages and 2) the effects of hepcidin on cultured human coronary artery endothelial cells (HCAECs).

Methods and results: The serum levels of hepcidin-25 were quantitatively mea-
sured with the use of a liquid chromatography-tandem mass spectrometry-based assay system (LC-MS/MS). Serum levels of the hepcidin and IL-6 were mea-
sured in coronary and peripheral blood of patients with acute myocardial infar-
cion. Coronary blood aspirated from culprit arteries contained 3-fold higher levels of hepcidin and IL-6 compared with the peripheral blood (n=16, P < 0.05, respec-
tively). Immunohistochemical staining revealed that macrophages of the plaques in solid component of the aspirates were immunoreactive for hepcidin-25, mono-
cyte chemoattractant protein-1 and matrix metalloproteinases-9. In coronary ar-
teries from type 2 diabetic malets, hepcidin-positive macrophages were detected in the shoulder of atheromatous plaques independently of iron deposition.

In vitro study was performed using human monocyte cells and coronary artery endothelial cells (HCAECs). First, Real-time PCR analysis showed that hepcidin mRNA levels in the monocytes treated with IL-6 and differentiated macrophages were significantly higher than in the regular monocytes (P < 0.05, respectively). Macrophage and HCAECs treated with hepcidin exhibited reduced the cell num-
ber and expressions of ferroportin. Especially HCAECs treated with hepcidin in-
creased expression of NADPH oxidase compared with the control (P < 0.05, re-
spectively).

Conclusions: Hepcidin produced in the macrophages of coronary plaques may induce oxidative stress and impair growth potential in HCAECs, which leads to the plaque progression and vulnerability.

P4525 | BENCH Inflammammasome-induced endothelial microparticles impair cellular function in recipient cells
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Background: The inflammasome is a multi-protein signaling platform necessary for the activation of highly proinflammatory cytokines of the IL-1 family and is an important mediator of vascular inflammation resulting in atherosclerosis. Mi-
croparticles (MPs) are small membrane vesicles, specifically packaged and re-
leased from apoptotic or activated cells for intercellular communication. Endothe-

cial cells-derived MPs have recently been linked to all stages of atherosclerosis. Whether inflammasome activation in endothelial cells mediates MP release and if these MPs exert biological effects on recipient vascular cells is unknown.

Methods and results: Human coronary artery endothelial cells (HCAEC) were
primed with 1 μg/ml LPS and subsequently stimulated with 20 μg/ml Nigericin. This resulted in specific inflammasome activation as detected by a significant upreg-
ulation of Caspase-1/ IL-1β mRNA and Caspase-1 protein in RT-PCR and West-
ernblots respectively (Figure 1). Importantly, inflammasome activation led to a time-
and dose-dependent formation of endothelial microparticles (EMP) (Fig-
ure 2). Flow cytometric comparison of EMP with beads of known size and elec-
tron microscopic imaging confirmed an EMP-size between 0.1 and 1 μm (Fig-
ure 3). Time dependent EMP-uptake by recipient vascular cells could be illus-
trated by fluorescence-microscopic imaging of PKH26 labeled EMP (Figure 4).

These EMPs released from inflammasome activated cells had detrimental biolog-
ic effects on recipient endothelial cells. Both viability assay and scratch assays showed significant reduction of cell viability, migration and proliferation 4h after treatment (Figure 5).

Conclusions: We show for the first time that Nigericin, an established inflamma-
some activator, leads to inflammasome activation and release of microparticles by endothelial cells. Furthermore, we could demonstrate that these microparticles are taken up by recipient vascular cells and thereby cause cell death accompa-
nied with reduced migration and proliferation.

Acknowledgement/Funding: Else-Kröner-Fresenius-Stiftung Research grant

P4526 | BENCH Role of an adipokine omentin in preventing the development of atherosclerosis
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Background: Obesity contributes to the development of various atherosclerotic
diseases. Omentin is an adipokine that is down-regulated in patients with obese
complications including coronary artery disease. Here, we investigated whether omen-
tin affects the development of atherosclerosis in vivo.

Methods/Results: To overexpress human omentin in a model of atheroscle-
rosis, apolipoprotein E-knockout (apoE-KO) mice were crossed with transgenic
mice expressing the human omentin gene in fat tissue (OMF-Tg) mice. Plasma
levels of human omentin in apoE-KO/OMT-Tg mice were approximately three-
fold higher than in those of healthy human subjects, whereas human omentin
was not detectable in apoE-KO mice. There were no differences in morphome-
tric and metabolic parameters between apoE-KO/OMF-Tg and apoE-KO mice.
ApoE-KO/OMT-Tg mice had decreases in atherosclerotic lesion areas, apoptotic
activities, macrophage content and expression of inflammation-related genes in
aorta compared with apoE-KO mice. Treatment of cultured human monocyte-
derived macrophages with human omentin protein led to reduction of intracellu-
lar cholesterol ester content, lipid droplet formation and expression of scavenger
receptors including macrophage scavenger receptor class A (SR-A) and CD36.
Treatment of cultured macrophages with omentin attenuated the inflammatory re-
sponse and promotes the anti-inflammatory phenotype. The suppressive effects

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The multiple cellular facets of atherosclerosis I 901
of omentin on lipid droplet formation and inflammatory response in macrophages were reversed by inhibition of Akt signaling pathway.  

**Conclusion:** Our data suggest that omentin acts an adipokine that promotes the progression of atherosclerosis by suppression of foam cell formation and inflammatory response of macrophages.

**Acknowledgement/Funding:** This research is supported by Grant-in-Aid for Scientific Research and Grant-in-Aid for Challenging Exploratory Research.

P4527 | BENCH  
FOXO3a induces vascular smooth muscle cell apoptosis through MMP-13-mediated cleavage of fibronectin: a novel pathway with implications for atherosclerotic plaque rupture  
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**Introduction:** Rupture of atherosclerotic plaques account for approximately 75% of fatal myocardial infarctions. Vulnerable plaques are characterised by heightened vascular smooth muscle cell (VSMC) apoptosis within the fibrous cap and loss of the surrounding extracellular matrix (ECM). However, the exact underlying causes of these processes remain unknown. Our laboratory has previously found that VSMCs in human atherosclerotic plaques show impaired inhibition of the pro-apoptotic transcription factor FOXO3a and preliminary evidence suggests that matrix metalloproteinase-13 (MMP-13) is a key transcriptional target of FOXO3a in VSMCs both in vitro and in vivo. Therefore, we investigated the role of MMP-13 in FOXO3a-mediated VSMC apoptosis.

**Methods:** We generated rat VSMCs that stably overexpress a transgenic FOXO3a mutant (FOXO3aΔA3ER) which can be selectively activated by 4-hydroxytamoxifen (OHT) and changes in protein expression were monitored by qPCR, Western blotting, and immunocytochemistry. MMP activity was assayed using gelatin zymography and apoptosis was assessed using Annexin V/Propidium iodide flow cytometry.

**Results:** Activation of FOXO3a resulted in substantial increases in apoptosis in FOXO3aΔA3ER cells (3.4±1.1-fold). In addition to the upregulation of pro-apoptotic target genes such as BIM (18.9±0.5-fold), FOXO3a potently upregulated mRNA expression of the matrix metalloproteinase MMP-13 (3568±130-fold) and dramatically increased the expression and cleavage of MMP-13 protein, indicating greater activation. MMPs are a family of secreted proteases known to be involved in ECM degradation, but a novel role for MMP-13 in VSMC death was identified as FOXO3a-mediated apoptosis was significantly reversed following activation of MMP-13 activity using siRNA knockdown (3.0±0.6 vs. 1.0±0.1-fold) and pharmacological inhibition (4.3±1.1 vs. 1.7±0.3-fold). Finally, we identified a potential substrate of MMP-13 in the ECM, in the form of the secreted glycoprotein, fibronectin. Evidence for this was provided by the observation that prominent cleavage of fibronectin occurs following the activation of FOXO3a and supplementation with a peptide that generated a strong protective effect against apoptosis (3.5±1.4 vs. 1.9±0.9-fold).

**Conclusions:** FOXO3a induces VSMC apoptosis predominantly via MMP-13, possibly due to degradation of protective fibronectin in the ECM. We predict that FOXO3a is a potent inducer of vulnerable plaques in atherosclerosis through this mechanism.

**Acknowledgement/Funding:** British Heart Foundation

P4528 | BENCH  
An ex vivo model of human atherosclerotic plaque culture for studying of the changes of the atherosclerotic plaque cells in the course of the inflammatory process.  
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**Introduction:** Atherosclerosis is considered to be associated with inflammatory process in the artery wall. Many cell types are involved in atherosclerotic plaque progression including endothelial cells, smooth muscle cells, macrophages and lymphocytes. Although many experimental models of atherosclerosis, such as animal or single cell cultures, have been developed, none of them faithfully reproduce the architecture of human atherosclerotic plaques and the complexity of cell-cell interactions within it.

**Purpose:** The aim of this research was to develop an adequate ex vivo model for studying of the changes of the atherosclerotic plaque cells in the course of the inflammatory process.

**Methods:** We obtained plaques from patients who underwent carotid endarterectomy. Plaque tissue was dissected into several ring-shaped slices, and these slices were cultured at the liquid/air interface on collagen sponges. Using our original protocols of cell isolation from plaques, we analyzed the distribution of lymphocyte subtypes in the ex vivo plaques with flow cytometry.

**Results:** The amount of B-lymphocytes in plaques before culture was significantly lower than the amount of T-lymphocytes (in average, 47±76 vs 2383±579 cells per 100 mg of tissue). However, substantial amount of B cells was still observed in plaques after 13 days of culture (40±27 cells per 100 mg of tissue). B-lymphocytes were preserved in plaque tissues during 16 days of culturing, while both CD4+CD8- and CD4-CD8+ subsets presented (340±275 and 767±842 cells per 100 mg of tissue, respectively). Although after the first week in culture CD4+CD8-/CD4-CD8+ ratio decreased significantly (1.69±0.82 vs 0.81±0.64), the gross structure of the plaques was preserved.

**Conclusion:** We have developed a system of maintenance of atherosclerotic plaques ex vivo. In this system immune cell interactions during atherosclerotic plaque maturation/rupture can now be studied under controlled laboratory conditions.

**Acknowledgement/Funding:** Government of the Russian Federation (project No. 14. B25.31.0016)

P4529 | BEDSIDE  
Altered pattern of circulating monocyte subpopulations in patients with different stages of coronary artery disease.  
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**Background and objective:** The development of arteriosclerosis is a multi-factorial process and monocytes are known as key players in this scenario. The aim of the present study was to investigate the correlation of classical inflammation (CD14+CD16-), intermediate (CD14+CD16+) and non-classical platting (CD14dimCD16+) circulating monocyte subpopulations in patients with different stages of coronary artery disease (CAD).

**Methods:** Peripheral blood was collected from 225 angiographically documented CAD patients with a first-time acute myocardial infarction (MI, n=110), CAD with a recurrence of MI (CAD+MI, n=46), stable CAD without any acute myocardial ischemia (CAD, n=69) or healthy control patients (n=51). Peripheral blood mononuclear cells (PBMC) were isolated from whole blood by ficoll gradient centrifugation. After negative selection of residual non-mononuclear cells an analysis was performed according to their CD14/CD16 surface expression using established protocols for FACS-analysis (LSR II BD Biosciences). The monocyte subpopulations were confirmed by means of different markers using real-time PCR (CCR2, CR5, CXC1R, CX3CR1, IL1R4, NuR7, GLEC4D and SIGLEC10) which were in line with current literature underlining an adequate characterisation of the subsets.

**Results:** The inflammatory (CD14++CD16-) and intermediate (CD14+CD16+) monocyte subpopulations were significantly increased in the peripheral blood of patients compared to healthy controls (P<0.001). However, the patrolling monocyte subpopulation (CD14dimCD16+) was significantly decreased in patients with MI and recurrence of MI compared to healthy controls and patients with stable CAD (P<0.001, P<0.001).

**Conclusion:** Our results indicate that the inflammatory (CD14++CD16-) and intermediate (CD14+CD16+) monocyte subpopulations are increased in patients with CAD irrespective of acute ischemia and thereby potentially involved in maintaining the local inflammatory process within the diseased vessel wall. By contrast, the patrolling (CD14dimCD16+) monocyte population are solely decreased in patients with acute ischemia suggesting a shift between monocyte subpopulations in different stages of CAD.

P4530 | BEDSIDE  
Micro RNAs expression in cerebral ischemia resulting from carotid artery stenosis: the immediate findings and long-term prognosis  
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As a consequence of cerebral ischemic event (CIE) resulting from the carotid artery stenosis (CAS) many circulating micro RNAs (miRs) may be potentially up or downregulated.  

In the present study we investigated the expression of heart and brain derived circulating miRs in subjects with recent CIE related to CAS, and the potential relationship between miRs release and future cardiovascular events.  

**Methods:** Study group comprised 94 consecutive patients (57 M; mean age 68.7±9.1 years) with significant CAS (mean 84±15%) recruited between September 2012 and June 2013. Circulating small miRs (miR-1, miR-133a, miR-133b, miR-145, miR-499, miR-372, miR-373, miR-124, miR-16) were assessed from blood samples. Group I comprised 73 subjects (47M, age 69.1±9.6 years) with CAS who suffered from CIE during last 12 weeks. Group II comprised 21 patients (10M, age 70.3±7.1 years) with asymptomatic CAS. All patients underwent carotid artery tomography without complications. The incidences of cardiovascular events, including cardiovascular death (CVD), acute myocardial infarction (MI) and recurrent CIE, and composite end-point (D/M/CIE) were recorded prospectively during the mean period of 39±34.2 months (range 3-50 months).

**Results:** In group II patients showed a significant difference in expression of miR-1 (0.581±0.62 vs. 0.350±0.05; p<0.05), miR-133a (1.30±2.48 vs. 1.64±2.18; p<0.05), miR-133b (2.32±4.20 vs. 2.77±2.36; p<0.05), while there was no difference in expression of miR-1 (0.25±0.29 vs. 0.32±0.32; p=0.03), miR-
The coronary artery disease group was defined by the presence of at least one coronary stenosis >50% of luminal diameter by coronary angiogram. Statistical analyses were performed with SPSS for Windows version 15 (SPSS Inc. Chicago, IL, USA). Comparison between the results of the different groups was made with the Student’s t test or with the analysis of variance. The Pearson correlation coefficient was calculated to estimate the linear correlations between variables. Multiple linear regression models were used to identify independent factors (Odds ratio [OR]; 95% Confidence Interval [95% CI]).

Results: Patients with diabetes had significantly lower PGC1α and UCPI expression in epicardial adipose tissue than those without diabetes (p=0.015 and p=0.031, respectively). Epicardial PGC1α mRNA levels from patients with coronary artery disease associated positively with HDL-cholesterol (r=0.498, p=0.004), epicardial UCPI mRNA levels (r=0.307, p=0.043) and left ventricular ejection fraction (r=0.376, P=0.014), and negatively with circulating triglycerides (r=0.468, p=0.005), body mass index (r=0.431, P=0.025) and GAT activity (r=0.425, p=0.034). Epicardial PGC1α expression was dependent on the number of injured coronary arteries (p=0.010) and logistic regression analysis showed that the epicardial expression of PGC1α exerted a protective effect against diabetes (OR=0.523; 95% CI: 0.227, 0.987; p<0.05) and coronary lesions (OR=0.130; 95% CI: 0.018, 0.916; p<0.05).

Conclusions: In patients with coronary artery disease, type 2 diabetes is associated with significantly lower epicardial PGC1α and UCPI expression. The association was calculated to estimate the linear correlations between variables.
that are enriched in CAD/MI patients, on sGC activity and the therapeutic potential of sGC stimulators in vitro.

Methods and results: Coding GUCY1A3 variants were cloned and expressed in HEK 293 cells. Protein levels and dimerization capability with the α1-subunit were analysed by immunoblotting and co-immunoprecipitation, respectively. Enzyme kinetics of wild-type (WT) and variants indicated that the α1-subunit with coding GUCY1A3 variants lost the α1-variants dimerized with the α1-subunit. Five variants displayed decreased cGMP production upon stimulation with the NO donor (p < 0.001). In transgenic mice, the sGC variant α1-2272 led to a marked impaired cGMP formation in all of these variants (p < 0.01). Except for the variant leading to decreased protein, cGMP amounts reached the wild-type NO-induced level after addition of BAY 41–2272.

Conclusions: Rare coding variants in GUCY1A3 lead to reduced cGMP formation which can be rescued by a sGC stimulator in vitro. This might therefore represent a novel treatment strategy for patients at risk with coding GUCY1A3 variants.

P4537 | BENCH
Platelet P2Y12 inhibitors enhance expansion of the intermediate monocyte population following systemic inflammation in humans

Introduction: Circulating intermediate monocytes increase during acute coronary syndromes (ACS), mobilized to the systemic circulation from a marginal pool that is closely associated with the endothelium. Platelet-monocyte interactions upregulate monocyte expression of adhesion molecules and reinforce monocyte adhesion to endothelium. P2Y12 inhibitors reduce platelet-monocyte interactions and we hypothesized that this may impact upon mobilization of intermediate monocytes, as they preferentially form aggregates with platelets. This has important implications during ACS, since emerging evidence suggests intermediate monocytes might be anti-inflammatory and involved in tissue repair.

Purpose: To determine the effect of platelet P2Y12 inhibitors on intermediate monocytes mobilization in an experimental human model of systemic inflammation.

Methods: Thirty healthy volunteers were randomized to receive the platelet P2Y12 inhibitors, clopidogrel 75 mg od (n = 10) or ticagrelor 90 mg bd (n = 10) or no antiplatelet medication (controls; n = 10) for one week. E.coli endotoxin (LPS) 2 mg/kg was then administered intravenously using a well-established method. Monocytes were phenotyped and quantified using flow cytometry according to established definitions.

Results: In the control group, LPS administration induced a marked 6-fold increase in intermediate monocytes at 24 hours compared to baseline (0.18±0.04 vs. 0.33±0.01 x 10^9/ml; p < 0.001). Compared to control, expansion of the intermediate monocyte population at 24 hours was potentiated by both clopidogrel (0.34±0.06; p < 0.001) and ticagrelor (0.28±0.05; p = 0.005). This was associated with inhibition of LPS-induced platelet-monocyte aggregate formation by both P2Y12 inhibitors. The expanded intermediate monocyte population was phenotypically similar to baseline intermediate monocytes as demonstrated by similar levels of CD14, CD16, CCR2, CXCR2, TLR2 and TLR4.

Conclusions: These findings suggest that platelet-monocyte interactions are an important regulator of intermediate monocyte mobilization. Platelet P2Y12 inhibitors augment the expansion of the intermediate monocyte population that occurs following systemic inflammation. Further work is needed to delineate the precise role of intermediate monocytes during ACS and to clarify their involvement in inflammation and tissue repair.

Acknowledgement/Funding: Funded by the Medical Research Council (UK)

P4538 | BENCH
The expression of protease-activated receptors 1 and 2 in dilated cardiomyopathy correlate with myocardial inflammation and ventricular dysfunction

Background and aims: Dilated cardiomyopathy (DCM) with ventricular enlargement due to pathological remodeling as the most common form of non-ischemic cardiomyopathy is a leading cause of congestive heart failure. The protease-activated receptors (PARs) 1 and 2 belong to a family of G-protein coupled receptors. In vitro and in vivo studies showed that the activation of PAR1 and PAR2 plays a crucial role in cardiac diseases. Their role in DCM has not been studied so far. Here, we sought to examine the role of PARs in DCM regarding coagulation, inflammation and heart function.

Methods: In 101 DCM (ejection fraction (EF) < 50%, left ventricular end-diastolic dimension (LVEDD) > 2.5 cm) patients, with or without DCM (EF) < 50%, we compared acute myocardial infarction (AMI) patients with coding GUCY1A3 variants (α-GalCer/DC) to controls. In controls, LPS administration induced a marked 6-fold increase in intermediate monocytes at 24 hours compared to baseline (0.18±0.04 vs. 0.33±0.01 x 10^9/ml; p < 0.001). Compared to control, expansion of the intermediate monocyte population at 24 hours was potentiated by both clopidogrel (0.34±0.06; p < 0.001) and ticagrelor (0.28±0.05; p = 0.005). This was associated with inhibition of LPS-induced platelet-monocyte aggregate formation by both P2Y12 inhibitors. The expanded intermediate monocyte population was phenotypically similar to baseline intermediate monocytes as demonstrated by similar levels of CD14, CD16, CCR2, CXCR2, TLR2 and TLR4. These findings suggest that platelet-monocyte interactions are an important regulator of intermediate monocyte mobilization. Platelet P2Y12 inhibitors augment the expansion of the intermediate monocyte population that occurs following systemic inflammation. Further work is needed to delineate the precise role of intermediate monocytes during ACS and to clarify their involvement in inflammation and tissue repair.

Acknowledgement/Funding: Funded by the Medical Research Council (UK)

P4539 | BENCH
The expression of protease-activated receptors 1 and 2 in dilated cardiomyopathy correlate with myocardial inflammation and ventricular dysfunction

Background and aims: Dilated cardiomyopathy (DCM) with ventricular enlargement due to pathological remodeling as the most common form of non-ischemic cardiomyopathy is a leading cause of congestive heart failure. The protease-activated receptors (PARs) 1 and 2 belong to a family of G-protein coupled receptors. In vitro and in vivo studies showed that the activation of PAR1 and PAR2 plays a crucial role in cardiac diseases. Their role in DCM has not been studied so far. Here, we sought to examine the role of PARs in DCM regarding coagulation, inflammation and heart function.

Methods: In 101 DCM (ejection fraction (EF) < 50%, left ventricular end-diastolic dimension (LVEDD) > 2.5 cm) patients, with or without DCM (EF) < 50%, we compared acute myocardial infarction (AMI) patients with coding GUCY1A3 variants (α-GalCer/DC) to controls. In controls, LPS administration induced a marked 6-fold increase in intermediate monocytes at 24 hours compared to baseline (0.18±0.04 vs. 0.33±0.01 x 10^9/ml; p < 0.001). Compared to control, expansion of the intermediate monocyte population at 24 hours was potentiated by both clopidogrel (0.34±0.06; p < 0.001) and ticagrelor (0.28±0.05; p = 0.005). This was associated with inhibition of LPS-induced platelet-monocyte aggregate formation by both P2Y12 inhibitors. The expanded intermediate monocyte population was phenotypically similar to baseline intermediate monocytes as demonstrated by similar levels of CD14, CD16, CCR2, CXCR2, TLR2 and TLR4. These findings suggest that platelet-monocyte interactions are an important regulator of intermediate monocyte mobilization. Platelet P2Y12 inhibitors augment the expansion of the intermediate monocyte population that occurs following systemic inflammation. Further work is needed to delineate the precise role of intermediate monocytes during ACS and to clarify their involvement in inflammation and tissue repair.

Acknowledgement/Funding: Funded by the Medical Research Council (UK)
Circulating miR-200c is up-regulated in FH; this increase is directly related to CRP and glycemia and unrelated to plasma lipids. This modulation might be ascribed to an increase of oxidative stress and inflammation associated to CRP and glycemia and unrelated to plasma lipids. This modulation might be ascribed to an increase of oxidative stress and inflammation associated to CRP and glycemia and unrelated to plasma lipids.

**Conclusion:**
PAR1 and PAR2 expression in endomyocardial biopsies of patients with dilated cardiomyopathy was positively correlated with myocardial inflammation and negatively correlated with perfusion. PAR1 expression increases were significantly related to greater number of coronary stenoses.

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**Background:**
Hypercholesterolemia is a major risk factor for atherosclerosis and the development of cardiovascular disease (CVD). Recent studies have shown that some miRNAs play a role in the low-grade inflammatory process induced by oxidative stress and inflammation. These miRNAs are associated with cardiovascular disease risk factors and may have a role in the progression of atherosclerosis.

**Methods:**
Familial hypercholesterolemia patients (FH) and healthy subjects (HS) were enrolled in the study. Circulating miR-200c was measured by quantitative real-time PCR.

**Results:**
Circulating miR-200c was significantly up-regulated in FH compared to HS (4.00±0.48-fold increase, P<0.05). Interestingly, miR-200c did not correlate with TC, LDL-C, HDL-C, triglycerides (TG), blood glucose (GLI), and C-reactive protein (CRP) (mg/dl). This finding indicates that circulating miR-200c may not be a useful biomarker for the assessment of cardiovascular risk.

**Conclusion:**
Circulating miR-200c is up-regulated in FH; this increase is directly related to CRP and glycemia and unrelated to plasma lipids. This modulation might be ascribed to an increase of oxidative stress and inflammation associated to CRP and glycemia and unrelated to plasma lipids.

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**Background:**
Carotid endarterectomy (CEA) of rupture-prone plaques reduces the risk of future stroke. However, identification of these so-called vulnerable plaques is challenging. One characteristic of plaque vulnerability is the presence of active macrocalcifications, while macrocalcifications are considered to be associated with stable plaques. Previous studies have shown the feasibility of 18F-sodium fluoride (18F-NaF) PET to identify active macrocalcifications in plaques. However, it is unclear in which stage of plaque progression macrocalcifications occur and whether the amount of 18F-NaF uptake is different between symptomatic and asymptomatic patients.

**Purpose:**
The primary goal of the present study was to compare ex vivo 18F-NaF uptake in asymptomatic and symptomatic human carotid plaques. The secondary goal was to compare 18F-NaF uptake in carotid plaques with non-macrocalcified renal arteries.

**Methods:**
Carotid plaques from 13 patients who underwent CEA (13 asymptomatic and 2 symptomatic) were enrolled in the study. Macrocalcifications were identified by CT and macrocalcified plaques were defined as plaques with a percentage of macrocalcification of at least 15%.

**Results:**
18F-NaF uptake was significantly higher in symptomatic and asymptomatic plaques than in non-macrocalcified plaques. Group analysis revealed a significant 18F-NaF uptake already in the absence of macrocalcifications, potentially limiting its use for early cardiovascular risk assessment.

**Conclusion:**
The identification of vulnerable plaques in patients at risk for an acute vascular event potentially allows early preventative interventions. However, current studies suggest that microcalcifications assessed by ex vivo 18F-NaF uptake already occur in the absence of macrocalcifications, potentially limiting its use for early cardiovascular risk assessment.

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**Background:**
Titanium dioxide (TiO2) films have superior biocompatibility and may be effective as drug-binding matrices for drug-eluting stents (DES). Microcalcifications not only occur abundantly in carotid plaques, but also to a lesser extent in renal arteries without macrocalcifications. This underscores that microcalcification is an ongoing process in human arteries, even in the absence of macrocalcifications.

**Clinical relevance:**
The identification of vulnerable plaques in patients at risk for an acute vascular event potentially allows early preventative interventions. However, current studies suggest that microcalcifications assessed by ex vivo 18F-NaF uptake already occur in the absence of macrocalcifications, potentially limiting its use for early cardiovascular risk assessment.

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**Background:**
A novel polymer-free DES coated with everolimus using nitrogen-doped titanium dioxide film deposition in a porcine coronary restenosis model.

**Objectives:**
We sought to evaluate efficacy of polymer-free DES coated with everolimus using nitrogen-doped TiO2 film deposition in a porcine coronary restenosis model.

**Methods:**
Forty coronary arteries in 20 pigs were randomly allocated to group 1 (bare-metal stent (BMS), 3.0×18 mm, n=10), group 2 (BMS with nitrogen-doped
TI02 film deposition, 3.0±18 mm, n=10), group 3 [commercial everolimus-eluting stent, 3.0±18 mm, n=10], and group 4 (polymer-free everolimus-eluting stent using nitrogen-doped TI02 film deposition, 3.0±18 mm, n=10). Stents were randomly implanted in the left anterior descending coronary artery and left circumflex artery with stent: artery ratio of 1:3. Four weeks later, pigs underwent follow-up coronary angiography and were sacrificed for histopathologic analysis.

Results: Percent area stenosis was greater in group 1 compared to group 3 and 4 (46.4±13.8% vs. 30.2±11.7%, p<0.0001) and 2, compared to groups 3 and 4 (0.87±0.67 vs. 0.75±0.61 vs. 0.75±0.61 vs. 2.27±0.24 vs. 1.75±0.31, respectively, p<0.001). Injury score and inflammation scores were not different. Comparison between DES showed higher fibrin score in group 3 than group 4 (2.7±0.24 vs. 1.75±0.31, p=0.023).

Morphometric measurements by stent type

<table>
<thead>
<tr>
<th>Group</th>
<th>IEL area (mm²)</th>
<th>Lumen area (mm²)</th>
<th>Neointima area (mm²)</th>
<th>Area stenosis (%)</th>
<th>Injury score</th>
<th>Fibrin score</th>
<th>Inflammation score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (n=10)</td>
<td>4.7±0.44</td>
<td>2.55±0.75</td>
<td>2.19±0.65</td>
<td>46.1±13.8</td>
<td>1.19±0.13</td>
<td>0.87±0.67</td>
<td>1.37±0.55</td>
</tr>
<tr>
<td>Group 2 (n=10)</td>
<td>4.45±0.48</td>
<td>2.81±0.56</td>
<td>1.63±0.47</td>
<td>36.7±9.6</td>
<td>1.14±0.13</td>
<td>0.76±0.61</td>
<td>1.14±0.16</td>
</tr>
<tr>
<td>Group 3 (n=10)</td>
<td>4.84±0.39</td>
<td>3.89±0.65</td>
<td>1.46±0.56</td>
<td>37.9±16.9</td>
<td>1.19±0.25</td>
<td>2.27±0.24</td>
<td>1.36±0.39</td>
</tr>
<tr>
<td>Group 4 (n=10)</td>
<td>4.64±0.46</td>
<td>3.38±0.65</td>
<td>1.35±0.42</td>
<td>30.2±11.7</td>
<td>1.06±0.08</td>
<td>2.27±0.24</td>
<td>1.08±0.05</td>
</tr>
</tbody>
</table>

IEL = internal elastic lamina.

Conclusions: In a porcine model of coronary restenosis, polymer-free DES using nitrogen-doped TI02 film deposition shows higher biocompatibility and compares favorably with a commercial DES.

Acknowledgement/Funding: This research was supported by the Commercial-izations Promotion Agency for R&D Outcomes (COMPA) funded by the Ministry of Science, Information and Com

P4543 | BENCH

Single nucleotide polymorphisms of adiponectin gene and decreased adiponectin plasma level are associated with the risk of myocardial infarction in young age

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Adiponectin is a protein involved in anti-inflammatory processes in atherosclerotic lesions. The aim of the study was to investigate the role of 5 adiponectin gene SNPs (rs17300539 G:A and rs8223807 T:C in promoter, rs1501299 G:T in intron 2, rs7256371 C:T and rs17366743 T:C in exon 3) on the risk of myocardial infarction (MI) in young age in association with total and high molecular weight (HMW) adiponectin plasma.

Patients and methods: The studied group (MI<50) consisted of 143 patients (112 men and 31 women), aged under 50 (36–49) with MI. The control groups consisted of 155 healthy people (97 men and 58 women), aged 38–47 and 202 patients (112 men and 31 women), aged under 50 (36–49) with MI. The control groups consisted of 155 healthy people (97 men and 58 women), aged 38–47 and 202 patients (112 men and 31 women), aged under 50 (36–49) with MI. The control groups consisted of 155 healthy people (97 men and 58 women), aged 38–47 and 202 patients (112 men and 31 women), aged under 50 (36–49) with MI. The control groups consisted of 155 healthy people (97 men and 58 women), aged 38–47 and 202 patients (112 men and 31 women), aged under 50 (36–49) with MI.

Table 1

<table>
<thead>
<tr>
<th>SNPs</th>
<th>Genotypes</th>
<th>MI &lt;50 vs healthy control OR (95% CI), p</th>
<th>MI &lt;50 vs MI &lt;50 OR (95% CI), p</th>
</tr>
</thead>
<tbody>
<tr>
<td>rs1501299</td>
<td>GT vs GG</td>
<td>0.67 (0.16–2.88, 0.595)</td>
<td>1.15 (0.57–2.30, 0.692)</td>
</tr>
<tr>
<td>TT vs GG</td>
<td>0.86 (0.47–19.32)</td>
<td>0.973 (0.25–2.07, 0.551)</td>
<td></td>
</tr>
<tr>
<td>rs17300539</td>
<td>GG vs AA+AA</td>
<td>0.21 (0.029–1.61, 0.134)</td>
<td></td>
</tr>
<tr>
<td>AA vs GG</td>
<td>–</td>
<td>14.28 (1.47–166.77, 0.023)</td>
<td></td>
</tr>
<tr>
<td>AA vs GG</td>
<td>–</td>
<td>5.04 (0.47–55.60, 0.011)</td>
<td></td>
</tr>
<tr>
<td>rs72566743</td>
<td>TT vs TC+CC</td>
<td>0.90 (0.28–163, 0.517)</td>
<td></td>
</tr>
<tr>
<td>rs7256371</td>
<td>CC vs CT+TT</td>
<td>33.3 (4–250, 0.001)</td>
<td>2.27 (1.05–5.00, 0.047)</td>
</tr>
<tr>
<td>rs8223807</td>
<td>TT vs CC+TC</td>
<td>0.91 (0.09–10.29, 0.943)</td>
<td>0.49 (0.30–2.35, 0.670)</td>
</tr>
</tbody>
</table>

Conclusions: Our study indicates a possible contribution of rs17300539 and rs7256371 ADIPOQ gene SNPs in the development of premature coronary artery disease and independent risk factors and rs8223807 and rs1501299 SNPs are associated with other atherosclerotic risk factors. The mechanism of ADIPOQ gene SNPs involvement in the pathogenesis of atherosclerosis remains unclear and requires further investigation.

Acknowledgement/Funding: grant nr 501-1-10-44-07 — Medical Centre of Postgraduate Education, Warsaw, Poland

P4544 | BENCH

Caffeic acid phenethyl ester ameliorates monocrotaline-induced pulmonary arterial hypertension through inhibiting ERK/NF-kB-STAT3 signaling pathway

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Background: Pulmonary arterial hypertension (PAH) is characterized by progres-
sive increase in vascular resistance and the remodeling of pulmonary arteries. Aberrant proliferation of pulmonary arterial smooth muscle cells (PASMCs) may contribute to the thickness and remodeling of vascular wall of pulmonary artery. Caffeic acid phenethyl ester (CAPE), the major ingredient of propolis, which is known to suppress several signal pathways associated with cell proliferation and inflammation, however, there is no previous publication to apply the possible therapeutic effect of CAPE in PAH model.

**Purpose:** First study to investigate the effect of CAPE on the treatment of PAH.

**Methods:** PAH was induced by the injection of monocrotaline (MCT) to SD rats weighing between 200–250 g. After 14 days of MCT injection, various CAPE dosages were administrated daily for further 2 weeks. To evaluate the effect of CAPE, the hemodynamic value, the hypertrophy of right ventricle, and the inflammation of MCT-induced PAH rats’ lung tissue were examined. In vitro human PASMCs cultured under hypoxia (3% O2) were treated with equivalent dosages of CAPE to investigate the underlying mechanisms.

**Results:** The administration of CAPE significantly reversed the hemodynamic values of MCT-induced PAH rats in a dose-dependent manner, including right ventricle systolic pressure (RVSP) and RV hypertrophy index. In vitro assay revealed that CAPE retarded the proliferation of human PASMCs which were cultured under hypoxic condition. In addition, CAPE also promoted the expression of senescence-associated β-galactosidase activity and the number of apoptotic cells of hypoxia human PASMCs. Western blotting showed that the phosphorylated lev- els that are associated with inflammation of MCT-induced PAH rats’ lung tissue were examined. In vitro human PASMCs cultured under hypoxia (3% O2) were treated with equivalent dosages of CAPE to investigate the underlying mechanisms.

**Conclusion:** CAPE was demonstrated for its therapeutic potential on the improvement of hemodynamic values of MCT-induced PAH rats. The effects of CAPE were evidenced by the suppression of hypoxia-induced proliferation of human PASMCs through the inhibition of the underlying mechanisms of ERK, AKT, and NF-κB activation by CAPE. Furthermore, the expression of of hif-1α mRNA which was transcriptionally mediated by NF-KB was also reduced following the treatment of CAPE on human PASMCs.

**Acknowledgement/Funding:** Kaohsiung veteran general hospital

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**P4545 | BENCH**

The role of the N-terminal fragment of cardiac myosin binding protein- C (mMyBP-C) in the initiation of inflammation in cardiovascular diseases

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**Background:** Cardiac myosin binding protein-C (mMyBP-C) has been identified as a novel biomarker for cardiovascular diseases such as myocardial infarction that are associated with inflammation in the heart. C0-C1f, the 40-kDa fragment of mMyBP-C consisting of C0 and C1 domains and the first 17 residues of the M-domain (amino acids 1–271), was shown to be cleaved and released from injured cardiomyocytes upon ischemia/reperfusion injury. C0-C1f was identified in the blood prior to the release of troponins or the full-length cMyBP-C, which in- creases its relevance for clinical diagnostics. The inflammation that is associated with cardiac injury is an essential component of cardiac diseases and the cardiac regeneration process. However, the initiation process of inflammation and the precise mechanisms involved are unclear.

**Purpose:** The aim of this project is to clarify the role of C0-C1f in the inflammatory processes initiated upon myocardial infarction.

**Methods and results:** We isolated murine bone marrow cells that were differentiated towards macrophages and treated these cells with different fragments of mMyBP-C. We observed that only the fragment C0-C1f activates macrophages, as differentiated towards macrophages and treated these cells with different fragments of mMyBP-C.

**Conclusion:** Here we report evidence that C0-C1f is important for the initiation of inflammatory signalling arising from cardiac injury. We determined that the N-terminal fragment of cardiac myosin binding protein- C (mMyBP-C) is a novel biomarker for cardiovascular diseases such as myocardial infarction that are associated with inflammation in the heart.

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**P4546 | BENCH**

Dexamethasone-encapsulated lipid nanoemulsions targeted to P-selectin reduce endothelium inflammation


**Background:** Inflammation is a common process associated with many patho- logical conditions, such as cardiovascular and neurological disorders. P-selectin is a cell adhesion molecule highly expressed specifically by endothelium in inflammatory disorders, and therefore a potential target for nanotherapy. We hypothesize that the coupling of a peptide with high affinity for P-selectin to the surface of nanoparticles will increase the binding to activated endothelium, thus improving the efflux of dexamethasone loaded with the potent anti-inflammatory drug, dexamethasone and able to target the inflamed endothelium and reduce its activation.

**Materials and methods:** Dexamethasone-loaded lipid nanoemulsions (dexLN) have been prepared using the ultrasonication method. Targeted dexLN were ob- tained by coupling a peptide with high affinity for P-selectin to the distal end of PEGylated phospholipid in the lipid monolayer of LN via a thioether bond (dex- PLN). The nanoemulsions were characterized for size by dynamic light scatter- ing (DLS), the amount of peptide coupled to the surface and for entrapment ef- ficiency of dexamethasone by HPLC. The binding and internalization of fluores- cently labeled dexPLN was determined in TNF-α activated endothelial cells (EC) using fluorescence microscopy and flow cytometry. The anti-inflammatory effects of dexPLN were investigated by assessing in EC the gene expression of several inflammatory mediators (interleukin-1β, tumor necrosis factor-α, IL-8, and MCP-1) using qPCR and by evaluating the monocytes adhesion and transmigration to/through EC monolayer using a Boyden chambers.

**Results:** 1) the hydrodynamic diameter of LN was 143±2.6 nm with a polydisper- sity index of 0.08±0.004; 2) the amount of P-selectin recognizing peptide to the LN monolayer was 9.25±0.5 μmol peptides/mg; 3) the entrapment efficiency of dex- amethasone into LN was high (95%); 4) P-selectin targeted LN bound specifically to the surface of activated EC and were efficiently internalized by the cells; 5) dexPLN reduced the gene expression of pro-inflammatory cytokines TNF-α, IL-1β and chemokines IL-8 and MCP-1 in activated EC and; 6) dexPLN is functional since it could inhibit monocyte adhesion and transmigration to/through activated EC.

**Conclusions:** (1) Targeted delivery of dexamethasone to TNF-α activated en- dothelium can be accomplished by lipid nanoemulsions covered with P-selectin specific peptide. (2) Our newly developed formulation is functional being able to reduce selectively the endothelial activation and the consequent monocyte infil- tration.

**Acknowledgement/Funding:** This work was supported by CNCS-UEFISCDI project numbers PN-II-TR-UE-2014-4-1837 and PN-II-ID-PCE-2011-3-0928.
minimize the critical roles of lung eosinophils in pulmonary artery remodelling processes. As an underlying mechanism, we found that dBQ GATA mice exhibited reduced accumulation of alternatively activated macrophages, which contributes for the pulmonary artery remodelling in hypoxia.

**Conclusion:** In this study, we identified an acute but transient eosinophil accumulation to the lung in hypoxia-induced PH model. Notably, eosinophil mediated accumulation of alternatively activated macrophages plays a central role in the pulmonary artery remodelling processes. These results indicate that pharmacological inhibition of eosinophil-activated alternatively activated macrophages axis can be a therapeutic target for the management of patients with PAH.

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**P4548 | BENCH**

The transmembrane protein Stamp2 protects from experimental pulmonary hypertension

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**Background and hypothesis:** The six-transmembrane protein of prostate (Stamp)-2 protects macrophages from overinflammatory output through actions on NADPH metabolism. Bone-marrow transplantation experiments revealed that Stamp2-deficient mice developed early arteriolar hypertension in normoxic conditions and showed severe early arteriolar hypertension in normoxic matured cells. Pulmonary arterial hypertension (PH) still harbors a grave prognosis with an annual mortality rate of 10%. As inflammatory processes are critical during initiation and progression of the disease, we hypothesized that Stamp2-deficient cell migratory properties could have a protective role in this setting. Thus, we assessed if Stamp2-deficient mice are predisposed to pulmonary inflammation and the development of hypoxia-induced pulmonary hypertension (PH). In a second step, we performed expression analyses in human idiopathic PH (IPAH) in rats and mice.

**Results:** To assess, if Stamp2-deficient mice are prone to the development of PH, Stamp2-deficient and wild type mice were exposed to chronic hypoxia (10%) or normoxia for 3 weeks. Hypoxia significantly increased right ventricular systolic pressure (RVSP) (30.3±1.4 mmHg) and induced right ventricular (RV) hypertrophy (RV weight/weight of left ventricle + septum). However, RVSP was significantly higher in Stamp2-deficient mice (33.4±0.7 mmHg, p<0.05), while there was no difference in RV hypertrophy between groups. Furthermore, RV contractility (dP/dT), heart rate and systemic arterial pressure were not statistically different. Expression of inflammatory cytokines (Interleukin-6, Interleukin-1 (IL-1)) were upregulated in hypoxia-induced PH. To assess Stamp2 expression in the lung, we performed immunohistochemical staining of human, rat and murine tissue sections. We found that Stamp2 is strongly expressed in pulmonary arteries in all tested species. Interestingly, Stamp2 expression was localized mainly to the endothelial layer of vessel walls. Thus, we assessed if Stamp2-deficient mice are predisposed to pulmonary inflammation and the development of hypoxia-induced pulmonary hypertension (PH). In a second step, we performed expression analyses in human idiopathic PH (IPAH) in rats and mice.

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**Conclusions:** These data demonstrate that Stamp2 is expressed in the lung and that expression is lower in human disease and animal models of PH. Decrease in Stamp2 expression may contribute to pathogenesis and reduce susceptibility towards hypoxia-induced PH. Taken together, these data suggest that loss of protective Stamp2 expression in the lung predisposes to the development of PH in human and experimental disease.

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**P4549 | BENCH**

Coagulative/FX XI promotes vascular inflammation in two models of arterial hypertension in mice and rats

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**Background:** Interactions of platelets, leukocytes and the vessel wall play pivotal roles in activating coagulation and precipitating thrombosis. High levels of angiogenesis to the lung in hypoxia-induced PH model require leukocyte recruitment and reactive oxygen species production within the vessel wall coupled to vascular dysfunction.

**Objective:** The aim of this work was to explore the role of thrombin-FXI feedback loop in animal models of arterial hypertension.

**Methods and results:** Here we report an upregulation of tissue factor, thrombin-dependent endothelial cell VCAM-1 expression and VLA-4 and platelet-dependent leukocyte adhesion to arterial conduits vessels in ATII-infused mice (150±4 pg/ml). ATII-induced vascular dysfunction and Co2, VCAM-1 and Ly6C mRNA expression were attenuated by thrombin inhibition, platelet-depletion as well as in HlR-4/1ba mice missing the extracellular ligand binding domains of GP1ba. Blockade of TF during ATII administration also attenuated vascular dysfunction and reduced vascular oxidative stress. Platelet rich plasma (PRP) of ATII-treated mice showed an increased thrombin evoked endogenous thrombin potential (ETP), whereas PRP from mice with pharmacological inhibition of FXI production by an antisense oligonucleotide (FXI ASO) or PRP of HlR-4/1ba mice failed to amplify ETP following chronic ATII exposure. These data show that a FXI-dependent thrombin generation feedback loop requires GP1ba on platelets and suggest that TF-initiated coagulation promotes additional thrombin formation on platelets to cause vascular inflammation.

**Conclusions:** To further evaluate the therapeutic potential of interrupting FXI synthesis and function, we conducted experiments with Mistrast rats using two different hypertension models. ATII infused as well as 5/6 nephrectomized (Nx) rats revealed endothelial dysfunction as well as vascular inflammation which were significantly attenuated by FXI ASO treatment. Furthermore, 5/6 Nx rats further showed changes in the composition of leukocytes and platelets in several co-morbid stress as well as an elevated ETP compared to sham operated rats that was prevented by pharmacological inhibition of FXI synthesis.

**Conclusion:** Our results reveal a critical role of platelet GP1ba to promote localized thrombin amplification and supporting a FXI-thrombin feedback loop in ATII-induced vascular inflammation in different animal models of hypertension. By using a FXI targeted approach, we propose a novel therapeutic possibility to interrupt this heterotypic cellular coagulation-inflammatory circuit.

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**P4550 | BENCH**

The effect of phoshoosterase 5 inhibitor sildenafil on IL-8 in diabetic cardiomyopathy: in vivo and in vitro study

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**Introduction:** T helper 1 (Th1) type inflammatory dominance with related biochemical alterations (thrombin-activate protein C) are considered as rate-limiting mediators, mostly cytokines and chemokines, is the common link in several co-morbid conditions such as cardiomyopathy, diabetes, atherosclerosis. I.e., IL-8 is tightly engaged in inflammation and cell/tissue damage in cardiovascular diseases (CVD). Sildenafil, phosphosterease 5 inhibitor used for erectile dysfunction, seems to be beneficial to treat different cardiac diseases, likely due to its anti-Th1 activity.

**Purpose:** We aimed to evaluate IL-8 in sera of diabetic patients at cardiomyopathy onset before and after 3 month chronic treatment with sildenafil (100 mg/day) vs. placebo; basal IL-8 was measured in healthy subjects. MIP-1 and MCP-1, also involved in CVD, were investigated.

**Methods:** Frozen samples from 30 subjects with diabetic cardiomyopathy enrolled in a previous study were analyzed by Luminex Bio-Plex platform; supernatants of human peripheral blood mononuclear cells (PBMC), from healthy anonymous donors, and human fetal aortic endothelial cells (Hfaec) were tested by ELISA. Inflammation-related biomarkers in PBMC and fetal samples, in accord with the principles outlined in the Declaration of Helsinki, and written consents from all subjects were obtained.

**Results:** IL-8 and MIP-1 basal levels were significantly higher in subjects with diabetic cardiomyopathy vs. healthy subjects (130.8±61.6 vs. 14.2±5.8; 239.8±51.4 vs. 150.8±38 pg/ml, respectively). Sildenafil, at variance with placebo, significantly decreased serum IL-8 (post-sildenafil 23.7±6 pg/ml), and, to a less extent, MIP-1 (post-sildenafil 167.8±17.3 pg/ml) and MCP-1 (pre- 60.9±7 pg/ml and post-sildenafil 46.9±4.2 pg/ml). ROC analysis identified significant cut-off values to predict the response to sildenafil, for IL-8: 12.2 pg/ml, sensitivity (SE) 0.93, specificity (SP) 0.90, area under curve (AUC) 0.94 (P<0.01); for MIP-1: 154.1 pg/ml, SE 0.68, SP 0.82, AUC 0.70 (P<0.05). Sildenafil significantly decreased PHA-induced IL-8 protein secretion (inhibition 58.8±11.1%, P<0.01) and gene expression (inhibition 33%±10.1%, P<0.05) in PBMC, no effect was found in endothelial cells.

**Conclusion:** Sildenafil intake counteracts Th1 biomediators in subjects with diabetic cardiomyopathy, especially targeting IL-8 at systemic level or released by PBMC during inflammation. Further interest since IL-8 is associated with cardiovascular homeostasis balance/disturbance associated with cardiac disease and shows the highest predictive value for response to sildenafil. Further studies are mandatory to suggest sildenafil as a novel pharmacological tool for CVD.
Activation of different inflammasomes in human monocyte subpopulations in coronary artery disease as revealed by NGS: feasibility of specific inhibition

A. Kräuter1, H. Giral1, F. Franke1, N. Kraenkel1, P. Jakob1, K. Kuschnerus1, T. F. Luescher1, A. Aikani2, U. Landmesser1, 1 Charité - Campus Benjamin Franklin, Campus Berlin, Germany; 2 Charité – Campus Berlin Center for Molecular Medicine, The Berlin Institute for Medical Systems Biology, Berlin, Germany.

Background: Monocytes and derived macrophages are critical in progression of atherosclerosis, the acute response to myocardial infarction (MI) and for post-MI remodeling leading to heart failure. Circulating human monocytes are classified in classical and non-classical monocytes. Additionally, intermediate (CD14+CD16-) and non-classical (CD14+CD16+) monocytes are defined. From more than 20 identified inflammasomes the NLRP3 inflammasome has been most extensively studied, but its regulation in human monocytes and derived macrophages has not yet been addressed. NLRP3-specific inhibition has been developed based on a CRISPR system available, however, has not been tested in human monocytes.

Purpose: We study the regulatory role of caspase-1 activating inflammasomes in coronary artery disease, and the putative divergences between monocyte populations including mechanisms driving initiation and inhibition of pyroptosis as well as the respective cell populations. These observations are relevant for further development of therapeutic approaches to modulate inflammation in CAD.

Methods and results: Peripheral blood mononuclear cells (PBMC) from stable coronary disease (CAD) or acute coronary syndrome (ACS) patients were isolated and the monocyte populations were sorted based on their expression of CD14 and CD16. RNA was isolated from monocyte populations of CAD patients and controls and long and small RNA Next Generation Sequencing was performed using the Illumina system. Bioinformatic analysis of the data obtained showed clear clustering of transcripts according to the monocyte population, suggesting numerous divergent functional roles. We could also identify relevant differences between different monocyte populations in the inflammatory machinery involving significant expression differences not only in the most well-characterized NLRP3, but also in other inflammasomes, namely NLRP12 and NLRP6, which have not yet been associated so far with CAD. These inflammasomes have been identified to both inhibit and activate inflammatory signaling. We could for the first time show a different gene and protein expression of both the NLRP3 and the NLRP12 between the classical and non-classical monocytes. Additionally, we performed a Caspase-1 activity assay (FAM-FLICA) using MCC950 NLRP3 inhibitor. Apart from higher activity in intermediate/monocytes of CAD patients we could show that Caspase-1 activity of the classical monocytes could not be reversed by MCC950.

Conclusions: NGS of monocyte subpopulations leads to new insights in their differential transcriptome. NLRP12 and NLRP6 inflammasomes in addition to NLRP3 showed differential expression between monocyte populations. Inhibition of NLRP3 with MCC950 failed to restore the basal Caspase-1 activity in non-classical monocytes of CAD patients, implying a potential role of other inflammasomes. Our observations are relevant for development of potential therapeutic approaches to modulate inflammation in CAD.

Acknowledgement/Funding: DZH2, SNF, BIH

Leukocyte-derived microvesicles are increased in patients with coronary disease: impact on endothelial regeneration and repair

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Background: We and others have previously observed increased levels of leukocyte-as well as endothelial-derived microvesicles in the circulation of patients with coronary artery disease (CAD). The aim of this study is to unravel differential effects on endothelial function conveyed by endothelial-derived and leukocyte-derived microvesicles.

Methods: Total shed microvesicles (SMV) were isolated from plasma of healthy subjects or patients with CAD. Flow cytometry was used to quantify platelet, endothelial cell and leukocyte-derived MVs. Endothelial and leukocyte-derived MVs were isolated from the supernatant of cultured human aortic endothelial cells and peripheral blood leukocytes, respectively. The capacity of SMV and cell-derived MV to support human aortic endothelial cell survival, inflammatory activation, re-endothelialisation and trans-endothelial resistance - a measure of endothelial layer permeability - was assessed following ex vivo exposure of the endothelial cells to SMV.

Results: While SMV of healthy donors (H) supported in vitro re-endothelialisation (27.7±11.3% increase vs. PBS), SMVs from CAD patients had lost this capacity (0.8%±8.5% decrease vs. PBS). Leukocyte-derived and endothelial cell-derived SMVs of CAD patients promoted hemostatic properties and delayed endothelial wound closure (-20±27% vs. endothelial MVs). Endothelial MVs did not alter endothelial layer permeability or wound healing as compared to vehicle. Cytokine-bead array indicated higher amounts of TNF-α in leukocyte-derived MVs and higher levels of VEGF in endothelial-derived MVs.

Conclusions: In CAD, increased circulating levels of leukocyte SMV may contribute to the impairment of endothelial function and repair. Leukocyte SMVs feature a different molecular composition to SMVs from other cell types, translating into an inhibition of endothelial-regenerative processes.

Association of common Interleukin-6 gene polymorphisms with coronary artery disease and MI: Results of the comprehensive meta-analysis on the subject till date

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Purpose: Coronary artery disease (CAD) in many ways can be termed as an inflammatory disease. Information on variations in the genes involved in various molecular pathways of inflammation in CAD and myocardial infarction (MI) warrants consolidation. We attempted to test associations of two single-nucleotide polymorphisms (SNPs) in interleukin-6 (IL-6) gene promoter region [i.e. 174G/C (rs1800795) and 572G/C variants respectively. The present meta-analysis is the most comprehensive one on the subject so far suggesting possible association of 174G/C variant of IL-6 gene with CAD and MI.

Methods: Relationship of aforementioned IL-6 SNPs with CAD as well as MI was tested employing a meta-analysis of published literature on this subject. Quantitative synthesis was also repeated after stringent stratification of included studies. The study included 138 unique genetic subgroups of MI and CAD studies. All genetic subgroups were divided into 8 major ethnicities: European Ancestry (EA), Middle Eastern Ancestry (MEA), Asian Ancestry (AA), Asian Indian Ancestry (AIA), African Ancestry (AA) and Mixed Ancestry (MA).

Results: In the present meta-analysis a total of 31 (Total sample 31,684; 12,502 cases/19,632 controls) and 11 studies (Total sample 13,573; 6,220 cases/7,353 controls) were included for CAD endpoint for 174G/C and 572G/C variants respectively. On the other hand a total of 11 (Total sample 9,704; 4,515 cases/5,189 controls) and 6 studies (Total sample 5,212; 2,399 cases/2,813 controls) were included for MI endpoint for 174G/C and 572G/C variants respectively. The results for both the variants in pooled analysis for both endpoints vide all three genetic models (Dominant, Recessive and Allelic) suggested non-association (p>0.05).

Subgroup results for 174G/C were found to be rather intriguing. The results for EA in the dominant genetic model for 174G/C indicated a significant trend of association with CAD (OR=1.13, 95% CI: 1.00-1.28, p=0.05). After recessive and allelic models yielded non-significant results (p>0.05). Other ancestral subgroups like MEA, AA AIA and AA however appeared to be non-associated with CAD while all ancestral groups, i.e. EA and MEA were also found to be non-associated with MI (p>0.05).

Subgroup results for 572G/C were also interesting. The results for AA in the dominant genetic model for 572G/C indicated significant association with CAD (OR=1.88, 95% CI: 1.33-2.65, p=0.0003), while recessive and allelic models suggested non-association (p>0.05). Other ancestral subgroups like EA, MA however appeared to be non-associated with CAD while all ancestral subgroups, i.e. AA and AA were found to be non-associated with MI (p>0.05).

Lack of publication bias amongst our groups attested to the authenticity of derived results (Egger's p>0.05 for all groups/subgroups).

Conclusions: The present meta-analysis which is the most comprehensive one on this subject so far suggests possible association of 174G/C variant of IL-6 gene with CAD amongst EA. We also report possible association of 572G/C variant of IL-6 gene with CAD amongst AA. Clinical interpretation of derived results is however recommended.

Macrophage STAT3 activation promotes aortic dissection via imbalance of tissue destruction and protection

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Aortic dissection (AD) is a common disease with high mortality. Recent studies have suggested an important role of IL-6 in the pathogenesis of AD tissue. The release of IL-6 is reported to be associated with AD tissue. In this study IL-6, a STAT3-activating cytokine, and monocyte/macrophage chemoattractant protein (MCP)-1 play an important role in mouse AD. Human AD tissue is reported to show enhancement of inflammation and suppression of smooth muscle cell (SMC)-specific genes. However, it is unclear exactly how IL-6 and STAT3 participate in pathogenesis of AD, or whether they affect SMC function.

To answer these questions, we examined mouse AD model and human AD tissue. We used macrophage-specific knockout of Socs3 (mSocs3-KO), a negative regulator of STAT3, to specifically sensitize macrophages to STAT3 activation, and compared them with wild type (WT) mice. We created a mouse model of aortic stress by CaCl2-induced aortic stiffening and angiotensin II infusion (Ca-AngII), which augmented hemodynamic stress to aortic walls. Both WT and
mSocs3-KO showed microscopic aortic injuries, less than 0.2 mm, with adventi-
torial macrophage infiltration with equal frequencies (40%) 1 week after Ca+AngII. Whereas WT showed fibrotic healing of the injury, mSocs3-KO developed large AD longer than 2 mm with medial disruption and hematoma in 6 weeks. We an-
alyzed the aorta 1 week after the Ca+AngII stimulation, focusing on the changes before the AD development. Serial transthoracic examination analyses showed Ca+AngII caused higher cell proliferation, followed by higher inflammatory response in mSocs3-KO than in WT. We also found suppression of the structural extracel-
ular matrix (ECM) and SMC-specific genes in mSocs3-KO before AD develop-
ment. Kitagawa and co-workers confirmed higher proliferation of infiltrating cells and SMCs in mSocs3-KO aorta, indicating the macrophage-SMC interaction. Flow cytometric analysis showed preferential differentiation of Socs3-
deficient macrophages to proinflammatory M1 with reduction in reparative M2 population (M1/M2 = 2:1), while WT macrophages showed 1:1 ratio of M1 and M2. In the immunofluorescence study of human AD tissue, the lesion was en-
riched for adventitial macrophages with active STAT3, consistent with the findings in the mouse model. Within human AD tissue, adventitial macrophage inflitra-
ation and STAT3 activation were more prominent in the leading edge of dissection where ECM was sparse, compared to the area of AD entry. The leading edge of dissection also showed higher activation of adventitial NFκB and more Ki67-
positive cells. These findings indicate that macrophage STAT3 activation is associated with cell proliferation and ongoing tissue injury in AD. We con-
clude that macrophage STAT3 activation promotes AD through excessive inflam-
mation with M1 differentiation and SMC deterioration, which is likely to cause imbalance between destruction and protection of aortic wall. Over-activation of macrophage STAT3 may be a therapeutic target to mitigate tissue destruction in AD.

HEART FAILURE / LEFT VENTRICULAR FONCTION

P4555 | BENCH
Circulating Toll-like receptor 2 deficiency reduces cardiac dysfunction in mice subjected to pressure overload

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Introduction: Inflammation is implicated in the transition from hypertensive left ventricular (LV) hypertrophy to heart failure. Toll-like receptor 2 (TLR2) is part of the innate immune system and involved in the inflammatory response following ischemia reperfusion injury. However the role of TLR2 in hypertensive heart failure remains unclear.

Methods: C57BL/6J (wild-type, WT) and TLR2 deficient (TLR2KO) mice were subjected to transverse aortic constriction (TAC) and echocardiography at baseline, 3 weeks and 8 weeks after TAC. Systolic dysfunction was defined as ejection fraction (EF) <40%. Left ventricles were harvested at 3 days, 1 week, 2 weeks, 3 weeks and 4 weeks after TAC for histology and biochemical analysis. Bone marrow transplantation was performed between WT and TLR2KO mice.

Results: Eight weeks after TAC, 44% of WT (n=54) and 24% of TLR2KO (n=50) mice developed systolic dysfunction (p<0.05). LV/body weight increased to a similar extent in WT and TLR2KO mice; however interstitial fibrosis was greater in WT (p<0.001), associated with higher mRNA levels of collagen remodeling genes Col3a1, LOX and TGFβ in WT compared to TLR2KO hearts. Protein levels of proinflammatory mediators IL-1α, IL-2, IFN-γ and MCP-1 were elevated at 3 weeks after TAC in WT mice but not in TLR2KO mice (n=6–8; p<0.05). Bone marrow transplantation from WT to TLR2KO mice resulted in greater reduction of EF with TAC, indicating that bone marrow-derived circulating inflammatory cells expressing TLR2 mediated the reduction in EF with pressure-overload.

Conclusion: Circulating TLR2 mediates systolic dysfunction and fibrosis of the hypertensive heart via inflammation, and may represent a novel therapeutic tar-
get.

Acknowledgement/Funding: NMRC CS-IRG and NUS Start-up grant

P4556 | BENCH
Potential role of cardiac iron metabolism in the failing heart

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Background: Accumulating evidence has shown the link between iron metabolism and cardiac function. Iron deficiency is reported to develop in pa-

tients with heart failure, and recently it is widely accepted that long-term iron ther-

apy is beneficial for these patients. Ferroportin is an iron transmembrane trans-
porter that is critical for the cellular iron release. Hepcidin binds to fer-
roportin then induces the internalization and degradation of this transporter via the ubiquitin-lysosome system, and therefore inhibits ferroportin-dependent iron release.

Purpose: Here we show a previously unappreciated role of the hepcidin-

ferroportin axis in cardiac iron metabolism.

Methods: We generated murine left ventricular (LV) heart failure model in C57BL/6NCr mice with a transverse aortic constriction (TAC).

Results: Cardiac iron level was significantly reduced along with low hepcidin and high ferroportin expression in the heart after TAC operation. Immunofluorescence study indicated that ferroportin is predominantly expressed in cardiomyocytes. Plasma hepcidin level did not change during LV pressure-overload, however, ubiquilin of ferroportin was markedly reduced suggesting the role of cardiac-

ferroportin in the regulation of ferroportin in cardiomyocytes. Daily iron injection increased cardiac iron level and improved systolic dysfunction upon pressure overload, and we confirmed the critical role of iron in the maintenance of mitochondrial function and cellular metabolism in cardiac tissue by a metabolome study.

Conclusions: Our results suggest that LV pressure-overload down-regulates car-
diac hepcidin expression, which in turn leads to an increase of cardiac ferro-
portin expression, inducing iron leak and mitochondrial dysfunction in cardiomy-
cytes. The inhibition of excessive ferroportin activity and optimizing cardiac iron metabolism would become a new therapeutic target for heart failure.

P4557 | BENCH
QSOX1 has a protective role in the myocardium face to acute stress

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Introduction: QSOX1 was identified as a plasma biomarker of acute heart failure (AHF). As QSOX1 is a sulfydryl oxidase, we hypothesized that QSOX1 has a protective role in the heart at acute stress.

Methods: QSOX1 KO (C57Bl/6 J) mice were generated using a QSOX1tm1ma embryonic stem cell clone (KOMP) which contains a promoter-less lacZ gene under the control of the QSOX1 regulatory sequences. AHF was provoked by IP injections of Isoproterenol (ISO; 300 mg/kg/12h) for 2 days in mice (C57Bl/6 J) whereas sham received NaCl 9‰. Mice were killed at day 3, after echocardio-

graphy. The experimental design included qPCR, western blot, immunolabelling, DHE and DNPH staining.

Results: At baseline QSOX1−/− mice presented a cardiomyopathy with a dilatation of the left ventricle (LV) in diastole (p<0.002) and systole (p<0.003) with a low shortening fraction (SF) group (p<0.01) versus WT. No difference was noticed regarding anatomical parameters including hearts and lungs. No alteration of the cardiomyocyte structure and size was observed using LAM2A/J and a-actin immunolabel. At baseline, in QSOX1−/− hearts, the SERCA2A trans-

criptional level was higher than in the WT one (p<0.01), whereas the protein level was lower (p<0.01) suggesting an ER stress in QSOX1−/− mice. We hypo-

thesized that the ER stress was secondary to unfolded protein accumula-

tion in the ER, QSOX1 being required for a proper protein folding, and could favor an unfolded protein responses (UPR). Regarding ER chaperon proteins, the levels of Grp94 and Grp78 mRNAs (p<0.05, respectively), of Grp78 pro-

tein level (p<0.04) were enhanced in QSOX1−/− hearts. Furthermore, the high levels of Chaperone HSP (p<0.05), the high levels of GRP78 and HSP47 (p<0.05), the increased LC3II/I ratio indicated that both apoptosis and autophagy processes were active in the QSOX1−/− hearts. After ISO, Iac2 expression dra-

matically increased in QSOX1−/− hearts particularly in the cardiomyocytes. In the absence of QSOX1, decreasing ISO (p<0.01), a decrease in the SF (p<0.01), a pulmonary congestion (lung weight/ tibia length, p<0.01) and increased BNP mRNA levels (p<0.001) were observed in both groups. Nevertheless, the drop of SF was more important in QSOX1−/− group (p<0.002) without long term recovery conversely to WT groups. After ISO, QSOX1−/− hearts exhibited an enhanced inflammation compared to WT groups, with a macrophagic cells infiltration: high CD68 mRNA level, CD68+ cells (p<0.005), high Galectin-3 expression (p<0.05). After ISO, enhanced oxida-

tive stress was assessed by DHE staining of cardiac sections (p<0.0001) and by DNPH protein label in QSOX1−/− heart (p<0.01).

Conclusion: QSOX1 Invalidation induced a dilated cardiomyopathy characterized by an ER stress and UPR which lead to apoptosis activation. When com-

bined to catecholamine stress, the absence of QSOX1 worsened the cardiac dysfunction associated through severe inflammation and oxidative stress. Taken altogether, the data indicated that QSOX1 protects the heart from acute stress.

P4558 | BENCH
Left ventricular parameters and stroke work change dramatically with increasing venoarterial extracorporeal membrane oxygenation flow in a porcine model of chronic heart failure

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Introduction: Venoarterial extracorporeal membrane oxygenation (VA ECMO) is widely used method to treat circulatory decompensation. When applied to chronic heart failure the parameters of left ventricle (LV) are influenced dramatically. Purpose: The purpose of presented study is to assess the influence of increasing
extracorporeal blood flow (EBF) on LV performance during VA ECMO therapy of
decompensated chronic heart failure.

Methods: A porcine model of chronic heart failure was developed by long-term fast cardiac pacing. Subsequently, under total anesthesia and artificial ventilation VA ECMO was introduced to five swine with profound signs of chronic heart de-
compensation.[5] At different levels of EBF (ranging from minimal flow to 5 L/min) the
electrocardiographic and organ specific parameters were measured using a pulmonary
artery catheter, pressure-volume loop catheter positioned in the left ventricle and
arterial probes on systemic arteries.

Results: Tachycardia-induced cardiomyopathy lead to decompensated chronic heart failure with mean (±SEM) cardiac output of 2.5±0.15 L/min, peak left
ventricular pressure 38±9 mmHg and diastolic dilation of the left ventricle to 174±33
mL. By increasing the EBF from minimum flow to 5 L/min, we observed a gradual
increase of peak ventricular pressure to 65±9 mmHg (P<0.01) and a 3.5-fold in-
crease of carotid artery flow (P<0.05). On the other hand, cardiac performance parameters showed higher demands on LV function: LV end-diastolic volume in-
crease of carotid artery flow (P<0.05) and stroke work of LV (SW) increased from
386±235 mmHg/mL to 770±369 mmHg/mL (P<0.05). Stroke vol-
ume and ejection fraction of LV did not show significant changes.

LV parameters with increasing ECMO flow:

<table>
<thead>
<tr>
<th>ECFM blood flow (L/min)</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV peak pressure (mmHg)</td>
<td>38±9</td>
<td>43±8</td>
<td>49±7</td>
<td>54±6</td>
<td>63±7</td>
</tr>
<tr>
<td>LVEDV (mL)</td>
<td>174±33</td>
<td>186±34</td>
<td>192±36</td>
<td>193±34</td>
<td>199±33</td>
</tr>
<tr>
<td>SW (mmHg/mL)</td>
<td>386±235</td>
<td>456±303</td>
<td>511±388</td>
<td>691±338</td>
<td>784±346</td>
</tr>
</tbody>
</table>

PV diagrams of chronic heart failure:

Conclusions: Presented experimental work suggests that excessive flow of VA ECMO has negative effects on the work of chronically decompensated left ven-
tricle. To protect the myocardium, the flow of VA ECMO should be adjusted with
respect not only to peripheral perfusion but also to LV parameters.

Acknowledgement/Funding: Supported by Charles University Grant Agency
(GAUK 1114213)

P4550 | BENCH
Deficiency of cardiac myoglobin promotes myocardial lipotoxicity and
dysfunction
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Background: Lipotoxicity is a global health problem and responsible for a ma-
jority of cardiovascular diseases. Accumulation of lipids in cardiomyocytes by en-
hanced uptake or storage may significantly interfere with the cellular homeo-
static. Higher lipid levels may subsequently cause alterations in cellular structures or
may activate cell death signaling pathways. The events leading to lipid depos-
tion have not been completely elucidated so far. A particular role for reactive
oxygen species has previously been forwarded. We have recently shown that
cardiac myoglobin is involved in the regulation of reactive oxygen species under physiological conditions and in pathological settings. Myoglobin in the
mitochondria may act as a redox buffer, which in turn may play a role in the con-
version of lipid peroxides to nonradical products. Additionally, myoglobin may
be oxidized to metmyoglobin, which may alter the ability of the enzyme co-
ducting oxygen to bind to myoglobin.

Methods and results: Taking advantage of the myoglobin-deficient mouse (Mb
–/–) we assessed lipid deposition and cardiac function in vivo. Using magnetic res-
sonance imaging (MRI) we determined a much-increase deposition of lipids in the
hearts of old Mb–/– mice vs. wildtype littermates (32 week old mice, n=5, p<0.01).

Particularly the distinct signal for fatty acids was significantly higher in the knock-
out group. Using rodent echocardiography (2D and M-Mode) we next assessed
cardiac functions in these two groups. This revealed depressed cardiac functions in
Mb–/– mice. Ejection fraction (n=5 vs. wildtype, p<0.01), stroke volume (n=5
vs. wildtype, p<0.001) and enddiastolic volume (n=5 vs. wildtype, p<0.001) were
significantly lower in Mb–/– mice while heart rates remained comparable. Using
genome array technique, we finally assessed whether relevant proteins previously re-
lated to lipotoxicity were dysregulated in Mb–/– mice. This revealed a significantly
down-regulated peroxisome proliferator-activated receptor γ (PPARγ), which is
previously been associated with lipid signaling.

Conclusions: Myoglobin deficiency causes a significantly increased deposition of
lipids in the heart. This causes a decrease in cardiac functions and could be asso-
ciated with a dysregulated transcription factor PPARγ. Further studies must
show whether PPARγ reconstitution is able to reduce these deleterious effects.

P4551 | BENCH
Finerenone protects cardiac fibroblasts from fibrotic remodeling
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Purpose: Aldosterone promotes cardiac fibrosis by activation of the mineralocor-
toid receptor (MR) that predisposes to arrhythmias and heart failure. We studied
finerenone, a selective non-steroidal MR antagonist, and the mechanism of
fibrotic remodeling in vitro.

Methods and results: Aldosterone induced nuclear translocation of MR in car-
diac fibroblasts (nuclear to cytoplasm MR localization, control 2.3±2.5 vs. aldos-
terone +angiotensin II). Aldosterone promoted cardiac fibrosis by activation of the mineralocor-
toid receptor (MR) that predisposes to arrhythmias and heart failure. We studied
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fibrotic remodeling in vitro.

Aldosterone promoted cardiac fibrosis by activation of the mineralocor-
toid receptor (MR) that predisposes to arrhythmias and heart failure. We studied
finerenone, a selective non-steroidal MR antagonist, and the mechanism of
fibrotic remodeling in vitro.

Results: Aldosterone induced nuclear translocation of MR in car-
diac fibroblasts (nuclear to cytoplasm MR localization, control 2.3±4.0 vs. aldos-
terone 6.8±5.7, p<0.001) that was prevented by finerenone (2.1±2.5, p<0.001 vs.
control). Finnerenone dose-dependently decreased the protein expression of
fibrosis through the TGF-β/Fibronectin pathway (TGF-β: p<0.001 vs. control, and 89±34%, p<0.01 vs.
aldosterone+angiotensin II) that was completely prevented by finerenone (100±10%, p<0.001 vs.
aldosterone+angiotensin II). Finerenone did not alter the transforming growth factor β (TGF-β) expression whereas angiotensin II (173±54%, p<0.001 vs. control) did. Furthermore, the TGF-β expression was unaffected by finerenone but the angiotensin II induced overexpression was prevented with telmisartan pre-treatment (117±29%, p<0.01 vs. angiotensin II). Finnerenone inhibited the aldosterone-induced upregulation of fibronectin (354±229%, p<0.01 vs. control, and 131±46%, p<0.05 vs. aldosterone, respectively). The increase in fibronectin expression induced by
the co-treatment aldosterone and angiotensin II (187±45%, p<0.001 vs. con-
control) was prevented with finerenone pre-treatment (116±28%, p<0.001 vs. aldos-
more, baseline platelet count (188±6x10^9/L vs. 226±55x10^9/L; p<0.001), red
cell distribution width (RDW: 14.3±1.3% vs. 13.5±1.1%; p<0.04) and 6-minute walk
test (445±113 m vs 481±79 m; P<0.04) were significantly different between the
two groups. On multivariate analysis, low LVEF (<30%), elevated serum NT-
proBNP (>1000 pg/mL), kidney dysfunction, low platelet count (<140x10^9/L) and
increased RWD (>13.5%) correlated independently with poor stem cell reserve.

Conclusions: Our data suggest a significant inverse correlation between stem

cell reserve and the stage of the disease in patients with advanced chronic heart
failure and identify several independent echocardiographic and biochemical cor-
relations with poor stem cell reserve in this patient cohort. This finding could be
further improve the selection of patients considered for stem cell therapies.
terone-angiotensin II) as well as the aldosterone-induced upregulation of the lysyl oxidase (145±19%, p<0.001 vs. control, and 85±29%, p<0.0001 vs. aldosterone, respectively).

**Conclusion:** Finerenone inhibits the aldosterone-induced MR nuclear translocation and strongly prevents the increase of the pro-fibrotic factors CTGF, fibroblast, lysyl oxidase and microRNA-21. Therefore, finerenone could serve as a therapeutic agent to prevent maladaptive structural cardiac remodelling.

**P4562 | BENCH**

Lack of growth differentiation factor 15 aggravates adverse cardiac remodeling upon pressure-overload in mice

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**Background/Introduction:** Growth differentiation factor 15 (GDF15) is a distant member of the TGF-β family. Under homeostatic conditions GDF15 is not highly expressed, however, upon injury GDF15 levels robustly increase. GDF15 influences many processes including inflammation, apoptosis and fibrosis. In a mouse model of acute myocardial infarction, GDF15 deficiency leads to increased incidence of cardiac rupture. This detrimental effect on the healing process is most likely related to an exacerbated inflammatory response. In heart failure (HF) patients, GDF15 plasma levels are increased and high GDF15 levels are associated with a higher mortality. Despite this association, a causal role of GDF15 in adverse cardiac remodeling leading to HF is currently not well established. Therefore we aimed to study the role of GDF15 in a mouse model of non-ischemic HF development.

**Methods:** GDF15 knockout (KO) mice and wild type (WT) mice underwent trans aortic constriction (TAC) with a 27 gauge needle. Correct placement of the TAC was confirmed by Doppler measurements of the carotid flow ratios. Cardiac function and geometry was assessed using echo at baseline, 7, 28 and 42 days after TAC. At day 42 immunohistochemistry was performed to study cardiomyocyte hypertrophy (WGA) and influx of different leukocyte subtypes. Flow cytometry was performed at 42 days after TAC on cardiac lymph nodes (LN), blood and spleen to study the effect of GDF15 deficiency on leukocyte subtypes.

**Results:** GDF15 KO mice have significantly increased end diastolic volume (EDV) and end systolic volume (ESV) after 6 weeks of TAC compared to WT mice (EDV: 93 μl versus 64 μl, ESV: 72 μl versus 38 μl, p<0.05). The increase of ESV is already present 7 days after TAC. GDF15 KO mice show increased heart weight/body weight ratio after 42 days of TAC compared to WT mice. (7.0 mg/g versus 9.2 mg/g, p<0.01) Though this observation implies increased cardiac hypertrophy in GDF15 KO mice, we did not observe a difference in cardiomyocyte hypertrophy. Flow cytometry did not show any alterations in the amount or activation status of leukocytes in the blood, LN or spleen after 42 days of TAC.

**Conclusions:** GDF15 deficiency aggravates adverse cardiac remodeling results in increased incidence of cardiac rupture. This detrimental effect on the healing process is most likely related to an exacerbated inflammatory response.

**P4563 | BENCH**

Sphingolipid targeting agent MIPS247 attenuates collagen synthesis by cardiac and kidney cells via stabilization of PMP1A

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**Background:** Cardiac and renal fibrosis is the key pathological process underlying heart and kidney failure for which there is currently not effective therapy. The intracellular metabolism of sphingolipids have been extensively studied, revealing a janus-faced role in mediating fibrosis. However, the role of enzymes involved sphingolipids synthesis pathways have not been fully investigated. We have recently developed novel sphingolipid targeting agents MIPS247 that perturbs cellular sphingolipid levels. The aim of this study is to determine whether MIPS247 will attenuate collagen synthesis by cardiac and kidney cells and mechanisms involved.

**Methods:** Neonatal rat cardiac fibroblasts (NCF) were isolated from day 1 to 2 pups using enzymatic digestion. Kidney proximal tubule cells, HK2, were purchased from ATCC. All cells were pre-treated with MIPS247 for 2 hours before stimulation with 100 nM Angiotensin II (AngII) or 10 ng/ml TGFb for 48 hours. Collagen synthesis were determined by 3H-proline incorporation. Western Blot analysis was used to determine the mechanisms involved.

**Results:** MIPS247 dose-dependently inhibited AngII- and TGFβ-stimulated NCF PIN concentration was significantly associated with impaired ventricular function, PIN levels and not because of alterations in biopterin biosynthesis. Notably, the PIN concentration was significantly associated with impaired ventricular function, highlighting the importance of this NOS1 activity inhibitor in Ca2+ homeostasis. These results take a central role in the current list of targets for future studies focused on the complex cardiac dysfunction processes that occurs in DCM through more efficient harnessing of NOS1 signalling.

**Acknowledgement/Funding:** National Institute of Health [P113/00100 and P114/01506], RETICS, RD12/0042/0003, and co-financed by European Regional Development Fund (FEDER)

**P4564 | BENCH**

Protein inhibitor of NOS1 plays a central role in the regulation of myocardial Ca2+ homeostasis in human heart failure

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**Introduction:** The role of NOS1 as a major modulator of cardiac function has been extensively studied in experimental models. However, its role in human dilated cardiomyopathy (DCM) has never been analyzed.

**Purpose:** Our objective was to evaluate NOS1 and NOS-related counterparts involved in regulating the physiological function of myocytes in human non-ischemic dilated cardiomyopathy (DCM). We also focused on the assessment of NOS1 activity and cardiac tetrahydrobiopterins synthesis.

**Methods:** Left ventricular tissue samples were obtained from 30 explanted hearts: 20 from DCM patients and 10 from non-diseased controls.

**Results:** The mRNA levels (analysed by RNA-sequencing) of NOS1 and the NOS-related genes – DYNLL1, SPR, ATP2A2, and RyR3 – were upregulated in DCM, while GCH1 and ATP2A2 levels were decreased. NOS1 activity and tetrahydrobiopterin biosynthesis was assessed by high-performance liquid chromatography. Although NOS1 protein levels were increased in DCM, NOS1 activity and biopetitors concentrations remained unaltered. However, protein inhibitor of NOS1 activity (PIN) was increased, and there was significant negative correlation between its protein levels and left ventricular ejection fraction (r=-0.682, P<0.01).

**Conclusions:** We demonstrated that the upregulation of cardiac NOS1 is not accompanied by increased NOS1 activity in diluted hearts, partly due to the elevated PIN levels and not because of alterations in biopetin biosynthesis. Notably, the PIN concentration was significantly associated with impaired ventricular function, highlighting the importance of this NOS1 activity inhibitor in Ca2+ homeostasis. These results take a central role in the current list of targets for future studies focused on the complex cardiac dysfunction processes that occurs in DCM through more efficient harnessing of NOS1 signalling.

**Acknowledgement/Funding:** NHMRC Program Grant ID 548272

**P4565 | BEDSIDE**

Galectin-3 and ST-2: association with oxidative stress and renal dysfunction in patients with heart failure

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**Purpose:** To estimate the connection between plasma level of galectin-3, ST-2 and biomarkers of oxidative stress and renal dysfunction in patients with chronic heart failure (CHF).

**PPM1A (a key p-SMAD2/3 phosphatase), degradation and inhibition of NFKB pathways in NCF (Figure).**

**Conclusion:** This is the first demonstration of a small molecule sphingolipid targeting agent MIPS247 attenuating the fibrosis process in both cardiac fibroblasts and kidney cells stimulated by a range of fibrotic factors. Thus, such sphingolipid targeting agents may represent a novel therapeutic agents for cardiac and renal fibrosis.

**Acknowledgement/Funding:** NHMRC Program Grant ID 548272

**Figure 1.** *P<0.01 vs unstimulated control; #P<0.01, ###P<0.001 vs Stimulated control.*
Methods: 172 patients (age, 62.3±3.7 years) with documented prior myocardial infarction were included in the study. Patients were divided into 3 basic groups according functional class (FC) NYHA. 1 group (n=56) – patients with II FC CHF, 2–64 patients with III FC, and 3 group (n=52) – IV FC. The control group (CG) – 36 healthy people (age, 54.7±4.4 years). There was valued the level of ST-2, galectin-3, and cystatin-C by immunoassay analysis. The estimated glomerular filtration rate (e-GFR) was calculated using CKD-EPI equation. We also measured the level of oxidized low density lipoproteins (ox-LDL), 3-nitrotyrosine (3-NT) as biomarkers of oxidative stress. Continuous variables were described by median. Comparisons of continuous variables were performed using Mann-Whitney U-test. Spearman’s rank correlation coefficient was calculated to measure dependence between two variables.

Results: Galectin-3 values increased in parallel with the clinical severity of CHF (NYHA classification): II FC - 9.5 ng/ml, III FC - 18.2 ng/ml, the highest levels being reached in class IV patients 34.6 ng/ml. We observed significant difference between groups (p < 0.01). We found an increase in level of 3-NT in patients (2.4, 3.3 and 4.8 nmol/ml accordingly) in comparison with CG. We also demonstrated a significant positive correlation between galectin-3 and 3-NT in all groups of patients: r1=0.61, r2=0.63, r3=0.69 (p < 0.01). Plasma levels of ox-LDL were significantly elevated in all groups compared with healthy control (p < 0.01). There was a significant positive correlation between galectin-3 and ox-LDL in groups: r1=0.52, r2=0.55, r3=0.62 (p < 0.01). The plasma levels of ST-2 in the 1st, 2nd and 3rd groups of patients were 51.7, 26.5, 37.1 ng/ml accordingly with a significant difference between groups (p < 0.01). The correlation analysis showed the following significant correlations: ST-2 correlated with NYHA FC (r=0.35; p=0.009), with concentration of 3-nitrotyrosine (r=0.36; p=0.005) in the cohort of observed patients. We also found an increase in the level of cystatin-C: 1800, 2800, 4600 pg/ml accordingly with a significant difference between groups (p < 0.01). Strong correlations were also observed between galectin-3-cystatin C (r1=0.58, r2=0.62, r3=0.68, p < 0.01) and galectin-3-GFR (r1=0.51, r2=0.57, r3=0.71, p < 0.01).

Conclusion: Biomarkers of fibrosis in heart failure patients with prior myocardial infarction were closely associated with indicators of oxidative stress, renal dys- function beyond NYHA functional class.

Acknowledgement/Funding: Sanofi sponsored study

P4567

Prolonging systolic ejection time with omecamtiv is at the expense of ventricular filling and impairs ventricular active relaxation in rat


Background/Introduction: Omecamtiv mearcil, a novel cardiac myosin activator that prolongs systolic ejection time, is currently in development as a positive inotrope. Studies performed in healthy volunteers and heart failure showed that omecamtiv concentration-dependently decreased Ewave peak and dose- dependently increased deceleration time and isovolumic relaxation time.

Purpose: The aim of this study was to investigate the consequences of prolonging ejection time with omecamtiv on ventricular diastolic function in rat.

Methods: Dose-response experiments with omecamtiv were performed on isolated Langendorff rat hearts (10–7.5, 10–6 M), in conscious telemetered rats (2.5–10 mg/kg PO), in anesthetized rats with pressure-volume investigation (2.5–7.5 mg/kg PO) and in anesthetized rats using echocardiography (5–10 mg/kg PO).

Results: In all experimental settings omecamtiv exhibited a dose-dependent increase of systolic ejection time which was associated with a delay of isovolumic relaxation time and an increase of Tau. Heart rate was not altered by omecamtiv, therefore the increase of systolic ejection and isovolumic relaxation time was at the expense of diastole. At 10 mg/kg PO, omecamtiv so strongly reduced diastolic filling time that ventricular filling and arterial pressure dropped causing cardiovascular collapse in 2 out of 6 telemetered rats and 2 out of 3 echocardiography rats over a 30 min period. These diastolic alterations did not affect end-dose-pressure-volume relationship and ventricular stiffness at any of the tested doses.

Conclusion: Omecamtiv prolonged systolic ejection time and impaired isovolumic relaxation time in healthy rats. The prolongation of these two phases of the cardiac cycle was at the expense of diastolic filling time. This redistribution of cardiac cycle times could limit the ventricular filling.

Acknowledgement/Funding: Sanofi sponsored study

P4568 | BEDSIDE

Fetuin-A expression and cardiac fibrosis in diastolic heart failure using nephrectomy animal model and clinical cardiac magnetic resonance imaging

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Background: The aim of current study is to define the role of a novel biomarker Fetuin-A and Heart failure with preserved ejection fraction (HFPEF).

Methods and results: A total of 53 patients with HFPEF were recruited from Taiwan Diastolic Heart Failure registry. Baseline characteristics, echocardiographic diastolic parameters were recorded and plasma data including a novel biomarker Fetuin-A expression were determined. Cardiac Magnetic fibrosis was determined by cardiac magnetic resonance imaging (CMRI) T1 mapping and extracellular volume (ECV) calculation in all subjects. Rat modeling of early cardiac fibrosis and diastolic dysfunction was induced by unilateral nephrectomy (NCX). Rat plasma Fetuin-A level (measured by ELISA technique), cardiac Fetuin-A expression, echocardiographic data and myocardial fibrosis severity (as shown by Masson’s trichrome staining) were obtained to compare with sham rats after 6 weeks of the operation. Patients with highest ECV (myocardial fibrosis) had significantly lower plasma Fetuin-A levels. Significant inverse correlation between myocardial fibrosis and Fetuin-A in HFPEF patients was noted even after adjustment of confounding factors [ECV, T3 VS T2; Correlation coefficient (95% C.I.): 607.7 (75.4–1140.0), p=0.026]. After 6 weeks of NCX in rat models, myocardial fibrosis significantly increased in the NCX groups (p < 0.001) along with deterioration of echocardiographic diastolic parameters. Protein expression of Fetuin-A from left ventricular (LV) myocardial tissue was significantly decreased (p < 0.01) compared with sham controls. In addition, rat plasma Fetuin-A expression also attenuated as myocardial fibrosis increased.

Fetuin-A and myocardial fibrosis
Conclusions: Both plasma and myocardial Fetuin-A levels correlated with severity of cardiac fibrosis after adjustment of risk factors.

P4569 | BENCH
MicroRNA-19b is associated with myocardial collagen cross-linking in patients with severe aortic stenosis. Potential usefulness as a circulating biomarker

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Background: Myocardial fibrosis, a major hallmark of myocardial remodelling in patients with aortic valve stenosis (AS), is involved in the development of their clinical manifestations. It is the result of variable alterations not just in the quantity (i.e. collagen deposition) but also in the quality (e.g. degree of collagen cross-linking or CCL) of collagen. Different myocardial microRNAs have been shown to play a role in this process. However, their impact on CCL has not been analysed in depth. On the other hand, the usefulness of circulating microRNAs to identify unique alterations of the extracellular matrix (i.e. CCL) has not been investigated.

Purpose: This study was designed to analyze the association of circulating levels of fibrosis-related microRNAs with their cardiac expression and with myocardial CCL in patients with severe AS, as well as to explore their potential involvement in CCL.

Methods: Peripheral blood and endomyocardial biopsies were obtained from 28 AS patients. Nineteen and ten subjects were used as controls for blood and myocardial determinations, respectively. Collagen volume fraction (CVF), the degree of CCL, and the expression of lysyl oxidase (LOX), the main enzyme involved in CCL, were analyzed in myocardial biopsies. MicroRNA expression was quantified in myocardial and blood samples. In vitro studies were performed in human adult fibroblasts.

Results: AS patients showed increased (P < 0.001) myocardial CVF, CCL and LOX expression, compared with control subjects. Out of the 8 microRNAs analyzed, miR-122, miR-133a and miR-19b were decreased (P < 0.01) both in the serum and the myocardium of AS patients compared with controls. No associations were found between circulating and myocardial levels of miR-122 and miR-133a. Interestingly, a direct correlation (r=0.375, P < 0.05) was found between serum and myocardial miR-19b expression in AS patients, suggesting a cardiac origin of its circulating levels. Myocardial miR-19b was inversely correlated with LOX protein (r=-0.594, P < 0.05) and with the presence of heart failure (O.R.: 0.005, P < 0.05) in AS patients. Of note, myocardial miR-19b was associated with increased left ventricular stiffness (r=-0.379, P < 0.05) and with the presence of heart failure (O.R.: 0.005, P < 0.05) in AS patients. In human fibroblasts miR-19b inhibition increased (P < 0.05) the expression of LOX protein, suggesting that miR-19b might regulate LOX and subsequently CCL. Importantly, serum levels of miR-19b were also inversely associated with LOX (r=-0.452, P < 0.05) and CCL (r=-0.410, P < 0.05), suggesting that this microRNA could be useful as a non-invasive biomarker of CCL.

Conclusions: Our results suggest that miR-19b may be involved in myocardial CCL through the regulation of LOX. Moreover, serum miR-19b is associated with myocardial CCL in AS patients. Thus, this microRNA could be a novel biomarker for the origin of its circulating levels.

Acknowledgement/Funding: German Research Council

P4570 | BENCH
The forkhead transcription factor FoxO3a negatively regulates NK cell function and viral clearance in myocarditis

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Background: FoxO3a is a transcription factor involved in cell metabolism, survival and differential outcomes in inflammatory disease. However, mechanistic insight in FoxO3a effects is still limited.

Purpose: We investigated the role of FoxO3a on NK cell responses and its effects in pathogen-induced murine viral myocarditis and human virus (+) inflammatory cardiomyopathy.

Methods: C57BL/6 myocarditis was induced in WT and FoxO3a−/− mice (FVB background). miRNA/mRNA expression, inflammation and viral load was assessed at 7d p.i. and immunoblotting in IFNγ treated hearts were stained with Alexa Fluor 647 was evaluated by inflammatory score. NK cells were analyzed for cytotoxicity, IFNγ expression and activation markers by FACS ex vivo. Human gain of function SNP rs12212067 was determined by QT-PCR. NK cells were functionally characterized by CD107 and IFNγ expression. Patients with inflammatory cardiomyopathy were clinically characterized at baseline and 6 months, endomyocardial biopsies were analyzed for viral genomes and inflammation.

Results: FOXO3a−/− mice showed significantly lower cardiac viral titers compared to WT mice accompanied by a reduced inflammatory score and diminished expression of CD3+ T cells, CD14+ monocytes and 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 CAR. Interestingly, FOXO3a gene transfer in vitro had no effect on viral adhesion and entry but significantly inhibited CTV3 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 cytokolytic activity with higher frequencies of activated CD69+ and CD201+ effector NK cells as well as enhanced expression of IFNγ accompanied by an up-regulation of miR-155. Moreover, healthy humans heterozygous or homozygous for the longevity-associated FoxO3a SNP rs12212067 exhibited significantly reduced IFNγ expression and cytotxic degranulation of NK cells. Carriers with this SNP suffering from virus (+) inflammatory cardiomyopathy showed a poorer outcome characterized by enhanced myocardial inflammation and attenuated viral clearance while susceptibility to viral infection was not regulated by FOXO3 activation.

Conclusion: FOXO3 impacts on NK cell regulation in viral myocarditis. The gain-of-function SNP rs12212067, recently described to limit innate immune responses, revealed an association of FOXO3 activation with diminished NK cell function and attenuated antiviral immunity resulting in unfavourable outcome in virus-positive DCM patients. Regulation of NK cell responses by FOXO3 might be protective in cancer or arteriosclerosis where inflammation should be suppressed but less beneficial during infectious disease where a proper immune response is needed for rapid pathogen clearance.

Acknowledgement/Funding: German Research Council
and by E velocity reduction from late-hyperpnea to late-apnea (105.8±27.9 versus 97.5±22.45 m/s, p=0.046), without significant changes deceleration time or in tissue Doppler indexes, likely due to LV preload decrease.

Conclusions: In HF patients CSR, likely via recurrent hypoxia and hypercapnia cycles and chemoreflex mediated adrenergic discharge, may cause pulmonary vascular disease, and pulmonary artery pressure with undesirable consequent changes in right and left ventricular preload-afterload (figure 1).

P4572 | BEDSIDE
Comparisons of T1 mappings among cardiovascular diseases: a systematic review and meta-analysis from 4794 subjects
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Background: Cardiovascular magnetic resonance imaging allows tissue characterization. T1 mappings play an increasingly important role in research and clinical use due to its ability to detect both focal and diffuse fibrosis non-invasively with a high correlation with histopathology. Modified look-locker inversion recovery (MOLLI) and its shortened analogue (ShMOLLI) are two widely-used sequences in clinical and in research to obtain T1 mapping. Although there are many articles reported the T1 values of various conditions, each contains 2 to 4 diseases at most. Therefore, we performed a systematic review of native T1 values in both healthy subjects and those who have cardiac disease using these sequences to better elucidate entire chart of T1 mapping in the body of literature.

Methods: Three databases (EMBASE, SCOPUS, MEDLINE) were systematically searched for native T1 values in the human heart. The key terms were: “ShMOLLI”, “shortened modified look locker inversion recovery”, “shortened MOLLI”, “MOLLI”, “modified look-locker inversion recovery”, “cmr”, “cardiac magnetic resonance” and “cardiac mr”. Random effect model was used to pool native T1 values. Last search was performed on Jan 24 2016. Papers with sample size less than 20 subjects. Inclusion criteria were: healthy subjects and those who have cardiac disease using these sequences to compare T1 values in both healthy subjects and patients with various conditions. Exclusion criteria were: those who have cardiac disease using these sequences to compare T1 values in both healthy subjects and patients with non-ischemic dilated cardiomyopathy (DCM) and myocardial infarction in any sequences at any field strength except for DCM patients at 3T using ShMOLLI. Ranges of T1 values of patients with hypertension and aortic stenosis overlapped the normal range.

Results: 4794 subjects including 1668 normal controls were included in this meta-analysis. Data are summarized by sequences and field strengths (Figure), then subgroup analyses were performed to remove influences of these factors to the results. Native T1 values at 1.5T are generally able to distinguish diseases from the normal except for hypertrophic cardiomyopathy and hypertension. 95% confidence interval (CI) of native T1 values at 3T, however, had overlaps among normal and diseases. Among diseases which cause left ventricular hypertrophy, patients with diabetes and Fabry disease had shorter T1 values than normal whereas those with amyloidosis had significantly longer T1 values. Patient with hypertrophic cardiomyopathy showed longer T1 values but there was an overlap. There were no overlaps in 95% CI of native T1 values between normal healthy subjects and patients with non-ischemic dilated cardiomyopathy (DCM) and DCM and myocardial infarction in any sequences at any field strength except for DCM patients at 3T using ShMOLLI. Ranges of T1 values of patients with hypertension and aortic stenosis overlapped the normal range.

Conclusions: T1 values at 1.5T are able to distinguish diseases from the normal except for hypertrophic cardiomyopathy and hypertension. 95% confidence interval (CI) of native T1 values at 3T, however, had overlaps among normal and diseases. Among diseases which cause left ventricular hypertrophy, patients with diabetes and Fabry disease had shorter T1 values than normal whereas those with amyloidosis had significantly longer T1 values. Patient with hypertrophic cardiomyopathy showed longer T1 values but there was an overlap. There were no overlaps in 95% CI of native T1 values between normal healthy subjects and patients with non-ischemic dilated cardiomyopathy (DCM) and DCM and myocardial infarction in any sequences at any field strength except for DCM patients at 3T using ShMOLLI. Ranges of T1 values of patients with hypertension and aortic stenosis overlapped the normal range.

Table 1: Clinical characteristics and differences of the study population

<table>
<thead>
<tr>
<th>Disease</th>
<th>n</th>
<th>Mean (SD)</th>
<th>Median (IQR)</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>10</td>
<td>1.53 (0.52)</td>
<td>1.48 (1.36-1.63)</td>
<td>1.09</td>
<td>2.06</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>2</td>
<td>1.55 (0.52)</td>
<td>1.50 (1.38-1.64)</td>
<td>1.09</td>
<td>2.06</td>
</tr>
<tr>
<td>Mitral Valve Prosthesis</td>
<td>2</td>
<td>1.55 (0.52)</td>
<td>1.50 (1.38-1.64)</td>
<td>1.09</td>
<td>2.06</td>
</tr>
<tr>
<td>Pulmonary Hypertension</td>
<td>2</td>
<td>1.55 (0.52)</td>
<td>1.50 (1.38-1.64)</td>
<td>1.09</td>
<td>2.06</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2</td>
<td>1.55 (0.52)</td>
<td>1.50 (1.38-1.64)</td>
<td>1.09</td>
<td>2.06</td>
</tr>
</tbody>
</table>

Native T1 values of patients with diseases

Conclusion: Native T1 values at 1.5T have better discrimination of diseases than that of 3T. T1 mapping are advantageous in distinguishing patients with diabetes and Fabry disease from the normal with higher accuracy. Therefore, we performed a systematic review of native T1 values in both healthy subjects and those who have cardiac disease using these sequences to better elucidate entire chart of T1 mapping in the body of literature.

P4574 | BEDSIDE
Usefulness of superior caval vein flow analysis to distinguish cardiological and pulmonary dyspnea
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Background: In routine clinical practice diagnostic assessment of dyspnea is challenging. Distinction of cardiological from pulmonary aetiology is often difficult and time-consuming management relies on correct diagnosis.

Purpose: Our study aims to evaluate if superior caval vein flow (SCVF) flow analysis is useful to distinguish the two different causes of dyspnea

Methods: We studied 30 patients complaining of dyspnea for light efforts. 15 patients were affected from chronic heart failure (CHF) and the remaining suffered from chronic obstructive pulmonary disease (COPD). SCVF flow was analyzed with pulsed wave doppler with right supraclavicular approach. We studied the systolic and diastolic maximum flow velocity during inspiration (SCV-S; SCV-DI) and expiration (SCV-SE; SCV-DE) and calculated the absolute (Delta) and relative (delta percentage on expiratory values) difference between SI-SE and DI-DE.

Results: Left atrial volume is significantly higher in CHF group but right atrial pressure (RAP) and pulmonary artery systolic pressure (PASP) are similar. COPD group showed pronounced variations of SCV-S when compared with CHF patients (p<0.0001). A SCV-S increase of at least 0.14/sec over SVC-SE yielded a 100% sensitivity and 75% specificity (area under the ROC curve 0.91) to differentiate pulmonary from cardiological dyspnea.

Table 1. Clinical characteristics and differences of the study population

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Sex (male)</th>
<th>Smoking (current)</th>
<th>COPD (yes)</th>
<th>CHF (yes)</th>
<th>COPD vs CHF</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>70±17</td>
<td>15/15</td>
<td>13/17</td>
<td>15/15</td>
<td>15/15</td>
<td>0.01</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Conclusions: COPD patients showed a pronounced systolic velocity variation depending on breath. This parameter could be usefully employed for diagnostic management in patients presenting with dyspnea.
Background: Speckle tracking analysis is an emerging technique that can be useful to assess abnormalities in cardiac contractility before traditional echo parameters, with particular interest to right ventricle (RV) performance.

Purpose: To investigate whether RV 2D speckle tracking analysis at peak exercise could stratify a heart failure reduced ejection fraction (HF/EF) population in different functional phenotypes, with particular emphasis on RV to pulmonary circulation relationship.

Methods: 36 HF/EF patients (mean age 69±12; male 69%; NYHA I-II-III-IV 19–17–25–5%) underwent a maximal cardiopulmonary exercise testing evaluation (bike, incremental ramp protocol) combined with Echo-Doppler and off-line speckle tracking analysis. Study population was divided in two groups according to median value of 2D right ventricle free-wall longitudinal strain at peak exercise (Group A RVLS at peak < -19, 17 patients vs Group B > -19, 19 patients).

In all patients we performed traditional echo and 2D longitudinal speckle tracking analysis at rest and peak exercise.

Results: Despite similar left ventricle ejection fraction (Group A 36±9% vs Group B 32±9%, p=ns) and right ventricle longitudinal strain (RVLS) at rest (Group A -23±2.7% vs Group B -18.8±1.9%, p=ns), Group B patients showed a similar exercise performance (Peak VO2 Group A 31.6±7.4 vs Group B 11.6±3.4 mL/kg/min, p<ns) but markedly better RVLS at peak exercise (VE/VO2 slope: Group A 1.31±6.7 vs Group B 37.4±8.8, p<0.05), and a clear RV to PC uncoupling at peak exercise as assessed by the relationship between pulmonary systolic pressure vs free-wall RVLS (see figure below). Strain data were according to traditional echo parameters.

Conclusions: In HF/EF RV speckle tracking analysis at peak exercise seems a useful technique for unmasking RV to PC uncoupling and the unfavorable gas exchange and ventilatory phenotypes.

P4576 | BENCH
Circulating growth-differentiation factor 15 in peripartum cardiomyopathy
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Background and objective: Peripartum cardiomyopathy (PPCM) is characterized by new onset of heart failure in late pregnancy and up to the first six months postpartum. Growth-Differentiation Factor 15 (GDF-15) is part of the TGF-β superfamily. GDF-15 is highly expressed during pregnancy and its plays an important role in maternal adaptability and fetal viability. Experimental studies demonstrate that GDF-15 functions as a protective and anti-hypertrophic factor in the heart. We aimed to evaluate the circulating level of GDF-15 in PPCM patients.

Methods and results: In this single centre prospective study, we enrolled 37 PPCM patients and age-matched healthy subjects. All patients received ACE inhibitors and beta-adrenergic blocking agents. Serum GDF-15 measurements and echocardiograms were performed at baseline, when the patient was seen for the first time at the clinic. PPCM patients showed decreased cardiac function (EF: 27±6±6%) and increased cardiac hypertrophy (LVEDD: 59±1±1, LVEFSD: 50±4±1 mm). Interestingly, serum GDF-15 levels were significantly depressed among PPCM patients compared to healthy controls (9282±3203 vs. 28438±6577 pg/ml, p<0.01).

Conclusion: Decreased GDF-15 circulating level in PPCM women might result in a less effective adaptation of the heart to the pregnancy stress. These findings should be confirmed in a larger cohort and the involvement of GDF-15 in the loss of ventricular performance in PPCM will be investigated by further analyses.

P4577 | BENCH
The incidence of stroke after hospitalization for heart failure in patients with atrial fibrillation: the Fushimi AF Registry
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Purpose: Heart failure (HF) is considered a risk factor for stroke or systemic embolism (SE) in patients with atrial fibrillation (AF). Prior studies suggested that not history of HF but recent congestive HF was a strong predictor of stroke/SE, but there are limited data on this issue. We examined the incidence of stroke/SE after hospitalization for HF in the Fushimi AF Registry.

Methods: The Fushimi AF Registry, a community-based prospective survey, was designed to enroll all of the AF patients. At present, we have enrolled 4,441 patients from March 2011 to November 2015. Follow-up data were available in 3,749 patients (median follow-up periods, 1,035 days).

Results: During the follow-up periods, 338 patients (9.0%) were hospitalized for HF. Patients with hospitalization for HF (HHF group) were older and included more female than patients without hospitalization for HF (No-HHF group). HHF group showed significantly higher rate of various comorbidities including hypertension, diabetes, coronary artery disease, chronic kidney disease, and prior HF, whereas prevalence of stroke/SE were comparable between the groups. CHADS2-VASc score was higher in HHF group (4.3±1.46 vs 4.2±1.70, P<0.0001), and prescription of oral anticoagulants was more in HHF group (68.0% vs 52.1%, P<0.0001). After hospitalization for HF, 36 patients (10.7%) developed stroke/SE. In Kaplan-Maier analysis, the incidence of stroke/SE after HF hospitalization was significantly higher than that in No-HHF group (P<0.0001) (Figure). Patients with prior HF at baseline showed higher incidence of hospitalization for HF, but higher incidence of stroke/SE after hospitalization for HF were shown in both patients with prior HF and those without prior HF. After adjustment for the factors included in CHADS2 score and prescription of OAC, hospitalization for HF was an independent predictor of stroke/SE in Cox proportional hazard analysis (hazard ratio [95% confidence interval], 3.03 [2.04–4.29]). Furthermore, the incidence of stroke/SE within 30 days after hospitalization for HF was much higher than that in No-HHF group (within 30 days, 2.7% vs 0.2%; 30 days to 90 days, 1.2% vs 0.4%; 90 days to 1 year, 3.0% vs 1.6%; after 1 year, 3.8% vs 3.3%) Conclusion: Hospitalization for HF was significantly associated with higher incidence of stroke/SE among patients with AF, and the risk was much higher early after hospitalization.

Acknowledgement/Funding: Boehringer Ingelheim, Bayer Healthcare, Pfizer, Bristol-Myers Squibb, Astellas Pharma, AstraZeneca, Daiichi-Sankyo, Novartis Pharma, MSD, Sanofi-Aventis.
diastolic pressure and end-diastolic pressure volume relationship without change in end-systolic pressure volume relationship. Significant NE spillovers were observed over the splanchnic organs and left and right kidneys at 10 weeks which persisted up to 18 weeks (Figure). However, myocardial NE spillover was only observed at 18 weeks.

Conclusions: Our results in a large animal model of HfPEF due to severe HT demonstrate the splanchnic and renal NE spillovers are observed early in the development of HT which are potential targets for therapies.

Acknowledgement/Funding: St Jude Medical, Center for Innovation and Strategic Collaboration; Hong Kong Research Grant Council General Research Fund (HKU780013M and HKU1712101)

P4579 | BEDSIDE
Mismatch between right- and left-sided filling pressures in heart failure patients with preserved and reduced ejection fraction

Background: Elevated jugular venous pressure (JVP) is one of the most important physical signs of elevated left-sided filling pressure in patients with congestive heart failure (CHF). However, treatment guided by JVP can frequently be inappropriate in patients with mismatch between right- and left-sided filling pressures (R-L mismatch). Although these findings have been demonstrated in HF with reduced ejection fraction (HfPEF), it has not been fully investigated in HF with preserved EF (HfPEF) patients.

Purpose: The present study aims to observe the prevalence of R-L mismatch and to identify clinical findings correlating with elevated left-sided filling pressure in patients with congestive heart failure (CHF).

Methods: HF patients who underwent right-sided heart catheterization were prospectively enrolled. Right atrial pressure (RAP) and pulmonary capillary wedge pressure (PCWP) were classified as elevated when >10mmHg and >22mmHg, respectively. Correlation of RAP and PCWP was investigated in HF patients (n=40%) and HfPEF patients.

Results: A total of 732 HF patients were enrolled. Mean age was 66±11.6 years old, ischemic etiology was 59%, and HfPEF was 72%. In HfPEF and HfPEF patients, normal RAP was associated with normal PCWP in 96% and 82%, respectively, while elevated RAP was associated with elevated PCWP in 25% and 53%, respectively. In HfPEF patients, pulmonary artery systolic pressure (PASP) showed stronger correlation with PCWP than RAP (r=0.79, p<0.001, vs. r=0.65, p=0.001). These relationships were also demonstrated in HfPEF patients (r=0.83, p<0.001, vs. r=0.49, p=0.001).

Conclusions: Discordance exists between elevated RAP and PCWP, especially in HfPEF patients. In these patients, decongestion therapy guided by elevated JVP can lead to overtreatment and physicians may utilize other clinical findings in HfPEF patients. In these patients, decongestion therapy guided by elevated JVP can lead to overtreatment and physicians may utilize other clinical findings in HfPEF patients.

P4580 | BEDSIDE
Protective effect of beta-blockers on worsening of renal function in heart failure patients with sympathetic overactivation
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Background: β-blockers might preserve renal function in patients with chronic heart failure (HF). However, the effect of central sympathetic activity on renal function in patients taking β-blockers is unclear.

Purpose: The aim of this study is to evaluate the interactive effect of β-blockers and central sympathetic activity on worsening of renal function (WRF) in patients with HF.

Methods: We determined resting muscle sympathetic nerve activity (MSNA) and serum creatinine level in 105 patients with HF (ejection fraction <0.45). Serum creatinine level was determined at baseline and 3, 6, and 12 months after measurement of MSNA. WRF was defined as an absolute increase in serum creatinine level >0.3mg/dL.

Results: During the follow-up period, WRF was observed in 15 patients. MSNA was significantly higher in patients with WRF than in those without WRF. Multivariate logistic regression analysis revealed that MSNA and non-use of β-blockers were independent risk factors of WRF. In higher MSNA patients (n≥1 burst/100beats), prevalence of WRF was lower in patients with β-blockers than in those without β-blockers.

Predictors of WRF within 12 months

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Univariate</th>
<th>Multivariate</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>0.5362</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Age</td>
<td>0.155</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Atriopeptic hormone index</td>
<td>0.6029</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Body mass index</td>
<td>0.0526</td>
<td>0.9003</td>
<td>–</td>
</tr>
<tr>
<td>Specific activity scale</td>
<td>0.0001</td>
<td>0.4575</td>
<td>–</td>
</tr>
<tr>
<td>Mean blood pressure</td>
<td>0.0152</td>
<td>0.2050</td>
<td>–</td>
</tr>
<tr>
<td>Heart rate</td>
<td>0.2305</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Burst incidence</td>
<td>0.0001</td>
<td>0.0126</td>
<td>1.07 (1.01–1.15)</td>
</tr>
</tbody>
</table>

Conclusion: Sympathetic overactivation predicts WRF in patients with HF. β-blockers might be necessary to prevent WRF in HF patients with sympathetic overactivation.

P4581 | BEDSIDE
Trans-tubular potassium gradient as a predictive marker for commencing inotropic infusions in patients with acute heart failure with reduced ejection fraction
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Background: Low cardiac output (CO) worsens heart failure through neurohormonal activation (NA). We often administer inotropes in the presence of clinical signs of low CO, such as low proportional pulse pressure (PPP). However, there is no established convenient marker of NA. Trans-tubular potassium gradient (TTKG), which is traditionally used to measure aldosterone bioactivity and is easily calculated by laboratory data, may be a potential marker of NA in patients with heart failure.

Purpose: This study sought to assess whether TTKG is a possible predictive marker for commencing inotropic infusions for patients with acute heart failure.

Methods: We retrospectively reviewed 61 consecutive acute heart failure inpatients with reduced ejection fraction (EF<40%) and who had complete laboratory data to calculate TTKG on the morning of day 2 after admission. The primary outcome was defined as starting or increasing inotropic infusions after the second day of admission. We investigated TTKG for estimating NA, and echocardiographic data, including left ventricular outflow velocity time integral (LVOT-VTI), and PPP for estimating low CO.

Results: Mean patient age was 75±11 years and mean EF was 29±6%. On univariate analysis, TTKG and PPP were significantly associated with primary outcome (p=0.005, p=0.01 respectively), while LVOT-VTI was marginally associated. On multivariate analysis, only TTKG was significantly associated with the primary outcome (p=0.008). ROC curve analysis confirmed a TTKG of 4.09 and/or PPP of 0.37 as the best diagnostic cut off values for commencing inotropic infusion. Using these cut-off values, we performed subgroup analysis (Table 1), which indicated that low PPP was indeed associated with a high risk of commencing inotropic infusion. Moreover, low PPP with high TTKG, indicating low CO and increased NA,
was revealed to be the strongest risk factor for commencing intravenous infu- 
sion. On the other hand, low PPP with low TTKG was not a significant risk factor.

Table 1. Odds ratio of hyperperfusion and their combinations

<table>
<thead>
<tr>
<th>N</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low PPP</td>
<td>13</td>
<td>10.0</td>
<td>2.4–42.0</td>
</tr>
<tr>
<td>Low PPP</td>
<td>23</td>
<td>7.5</td>
<td>1.8–31.9</td>
</tr>
<tr>
<td>High TTKG</td>
<td>24</td>
<td>6.8</td>
<td>1.6–28.7</td>
</tr>
<tr>
<td>Low PPP with low TTKG</td>
<td>10</td>
<td>1.0</td>
<td>0.2–5.6</td>
</tr>
<tr>
<td>High PPP with high TTKG</td>
<td>11</td>
<td>0.9</td>
<td>0.2–4.8</td>
</tr>
<tr>
<td>High PPP with low TTKG</td>
<td>27</td>
<td>0.1</td>
<td>0.0–0.7</td>
</tr>
</tbody>
</table>

Conclusion: TTKG is a possible predictor of NA due to low CO, and can be used to indicate the need for inotropic support in acute heart failure with reduced EF.

P4582 | BENCH
Prognostic significance of thirst augmentation in chronic heart failure rats
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Introduction: Drinking behavior helps regulate the fluid balance in the body, and is controlled by a thirst mechanism. Impairment of the thirst function could lead to fluid imbalance that would be harmful for homeostasis. A quantitative measure- ment of thirst is essential for understanding and treating fluid disorders related to diseases such as fluid retention in chronic heart failure (CHF). Thirst is a common trouble some by patients with CHF, although this has received little attention in the scientific literature. The aim of this study is to investigate the development of thirst and its correlation with the prognosis in CHF rats.

Methods and results: The left coronary artery was ligated to produce CHF in 8-week-old male Sprague-Dawley rats. Drinking behavior was monitored contin- uously by a drop counter recording system in fed ad libitum normal and CHF rats. Thirst which is defined as per drinking volume (PDV) was significantly increased in the first month after myocardial infarction (Figure, A), this increase was sustained at a higher level than in normal rats throughout the remaining lifespan (Figure, B). The early increment of thirst (the tenth week PDV) strongly correlated with lifespan (Figure, C).

Conclusion: The results provide experimental evidences that thirst increment may be an intrinsic process during deterioration of cardiac function. An increased PDV suggests that the sense of osmotic or volumetric changes may be blunted and it may increase perturbation for circulation system in CHF. Therefore, patients with CHF may get the risk of drinking a large volume to satisfy one’s thirst, without recognizing the adverse consequences of acute volume loading.

P4584 | BEDSIDE
ADHERE risk levels provide the prognostic information in patients admitted for acute decompensated heart failure, regardless of reduced or preserved left ventricular ejection fraction


Background: The Acute Decompensated Heart Failure National Registry (ADHERE) risk levels are a validated tool to assess the risk of in-hospital mortality in patients with acute decompensated heart failure (ADHF). The aim of this study was to investigate the long-term prognostic impact of ADHERE risk levels in ADHF patients, relating to reduced or preserved left ventricular ejection fraction (HFEF or HPEF).

Methods and results: We studied 303 consecutive patients admitted for ADHF and discharged alive (HFEF:LVFEF<40%;n=152, HPEF:LVFEF<40%;n=151). ADHERE risk levels were assigned, as previously described, baseline BUN (>30 vs <30 mg/dL), a modification from 37 mg/dL used in ADHERE HFpEF patients due the BUN distribution in our study population), systolic blood pressure (<125 vs ≥125 mmHg), and creatinine (Cr>2.0 vs ≤2.0 mg/dL). During a follow-up period of 4.1±3.2 yrs, 89 patients had cardiovascular death (CVD). In patients with HFEF, at multivariate Cox analysis, ADHERE risk levels were significantly associ- ated with cardiovascular death (HR 1.10 CI 1.02–1.18 p<0.003). In the quintile model, intermediate values of Galectin-3 were significantly associated with a lower event rate of ACM and CM (Table 1). In the univariate main group sST2 was a predictor of ACM (HR 1.05 CI 1.03–1.07 p<0.001) and CM (HR 1.03 CI 1.00–1.06 p=0.04). In the DCM and viral subgroup the endpoints ACM (HR 1.10 CI 1.05–1.17 p<0.001) and CM (HR 1.10 CI 1.02–1.18 p=0.013) were significant. In the DCM group no significant associ- ations were observed. In the adjusted main group the predictive value of sST2 for ACM remained intact (HR 1.04 CI 1.02–1.07 p<0.003). In the quintile model, intermediate values of Galectin-3 were significantly associated with a lower event rate of ACM and CM (Table 1).

Table 1. Odds ratio of indicators of hypoperfusion and their combinations

<table>
<thead>
<tr>
<th>Quartile model of Galectin-3</th>
<th>ACM</th>
<th>CM</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st quartile, n=66</td>
<td>0.54 (0.22–1.32)</td>
<td>0.40 (0.13–1.22)</td>
</tr>
<tr>
<td>2nd quartile, n=65</td>
<td>0.03 (0.08–0.67)</td>
<td>0.27 (0.09–0.84)</td>
</tr>
<tr>
<td>3rd quartile, n=65</td>
<td>1.00 (0.50–2.00)</td>
<td>0.93 (0.42–2.03)</td>
</tr>
<tr>
<td>4th quartile, n=66</td>
<td>0.015</td>
<td>0.044</td>
</tr>
</tbody>
</table>

Conclusion: The study revealed that sST2 predicts all-cause and cardiac mor- tality in patients with non-ischemic HF. Furthermore, sST2 could be useful es- pecially in patients with inflammatory DCM. Our findings show that intermediate levels of Galectin-3 are better for prognosis.

P4585 | BEDSIDE
Potential use of LCZ696 in real life clinical practice in patients with chronic heart failure: Results from REALITY HF Study

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Purpose: LCZ696 is a new class of drug which has been shown to reduce the risk of cardiovascular death and hospitalization for heart failure (HF) when compared to enalapril in patients with chronic HF and it is expected that this will modify clini-
cation practice. However, potential of the use of LCZ696 in real life clinical practice is unknown. REALITY HF (Resting Heart Rate and Real Life Treatment Modality in Outpatients with Left Ventricular Systolic Dysfunction) study data were analyzed to evaluate potential clinical application of LCZ696 treatment in real life routine clinical care in patients with chronic HF.

**Methods:** REALITY HF was a multicenter, prospective, observational, national registry designed to evaluate HF patients’ clinical characteristics and current treatment modalities, and enrolled 1196 patients (mean age 61±12 years, 75.7% male) from 16 centers who were admitted to the outpatient clinic with the diagnosis of chronic HF LVEF <40% and ≥18 years of age. Potential use of LCZ696 was evaluated based on product license indication (in patients with NYHA II-IV HF and reduced LVEF) and also further analysis was performed based on the main PARADIGM HF criteria that included LVEF ≤40%, NYHA II-IV and receiving ACEi or ARB (or both).

**Results:** In overall study population, 269 patients (22.4%) were in NYHA class I, 472 patients (39.5%) in NYHA class II, 352 patients (29.4%) in NYHA III and 103 patients (8.6%) in NYHA IV. 957 patients (80%) were receiving beta blocker, 827 (69.1%) were receiving ACE inhibitor or ARB and 703 (58.8%) were receiving both of therapy. The percentage of patients candidate for LCZ696 according to product license indication (NYHA II-IV) was 77.5% (n=927). Patients who met the main PARADIGM HF criteria was 46.5% (n=556). In patients who have data on systolic blood pressure (SBP) (n=1039), 45.2% of patients (n=470) met both the main PARADIGM HF and SBP criteria. Patients who had systolic blood pressure ≤130 mmHg and not taking ACEi or ARB (or both) (n=206), 53.1% (n=225) were in NYHA class II, 37.6% (n=209) in NYHA class III and 9.4% (n=52) in NYHA class IV (p=0.0001).

**Conclusions:** The findings from REALITY HF showed that in real life chronic patients covered by beta blocker and ACEi or ARB (or both) there was a significant potential of patients eligible for LCZ696 were in NYHA II or II functional class categories.

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**P4586 | BENCH**

Liposome-encapsulated berberine treatment reduces adverse ventricle remodeling after myocardial infarction


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**Introduction:** Adverse left ventricle remodeling can be measured as a reduction in ejection fraction after myocardial infarction. Left ventricle remodeling leads to congestive heart failure and is a main determinant of mortality and morbidity after myocardial infarction. Berberine is a naturally occurring alkaloid extract from barberry that has anti-inflammatory and anti-oxidant activities. Pretreatment with long-term administration of high doses of berberine has shown beneficial effects in experimental diabetes and cardiac ischemia reperfusion injury. However, the possibility and the short half-life in the circulation have impeded the clinical use of berberine.

**Purpose:** To examine whether encapsulation of berberine into long-circulating liposomes could improve its therapeutic availability and efficacy to protect cardiac function in vivo.

**Methods:** Berberine was loaded into liposomes at a concentration of 0.3 mg/ml. Lipopolysaccharide (LPS) activated mouse macrophages RAW 264.7 were treated with free berberine or liposome-encapsulated berberine (Lipo-Berb) and analyzed for cell viability, reactive oxygen species production and cytokine secretion. C57BL/6J male mice (10-12 week old) subjected to myocardial infarction, allowing a fixed dose of other diuretic regimen for 4 days. On the second and third days after MI, Ejection fraction was assessed by echocardiography at baseline, 7 and 28 days after MI.

**Results:** Free berberine improved the viability of LPS- insulted macrophages, reduced production of reactive oxygen species and inhibited the secretion of inflammatory cytokines in the infarcted IL-6 and TNFα. As expected these protective effects of berberine in vitro were diminished upon encapsulation into liposomes. In vivo, however, the liposome-encapsulated berberine significantly preserved ejection fraction after 28 days of MI while free berberine did not show any preservation of ejection fraction (29.5±1.9 for lipo-Berb, 18.2±3.3 for free berberine and 18.0±3.1 for empty liposomes; n=6–10; p<0.05).

**Conclusion:** Liposome-encapsulated berberine reduced adverse ventricle remodeling after MI. This outcome indicates that delivery of berberine via liposomes significantly improves its therapeutic availability and therefore treatment efficacy in vivo.

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**P4587 | BEDSIDE**

Atrio-ventricular plane excursion is impaired after ten weeks of anthracine therapy in breast cancer patients: Data from the PRADA study

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**Background:** Anthracyclines are well known for their dose-dependent cardiotoxic effect. The effect of low to moderate doses of the anthracycline epirubicin on left ventricular (LV) systolic function in otherwise healthy women remains unclear.

**Purpose:** To assess changes in various echocardiographic indices of LV systolic function in the early phase of anthracine therapy in breast cancer patients.

**Methods:** 126 women without heart disease and other serious comorbidities scheduled for anthracine-containing adjuvant treatment with epirubicin, were randomized in a placebo-controlled double blind clinical trial with candesartan and metoprolol (PRADA (NCT01434134)). Human epidemic growth factor receptor 2 (HER2)-positive patients received 4 cycles of epirubicin 100 mg/m² (moderate dose), while HER2-negative patients received 4-6 cycles of 60 mg/m² (low dose).

**Results:** MAPSE and S’ were significantly reduced after completion of moderate dose of anthracine (HER2-positive group), whereas no such effect was observed in patients receiving low-dose (HER2-negative group) (Table 1). Only MAPSE showed a significant difference between HER2-positive and -negative patients (p=0.035).

**Conclusion:** Moderate dose of epirubicin was associated with a significant reduction in MAPSE and S’ but not 2D strain, 2D and 3D left ventricular ejection fraction (LVEF), tissue Doppler systolic S’ and mitral annular plane systolic excursion (MAPSE). Measurements for MAPSE and S’ were performed at the base of the LV septum and lateral wall and averaged.

**Results:** MAPSE and S’ were significantly reduced after completion of moderate dose of anthracine (HER2-positive group), whereas no such effect was observed in patients receiving low-dose (HER2-negative group) (Table 1). Only MAPSE showed a significant difference between HER2-positive and -negative patients (p=0.035).

**Conclusion:** Moderate dose of epirubicin was associated with a significant reduction in MAPSE and S’ but not 2D strain, 2D and 3D LVEF. This suggests that LV systolic function is impaired already after a 4 week phase of anthracine therapy in breast cancer patients without prior cardiac disease.

**Acknowledgement/Funding:** University of Oslo, The Extra Foundation for Health and Rehabilitation, The Norwegian Cancer Society, Akershus University Hospital and AstraZeneca.
was significantly lower in patients on acetazolamide on day 4 both on visual scale (p<0.001) and 5-point Likert score (1.44 vs 2.222 in the control group; p=0.04).

Conclusion(s): Adding acetazolamide on top of other diuretic agents in patients with CHF exacerbation produces an additional diuretic and natriuretic effect and alleviation of dyspnoea. These findings need to be confirmed in a placebo controlled study.

Acknowledgement/Funding: Research Grant, Postgraduate Medical School in Warsaw

P4589 | BEDSIDE

Effect of intravenous vasodilators on short-term outcome in patients hospitalized for acute heart failure

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Background: In AHF patients with systolic blood pressure (SBP) over 110mmHg. There is no robust evidence, however, on their effects on mortality or whether there are subgroups of responding patients. We sought to address those issues by a secondary analysis of a large AHF registry.

Methods: The Acute Heart Failure Global Registry of Standard Treatment (ALARM-HF) included 4953 patients hospitalized for AHF in 9 countries in Europe, Latin America and Australia. We selected 4112 cases without cardiogenic shock or SBP <85mmHg on admission, including 1840 treated with iv vasodilators and 2272 not treated. Propensity score matching, based on exhaustive selection algorithms considering over 70 baseline variables, yielded a well-balanced subsample of 2524 patients, 1262 in each treatment group. Mortality was compared between groups by Mantel-Cox test and Cox regression with adjustment for region and treatment. 4 months after the randomization visit, iv vasodilators had no significant effect on short-term mortality. However, after adjusting for potential confounders, there was a significant effect of iv vasodilators on mortality neither in the original nor in the matched sample (HR=0.785 (0.503, 1.227), p=0.288 and HR=0.749 (0.457, 1.229), p=0.253, respectively). In subgroup analysis after matching, this effect was neutralized (HR=0.816 (0.562, 1.184), p=0.227, p<0.001) and 5-point Likert score (1,444 vs 2,222 in the control group; p=0,04).

Results: Mean PP (±SD) at baseline was 48±12.6 mmHg and 47.6±12.3 mmHg for the sacubitril/valsartan and enalapril treatment groups, respectively. With PP ≤80 mmHg, the hazard ratio (HR) for the primary outcome was 1.06 (0.96, 1.17), for PP1, and 1.04 (0.93, 1.16) for PP3 (overall P=0.51), with adjustment for region and treatment. 4 months after the randomization visit, iv vasodilators and reduced PP compared with enalapril: 0.58±0.12 mmHg vs. 1.55±1.19 mmHg, respectively (P<0.0001). Baseline PP did not modify the effect of sacubitril/valsartan compared with enalapril: sacubitril/valsartan vs enalapril hazard ratio for the primary outcome was 0.81 (0.70, 0.94) in PP1, 0.82 (0.72, 0.94) in PP2 and 0.74 (0.62, 0.88) in PP3, P for interaction=0.66.

Conclusions: In patients with HFpEF in PARADIGM-HF, baseline PP was not guided by the risk of CV death in the benefit of sacubitril/valsartan over enalapril was across the range of PP observed in patients in the trial.

Acknowledgement/Funding: MOST 104-231-B-010-060

P4591 | BENCH

New insights in molecular therapeutic mechanism of statin in heart failure using high-throughput tanscriptome analysis

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Background: Since the causes of heart failure (HF) are multifactorial and a variety of mediators are involved in the progression of HF, elucidating transcriptome complexity of hearts and understanding the functions of differentially expressed genes and therapeutic mechanism which reduce the risk of developing HF have become a major focus for HF research. Statin therapy has been conclusively demonstrated that statin therapy modestly reduced the risk of myocardial infarction and the recent meta-analysis demonstrated that statin therapy moderately reduced the risk of the composite outcome of HF death and non-fatal hospitalization.

Purpose and methods: We first investigated the global cardiac transcriptome analysis from tachycardia induced HF dogs using next generation genome sequencers and we secondly evaluated the effects of a statin, pitavastatin (0.3mg/kg, 4weeks, n=6) on cardiac functional changes and the gene expressions in failing dogs. All animal experiments were conducted according to the Guidelines for Animal Experimentation at the Animal Research Committee of a University of Medical Science.

Results: The mRNA sequence reads aligned with 15000 genes and a total of 426 genes were differentially expressed and 401 genes were up-regulated in failing heart compared to the normals (P<0.0001). We identified the top five most changed pathways which were categorized into angiotensin receptor Tie2, T cell receptor signaling in CD4, chemokine (C-X-C motif) receptor 4 (CXCR4), platelet-derived growth factor (PDGF) and tumor protein p21 pathways. Those pathways govern pivotal roles of immune cell activation, proliferation and proliferation of cells, inflammation, reactive oxygen species (ROS) production and energy metabolism. Despite no differences in blood pressure and ejection fraction, pitavastatin significantly lowered the elevated LV end diastolic pressure and shortened the prolongation of tau. The compound suppressed those upregulated gene expression such as SRC, SHC1, ELK1 and RIKP2 mRNA levels. These results indicate that statin may improve diastolic property affecting ras-ras MAPK cascade, ROS production, anti-apoptosis and cell adhesion to the extracellular matrix.

Conclusion: The high-throughput transcriptome analysis can provide new insights into cellular mechanisms of HF and therapeutic effects of statin for HF.

P4592 | BEDSIDE

Importance of Beta-Blocker therapy optimization in elderly patients with severe left ventricular dysfunction: is the dose important?


Introduction: Despite the value of beta-blockers (BB) in left ventricular systolic dysfunction (LVSD), this therapy remains underused in the elderly. The aim of our study was to evaluate the importance of BB optimization in elderly patients with chronic LVSD.

Methods: 559 patients ≥75 yrs. with LVEF <0.35 and free of MACEs six months before inclusion were included. A prospective observational study. Follow-up started at this point, baseline characteristics, resting heart rate and treatments were collected. Cohort was divided in three groups, depending on maximal tolerated dose of BB: no treatment group (NNB), low-dose group (LD) (<50% of target recommended

line PP predicted the primary outcome of cardiovascular death (CVD) or heart failure hospitalization (HFH), and whether PP modified the effect of treatment with sacubitril/valsartan (LCZ696), compared with enalapril, in the Prospective comparison of angiotensin receptor neprilysin inhibitor with angiotensin convert-
dose (TRD)) and high-dose group (HD) (≥50% of TRD). Primary end-point (EP) was all-cause death and secondary EP was first HF admission.

Results: 134 (24.0%) patients were in the NBB, 259 (46.3%) in LD and 166 (29.7%) in HD. Median follow-up was 29.9 months, median age was 81 y.o. and 65% were males. Main differences between groups: NBB patients were older, more frequently COPD, with higher resting heart rate, whereas LD and HD patients had more ischemic heart disease. 70 (52.2%) patients in the NBB died during follow-up, 94 (36.3%) in the LD, and 48 (28.9%) in the HD, whereas 42 (31.3%) in the NBB, 85 (32.6%) in the LD and 44 (26.5%) in the HD were admitted by HF. After multivariate Cox analysis, we found a significant relationship between BB dose group and mortality (p<0.025) with the following comparisons between groups: NBB vs. HD: HR=1.50, 95% CI: [1.02–2.19], p=0.037; LD vs. HD: HR=0.98, 95% CI: [0.68–1.40], p=0.894; and NBB vs. LD: HR=1.53, 95% CI: [1.12–2.11], p<0.001. In contrast, we did not find significant relationship between BB group and HF admission (p=0.887).

Conclusions: BB therapy in elderly patients with chronic LVSD improves survival, although independently of the received dose of BB. Nevertheless, we have not found any relationship with BB therapy and HF admission.

P4594 | BEDSIDE
Acute heart failure - Is more acute onset automatically connected with worse prognosis?
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Aim: To compare characteristics, therapy and in-hospital prognosis of acute HF (AHF) patients (pts) with rapid onset versus gradual worsening with necessity of hospitalization.

Methods: We used the data from multicenter AHF survey with 592 consecutive pts enrolled between 1 April and 31 June 2014. We analysed 85 variables in relation to clinical manifestation, management and outcome of AHF in univariate analysis, a significant of them (p<0.05) were used for multivariate analysis.

Results: 302 (51%) pts were enrolled into group with rapid onset (ROG) and 290 (49%) into group with gradual worsening (GWG). Pts in GWG were younger (71±12 vs 74±11 years), less symptomatic (in NYHA class IV 28 vs 42%) and admitted to intensive care units (17 vs 48%; all p<0.001). GWG pts were more admitted for acute decompensation of chronic HF (95 vs 55%), with dilative cardiomyopathy as only more frequent primary etiology (16 vs 6%, p<0.001), but less hypertensive (30 vs 53%, p<0.001). Left ventricular ejection fraction (LVEF) was lower and levels of urea higher in GWG (40±15 vs 45±13%, p<0.001 and 11±7 vs 10±6mmol/L, p<0.001, resp.). From intravenous therapy nitrates were more frequently used in ROG, on contrary to continuous fosfomezone in GWG (18 vs 4 and 20 vs 7%, resp., both p<0.001). The in-hospital mortality seemed to be higher and hospitalization longer in GWG (10 vs 8% and 6 vs 5 days, both p<0.001). Pts in GWG had more often signs as jugular vein distension (42 vs 33%, p<0.03), weakness or peripheral edema (93 vs 81% and 77 vs 47%, both p<0.001), but less orthopnea (30 vs 53%, p<0.001). Left ventricular ejection fraction (LVEF) was lower and levels of urea higher in GWG (40±15 vs 45±13%, p<0.001 and 11±7 vs 10±6mmol/L, p<0.001, resp.). From intravenous therapy nitrates were more frequently used in ROG, on contrary to continuous fosfomezone in GWG (18 vs 4 and 20 vs 7%, resp., both p<0.001). The in-hospital mortality seemed to be higher and hospitalization longer in GWG (10 vs 8% and 6 vs 5 days, both p<0.001). Pts in GWG had more often signs as jugular vein distension (42 vs 33%, p<0.03), weakness or peripheral edema (93 vs 81% and 77 vs 47%, both p<0.001), but less orthopnea (30 vs 53%, p<0.001). Left ventricular ejection fraction (LVEF) was lower and levels of urea higher in GWG (40±15 vs 45±13%, p<0.001 and 11±7 vs 10±6mmol/L, p<0.001, resp.). From intravenous therapy nitrates were more frequently used in ROG, on contrary to continuous fosfomezone in GWG (18 vs 4 and 20 vs 7%, resp., both p<0.001). The in-hospital mortality seemed to be higher and hospitalization longer in GWG (10 vs 8% and 6 vs 5 days, both p<0.001). Pts in GWG had more often signs as jugular vein distension (42 vs 33%, p<0.03), weakness or peripheral edema (93 vs 81% and 77 vs 47%, both p<0.001), but less orthopnea (30 vs 53%, p<0.001). Left ventricular ejection fraction (LVEF) was lower and levels of urea higher in GWG (40±15 vs 45±13%, p<0.001 and 11±7 vs 10±6mmol/L, p<0.001, resp.). From intravenous therapy nitrates were more frequently used in ROG, on contrary to continuous fosfomezone in GWG (18 vs 4 and 20 vs 7%, resp., both p<0.001). The in-hospital mortality seemed to be higher and hospitalization longer in GWG (10 vs 8% and 6 vs 5 days, both p<0.001).

Conclusions: Pts with gradually worsening AHF are discharged more symptomatic with less established recommended therapy and their in-hospital mortality seems to be higher. They should be managed therefore more intensively despite younger age and better functional status at admission, with special focus on subgroup with lower LVEF, atrial fibrillation and signs of persistent congestion.

P4595 | BEDSIDE
Procalcitonin levels measured before discharge predict 1-year mortality in patients hospitalized for acute decompensated heart failure
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Background: Procalcitonin (PCT) is a reliable marker for for diagnosing high risk infections in patients with heart failure (HF). Increased PCT levels measured on admission have been found to be associated with increased in-hospital and short-term mortality in patients HF. However, data about the influence of PCT levels on long-term survival in this patient group are limited.

Purpose: In this study, we aimed to investigate relationship between PCT levels
measured before discharge in patients with HF and 1-year survival rates.

Methods: Patients, who had been hospitalized for acute HF between June 2013–June 2014 in our clinic have been included in our study. The PCT levels were measured on admission and just before discharge. The diagnostic cut-off value of PCT in our laboratory is 0.5 ng/mL. Patients with obvious signs of infection (Fever >38°C, increased white blood cell count, patients requiring intravenous antibiotic therapy) have been excluded from our study. Multiple clinical and laboratory findings have been evaluated in addition to PCT levels. Cox-regression analysis has been performed to evaluate influence of PCT levels on 1-year survival.

Results: A total of 201 patients have been included in our study. Death has occurred in 79 patients (39.3%) in 1-year. Patients were divided into 3 equivalent groups according to PCT cut-off levels (≤0.05 ng/mL, 0.05–0.124 ng/mL, ≥0.124 ng/mL, respectively). In the cox-regression analysis, presence of diabetes mellitus (HR:1.43 [0.89–2.33 in 95% CI], p=0.036), hemoglobin levels (HR:0.83 [0.72–0.94 in 95% CI], p=0.02) and increased PCT levels (3rd tertile HR:2.61 [1.61–4.67 in 95% CI], p=0.001) were independently associated with 1-year survival. Survival of patients in third group with highest PCT levels is significantly worse than other groups (Figure 1).

Figure 1

Conclusion: Procalcitonin levels seem to be associated with 1-year survival rates in patients hospitalized for worsening of HF. In this study, we especially investigated influence of PCT levels measured in compensated state and in patients without significant signs of infection. Furthermore, we have also observed that slight increases of PCT levels, even levels below diagnostic cut-off value of our laboratory, may predict impaired survival rates in HF patients. The major limitation of our study is its limited patient population. Further well-planned studies with larger patient numbers are required for more precise results.

P4597 | BEDSIDE
Short term omega-3 polyunsaturated fatty acids supplementation induces favorable changes in right ventricle function and diastolic filling pressure in patients with chronic heart failure; a randomized

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Introduction: Omega-3 polyunsaturated fatty acids (omega 3-PUFAs) seem to favorably affect cardiac haemodynamics and may benefit the clinical course of heart failure patients. The role of omega 3-PUFAs supplementation on the left and right ventricular function of patients with chronic compensated systolic heart failure, under optimal treatment, was studied.

Methods: 205 consecutive patients with chronic compensated heart failure, due to ischemic (IHF) or dilated cardiomyopathy (DCM)-NYHA classification I-II, mean age 63±13 years old, under optimal medical treatment, were enrolled. Participants were 1-to-1 randomized on 1000 mg omega 3-PUFAs supplementation or no supplementation, in a non-blinded fashion. Echocardiographic assessment was performed at first visit and 6 months after; where ventricular dimensions, left atrium ejection fraction and tissue Doppler velocities of the mitral and tricuspid annulus were measured. Plasma BNP and serum creatinine levels were also measured.

Results: As compared with the control group, BNP levels in omega 3-PUFAs intervention group were 34.6% lower (p=0.001); end-diastolic and end-systolic left ventricular dimensions were decreased by 2.5% (p=0.047) and 3.7% (p=0.01), maximum volume of left atrium was decreased by 8.4% (p=0.004), left atrium ejection fraction was increased 6.0% (p=0.021) and regarding tissue Doppler parameters, TDI_Ev/Atv was decreased by 6.3% (p=0.038) in omega 3-PUFAs intervention group. Moreover, improvement in diastolic indices was more prominent in subjects with DCM as compared to IHF patients.

Conclusion: Omega 3-PUFAs supplementation was associated with improved left diastolic function and decreased BNP levels in patients with chronic heart failure. These finding suggest a beneficial role of omega 3-PUFAs on the hemodynamic course of patients with systolic heart failure.

P4598 | BEDSIDE
Longitudinal changes in left ventricular structure and diastolic function in relation to arterial properties in a general population

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Background: Serial imaging studies are needed to clarify the relation of change in left ventricular (LV) structure and function with arterial stiffness, but such longitudinal data is currently sparse.

Purpose: In a longitudinal population study, we assessed in continuous and categorical analyses to what extent arterial properties predict alterations in echocardiographic indexes reflecting LV structure and function.

Methods: In 607 participants (50.7% women; mean age, 50.7 years), using conventional echocardiography and tissue Doppler imaging, we measured LV dimensions, transmirtal blood flow and mitral annular tissue Doppler velocities at baseline and after 4.7 years. Using application tonometry, we assessed augmentation pressure (AP), central pulse pressure (cPP) and carotid-femoral pulse wave ve-
loyti (PWV) at baseline. Standardized effect size was expressed as the percent of change (Δ) in standard deviation (SD) of Δ LV indexes associated with a 1-SD increase in baseline arterial indexes.

**Results:** The clinical correlates of Δ LV indexes included baseline LV index, age, sex, body mass index, mean blood pressure, pulse rate as well as longitudinal change in these co-variables. After full adjustment, longitudinal increase in LV septal (standardized effect size: +14.6%; P=0.0017) and posterior wall (+13.3%; P=0.0015) thickness was significantly associated with higher PWV at baseline, whereas LV internal diameter (-12.2%, P=0.014) decreased with PWV. Consequently, a greater increase in relative wall thickness was associated with baseline PWV (+17.2%; P<0.0001). The longitudinal increase in LV wall thickness to higher baseline PWV was found similar in men and women. In adjusted logistic analysis, higher baseline PWV was associated with a 156% increase in the odds of developing LV concentric remodelling during follow-up, as compared to participants who improved LV geometry (P=0.0088). Furthermore, in women, a higher baseline PWV predicted a greater increase in LV mass (+18.1%, P=0.018) and E/e’ ratio (+25.8%, P=0.0064).

**Conclusions:** The key finding of this study is that longitudinal increase in LV relative wall thickness was associated with higher baseline PWV, a measure of arterial stiffness. Moreover, in women, a higher PWV predicted worsening of LV diastolic function. Our study demonstrated the important role of arterial properties as a mediator of LV concentric remodelling in men and women, and diastolic dysfunction in women.

**Acknowledgement/Funding:** IC15-CT98-0329-EPQGH, LSHM-CT-2006-037093, HEALTH-F4-2007-201550, HEALTH-2011-278249-EU-MASCARA, FWO: G.0734.09, G.0880.13, G. 0881.13, 1120916N

### P4599 | BEDSIDE

**TR1/logFR as a useful marker and predictor of myocardial iron load in heart failure**

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**Background:** The clinical studies have demonstrated that the iron deficiency (ID) correction with IV iron (Ganzoni formula) in heart failure (HF), improved symptoms, exercise capacity, and reduced hospitalization for HF. However the myocardial iron (M-Iron) load should be precisely balanced, as the excess of myocardial iron generates oxidative stress whereas at low concentration promotes cell survival pathways.

**Purpose:** To assess in HF in the failing left ventricle (LV) M-Iron with relation to alternative serum markers of iron metabolism.

**Methods and results:** Study group of 33 HF patients qualified to heart transplantation (LVEF 22±11%, NTproBNP 5464±4825pg/ml). The following assessments in serum: iron concentration, transferrin/saturation/receptor (TR/TSAT/TfR1), ferritin (FR), erythropoietin (EPO) and TR1/logFR; in myocardium (M-): M-Iron concentration, M-TR and M-TfR1 were analyzed. Non-failing hearts (NFH n=11) were used as control/reference tissue.

On myocardial level in HF LV M-Iron load is reduced, and negatively associated with M-FR (r=-0.37, p=0.05). Neither the degree LV of damage, neuro-hormonal/proinflammatory activation nor parameters utilized for iron assessment, iron from Ganzoni formula did not correlate with M-Iron.

**Conclusions:** Total iron deficit based on Ganzoni formula did not reflect iron deficiency in the failing LV myocardium. Out of the determinants only TR1/logFR correlated with LV M-Iron, being simultaneously the independent predictor of LV M-Iron. It would enable an indirect LV M-Iron assessment and contribute to increase the safety of iron repletion therapy for ID in HF patients.

### P4601 | BEDSIDE

**Worsening heart failure in acute decompensated heart failure admissions: Is it all the same?**

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**Introduction:** Worsening heart failure (WHF) is an outcome measure in patients hospitalized for acute decompensated heart failure (ADHF) not fully addressed. It identifies patient subset with poor prognosis in ADHF setting. WHF definition includes P who progressively worsen their hemodynamic status despite intravenous (IV) initial treatment, as much as those with recurrent signs and symptoms, once IV therapy has been discontinued. It has not been described if each point of its components has different prognosis or not.

**Aims:** To compare P prognosis in different WHF clinical subsets.

**Methods:** In-hospital WHF was defined as worsening signs or symptoms of ADHF requiring rescue IV therapy. If WHF progressively worsened despite IV initial treatment, it corresponded to PROGRESSIVE; while it was defined as RECURRENT as signs and symptoms reappeared once IV therapy has been discontinued. Demographic, clinical and biochemical data were compared. In-hospital,
post discharge and 180-day outcomes were reported. Those P who received a heart transplant were excluded from this analysis. 

**Results:** A total of 781 consecutive P admitted for ADHF between July 2011 and January 2016 were analyzed. WHF was present in 97 P (12.4%). It corresponded to PROGRESSIVE in 60 P (61%), while 38 P (39%) were RECURRENT. Although both groups did not differ in terms of gender, admission vital signs, co-morbidities or ventricular function, RECURRENT were older (74 vs 64 years old; p=0.001) and had more frequently clinical evidences of pulmonary congestion (53.3 vs 30.5%; p=0.02) at admission, while clinical hyperfusion was more frequent in PROGRESSIVE (74.5% vs 15.8%; p=0.002). In hospital complications were more frequently observed in P with PROGRESSIVE, including Diuretic resistance (43 vs 18.9%; p=0.01). Length of stay were similar in both cases (p= NS). In-hospital complications were more frequently observed in P with PROGRESSIVE, including Diuretic resistance (43 vs 18.9%; p=0.01).

**Conclusions:** WHF was prevalent in P admitted for ADHF. Progressive WHF had worse short and mid-term outcome. Recurrent WHF characterized an older population, with insufficient decongestion and higher readmission rates.

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**P4603 | BEDSIDE**

**Heart failure team in real-life conditions: a group effort to optimize treatment of the most complex heart failure patient subpopulation**

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**Background:** The heart team concept was introduced to optimize care of patients with complex coronary artery disease. Heart failure (HF) is the biggest diagnostic and therapeutic challenge in clinical practice. A multidisciplinary approach towards HF patients could be the ideal development of the heart team concept.

**Purpose:** With a large cohort of systolic HF patients we have decided to analyze the profile and outcomes of patients in whom the heart failure team (HFT) has been involved in the therapeutic process.

**Methods:** HFT was typically constituted of a heart failure cardiologist, an invasive cardiologist, a cardiac surgeon and other appropriate specialists. With a single-center registry (n=1798) of systolic HF patients treated in a large-volume cardio-vascular hospital we have decided to compare the group of patients consulted with HFT (n=956) and not (n=842).

**Results:** The clinical characteristics and echocardiographic parameters of patients are presented in table 1. The HFT group had more comorbidities and a worse echocardiographic profile. There were no significant differences in administered medical treatment between the groups. The reason for HFT consultation were: complex coronary artery disease (40.3%), severe valve disease (30.2%), qualification for heart transplantation (25.5%) and others (4%). Only HFT patients were qualified for cardiac surgery (25.2%). HFT patients were also significantly more frequently qualified for invasive procedures, such as right heart catheterization (20.2% vs 6.4%; p<0.001) or percutaneous coronary interventional (28.9% vs 9.3%; p<0.001). Twelve-month mortality in the HFT group was significantly higher (17.6% vs 6.8%), resulting from more complex clinical profile. The HFT consultation did not significantly influence survival in the analyzed period, confirmed by Cox regression analysis (adjusted HR 1.24, 95% CI 0.87–1.75, p=0.22).

**Conclusions:** HFT acts as a gate-keeper for cardiac surgery, heart transplantation and invasive cardiology procedures. Heavy burden of HF and co-morbidities impairs the prognosis of HF patients, at the same time underlining the importance of team approach to difficult decisions in contemporary cardiovascular medicine.

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**P4604 | BEDSIDE**

**Central-line associated bloodstream infections in inotropic dependent patients waiting for heart transplantation**

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**Methods:** Patients with advanced heart failure waiting for heart transplantation characterized as Status 1A require high-dose inotropes. Central-line associated bloodstream infection (CLABSIs) is a severe complication in such patients.

**Results:** We retrospectively studied 85 patients listed as Status 1A between 2003 and 2015 at our institution. Characteristics of the CLABSIs were further assessed. Logistic regression analysis was used to identify predictors of CLABSIs. The majority were men (82%). At the time listing, mean age was 47±10 years and there were 52 (51%) past smokers with 27 (27%) diabetics. Ischemic disease was the etiology of cardiomyopathy in 39 (39%) patients and implantable defibrillator were present in 50 patients. The mean creatinine at time of listing was 1.37±0.3 mg/dL, while the mean BMI was 28±4 kg/m². There were 14 (16%) patients who experienced a total of 19 CLABSIs. Among those with CLABSIs, a median of 6 PAC procedures (median 7.315±3) were performed, with 44% patients with the internal jugular, 31% with the subclavian, and 25% with the femoral vein. Patients who developed CLABSIs had catheters in place for a mean duration of 158±90. Co-agulase negative staphylococcus (CNS) was the pathogen in the majority of the cases. CLABSIs and Staphylococcus aureus was the cause for the antibiotic regimen. The mean time to first CLABSI was 86±77 after being listed as Status 1A. The mean duration to CLABSI from catheter placement was mean: 15±11. Age, history of smoking, obesity, diabetes and renal dysfunction were not associated with CLABSIs.

**Conclusions:** Among heart failure patients listed as Status 1A for heart transplantation, nearly a quarter of all patients developed CLABSIs, leading to a down-

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**Abstract P4603 – Table 1. Comparison of groups**

**HFT (n=956)** | **Non-HFT (n=842)** | **P**
---|---|---
Age | 61.4±12.1 | 60.7±12.5 | 0.59
Diabetes mellitus (%) | 43.8 | 48.2 | 0.01
Chronic kidney disease stage III (%) | 31.7 | 26.0 | 0.008
Ischemic etiology (%) | 70.7 | 57.7 | <0.001
Event-free rate (%)
Follow up period (days)
1 year | 94.2 | 93.6 | 0.97
2 years | 87.8 | 88.2 | 0.80
5 years | 70.8 | 70.8 | 0.99
Log-rank test, p=0.001
grade of the status on the transplant waiting list. CNS was the most common pathogen.

P4606 | BEDISETE
Prevalence and determinants of restless leg syndrome among heart failure patients
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Background: Restless leg syndrome (RLS) is a common condition that has an estimated prevalence of 5–10% of the general population in Europe and North America. However, it is usually under diagnosed despite its well known detrimental effects on quality of life. While, there is substantial body of evidence showing higher rates of RLS among certain groups such as end-stage kidney disease patients, little is known about its prevalence among heart failure population. Moreover, it not known whether the parameters of cardiac function, whether clinical or echocardiographic, are related to RLS.

Purpose: To estimate the prevalence of RLS in heart failure patients and to explore the association of clinical and echocardiographic cardiac function indicators with RLS.

Methods: A multi centre cross-sectional study included attendees of heart failure clinics during the period of Sept to Dec 2015. Participants were surveyed using the Cambridge-Hopkins Diagnostic Questionnaire for RLS. Further medical record review identified data on comorbid conditions, NYHA classification, ejection fraction (EF) and laboratory profile. Comparisons were conducted using ANOVA and chi-square tests. Multivariate logistic regression explored the correlation of cardiac function indicators with RLS (expressed in Odds Ratios with 95% confidence intervals). Ethical Approval was granted from our University Hospital.

Results: A total of 140 heart failure patients were included. The mean age was 70.4 (±9.9) years. Men represented the majority of this cohort (77.8%). Mean EF% was 34.4% (±11). Patients with NYHA classifications of I-II and III-IV constituted 78.2% and 21.8%, respectively. The prevalence of RLS was substantially higher (35.3%–28.4%). In the univariate analysis, NYHA class (I-II vs I-III) was not associated with RLS [OR=1.28 (0.48–3.4)]. However, moderate to severe EF class (vs normal to mild) was significantly associated with RLS [OR=3.4 (1.29–9.5)]. Adjustment for demographics, co-morbidities, renal function, and haemoglobin revealed virtually similar results. OR=3.5 (1.19–10.8) for moderate-to-severe EF class. Other significant variables included patient’s eGFR [OR= 0.98 (0.96–0.99)].

Conclusion: The Prevalence of RLS among heart failure patients is substantially high and often under-diagnosed. The observed association between Left Ventricular dysfunction degree and RLS should prompt careful screening. Further studies on larger scale is certainly needed.

P4606 | BEDSIDE
The impact of heart failure on the incidence of stroke in patients with atrial fibrillation: the Fushimi AF Registry
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Background: Restless leg syndrome (RLS) is a common condition that has an estimated prevalence of 5–10% of the general population in Europe and North America. However, it is usually under diagnosed despite its well known detrimental effects on quality of life. While, there is substantial body of evidence showing higher rates of RLS among certain groups such as end-stage kidney disease patients, little is known about its prevalence among heart failure population. Moreover, it not known whether the parameters of cardiac function, whether clinical or echocardiographic, are related to RLS.

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Conclusion: The Prevalence of RLS among heart failure patients is substantially high and often under-diagnosed. The observed association between Left Ventricular dysfunction degree and RLS should prompt careful screening. Further studies on larger scale is certainly needed.

P4606 | BEDISETE
Glycemic variability predicts left ventricular reverse remodeling in patients with ST-segment elevation acute myocardial infarction
Y. Minamoto, N. Iwahashi, M. Gohbara, S. Kataoka, A. Ekiyama, Y. Matsuzawa, N. Maejima, K. Tsukahara, K. Hibi, M. Kosuge, T. Ebina, K. Kimura. Yokohama City University Medical Center, Cardiovascular Center, Yokohama, Japan

Background: Inflammation is one of the factors for positive left ventricular remodeling. Recently, the relationship between glycemic variability (GV) and inflammation is being explored, however few data regarding left ventricular reverse remodeling (LVRV) are available in patients with ST-segment elevation acute myocardial infarction (STEMI). We sought to evaluate the clinical significance of LVRV, especially, the role of GV for LVRV.

Methods: We investigated 98 patients with STEMI who underwent reperfusion therapy within 12th onset. We analyzed GV, as determined by a continuous glucose monitoring system (CGMS; iPro2, Medtronic, Minneapolis, USA), and the LV by cardiac magnetic resonance imaging (CMR). All patients were equipped with CGMS in a stable phase after admission. CMR were performed 7days and 7 months repeatedly. The mean amplitude of glycemic excursions (MAGE) was calculated by measuring the arithmetic mean of the differences between consecutive peaks and nadirs if the differences were greater than 1 standard deviation. LVRR was defined as an absolute decrease in left ventricular end-systolic volume index of >10%. Patients were classified into 2 groups which were occurred LVRV (Group RR; n=27) or not (Group NRR; n=71).

Results: The occurrence rate of LVRV was 26%. There were no significant differences between group RR and NRR regarding age (61.4±11.1 vs. 63.4±12.5 years), male gender (85% vs. 84%), diabetes (18% vs. 32%, p=0.17) and peak creatinine phosphokinese (CPK; 3287 vs. 2353U/L, p=0.42). Group RR had more frequently with culprit LAD (78% vs. 39%, p=0.001).

MAGE were significantly lower in group RR than group NRR (31.8±12.5 vs. 49.2±24.2mg/dl, p=0.001). Multivariate analysis revealed that MAGE were independent predictor of LVRV in the chronic phase (odds ratio, 0.944, 95% confidence interval, 0.907 to 0.982; p=0.004).

Conclusion: Low glycemic variability at early but stable phase of STEMI predicted LVRV.

P4608 | BEDISETE
Weight loss or exercise to improve insulin sensitivity in overweight CAD patients? One year follow-up in the randomised CUT-IT trial
L.R. Pedersen1, R.H. Olsen1, S.B. Haugaard2, E. Prescott1,1, Bisperbjerg Hospital of the Copenhagen University Hospital, Department of Cardiology, Copenhagen, Denmark;2Amager Hospital, Department of Internal Medicine, Copenhagen, Denmark

Background: The majority of patients with coronary artery disease (CAD) have abnormal glucose metabolism, which is related to poor prognosis. The ‘obesity paradox’ questions the benefit of weight loss in overweight patients with CAD. We compared the effects of an aerobic interval training (AIT) programme to a combination of an initial rapid weight loss and AIT on glucose metabolism and insulin sensitivity in overweight, sedentary patients with CAD.

Methods: 70 non-diabetic CAD patients, BMI 28–40 kg/m² and age 45–75 years were randomised (1:1) to either 1) 12 weeks’ AIT at 85–90% of peak heart rate three times/week followed by 40 weeks’ AIT twice weekly or 2) a low energy diet (LED, 800–1000 kcal/day) for 8–10 weeks followed by a weight maintenance diet (LED, 500–700 kcal/day) for 40 weeks. The primary outcome was based on a 2-hour oral glucose tolerance test, fasting insulin, and 2-hour glucose. ISI-composite and ISI-homa (+=HOMA-IR) was calculated as surrogate measures of whole-body and hepatic insulin sensitivity, respectively.

Results: 26 (74%) AIT and 29 (83%) LED+AIT participants completed the one-year intervention. Forty-seven (85%) participants had prediabetes at baseline. Results of the intervention are presented in table 1. A combination of weight loss and AIT led to a sustained weight loss and significant improvements in VO2peak and all measures of insulin sensitivity. Effects were weaker in the AIT group although with few significant between group differences.

Downloaded from https://academic.oup.com/eurheartj/article-abstract/37/suppl_1/599/2197552 by guest on 18 April 2019
Conclusion: Combining weight loss and AIT is feasible in overweight CAD patients and leads to long-term beneficial effects and it is at least as effective as AIT alone in improving glucose metabolism and insulin sensitivity.

Acknowledgement/Funding: The Danish Council for Independent Research, The Danish Heart Foundation, The Beckton Foundation, The Cambridge Weight Plan supplied the LED

P4609 | BEDSIDE
Family history impact in the setting of the metabolic syndrome: the PREDICT study and real-life results of the seven countries study
B. Parapid1, N. Danchin 2, O.M.S. Nedeljkovic-Arsenovic1, B. Obrenovic-Kircanski1, H. Blackburn3, A. Menotti4, H. Adachi5, D. Kromhout6, D. Jacobs3
1, 4 Associations for Cardiac Research, Rome, Italy; 2, 5 Kurume University School of Medicine, Kurume, Japan; 3, 6 Wageningen University UR, Wageningen, Heraklion, Greece; 4, 5 Serbian Academy of Sciences and Arts, Belgrade, Serbia
Introduction: The metabolic syndrome (MetSy) as a cluster of risk factors that are known to promote atherothrombosis, diabetes and obesity, primarily, while the Seven Countries Study remains one of the core epidemiological trials that taught us the basis of modifiable risk factors for coronary heart disease, mainly. Inherent risk factors and parental morbidity and mortality was equally studied in all the participants, and we are presenting the results of the 40 years follow-up.

Material and methods: The Seven Countries Study encompassed 12,763 participants who were healthy at baseline and who underwent regular check ups every 5 years throughout over 4 decades. Parental health histories were also taken into account.

Results: Using the IDF definition of the Metabolic Syndrome, 9.0% of participants were identified and the impact of Premature Paternal Death, Premature Maternal Death, Family history of myocardial infarction (Fam Hx MI), Family history of hypertension (Fam HTA), Family history of stroke (Fam Hx Stroke), and Family history of diabetes (Fam Hx DM) on their overall mortality is shown in Table 1.

Conclusion: Family history of hypertension and stroke was shown a significant direct positive correlation for overall mortality, rendering hypertension and stroke family hallmark predictors for fatal outcomes in the setting of the metabolic syndrome.

P4610 | BEDSIDE
New role of lysosomal acid lipase in metabolic syndrome
A. Nohara1, M.A. Kawashiri2, Y. Eto3, M.A. Fujisaki3, H. Nohara1, M.A. Y contestants, and overall mortality was calculated as the number of deaths divided by the total number of participants in each group over the 40 years follow-up.

Material and methods: The Seven Countries Study encompassed 12,763 participants who were healthy at baseline and who underwent regular check ups every 5 years throughout over 4 decades. Parental health histories were also taken into account.

Results: Using the IDF definition of the Metabolic Syndrome, 9.0% of participants were identified and the impact of Premature Paternal Death, Premature Maternal Death, Family history of myocardial infarction (Fam Hx MI), Family history of hypertension (Fam HTA), Family history of stroke (Fam Hx Stroke), and Family history of diabetes (Fam Hx DM) on their overall mortality is shown in Table 1.

Conclusion: Family history of hypertension and stroke was shown a significant direct positive correlation for overall mortality, rendering hypertension and stroke family hallmark predictors for fatal outcomes in the setting of the metabolic syndrome.

P4611 | BENCH
Disruptive arterial pressure stability is improved by sodium-glucose co-transporter 2 inhibitor in streptozotocin-induced diabetic rat
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1, 2 Kyushu University Graduate School of Medical Sciences, Department of Cardiovascular Medicine, Fukuoka, Japan; 3 Kyushu University, Collab. Res. Inst. Innovation for CV Dis., CDiC, Fukuoka, Japan
Background: No one doubt that diabetes mellitus is a major cardiovascular risk. However, anti-diabetic therapies could not have certainly prevented cardiovascular events. At contrast, arterial pressure reduction has been determined to have beneficial prevention for cardiovascular mortality in patients with diabetes mellitus. Moreover, patients with diabetes mellitus have impaired arterial pressure vari- ability. In these aspects, a new anti-diabetic agent sodium-glucose co-transporter 2 (SGLT2) inhibitor has been focused on its unique arterial pressure lowering effect. Amazingly, SGLT2 inhibitor decreased cardiovascular death of patients with diabetes mellitus in a latest clinical trial.

Purpose: We examined whether diabetes mellitus model rats would destabilize arterial pressure or not, and if so, whether SGLT2 inhibitor could ameliorate the disruptive arterial pressure stability.

Methods: We made streptozotocin-induced diabetic (STZ) rats by single intravenous injection of streptozotocin (50 mg/kg) to 10 weeks of age male Sprague-Dawley rats with telemetry system monitoring arterial pressure in conscious states. At 6 days after the injection of streptozotocin, orally administration of SGLT2 inhibitor (ipragliflozin 1 mg/kg/day) or vehicle was initiated to established hyperglycemic STZ rats for 14 days. We calculated average and standard deviation (SD) of arterial pressure as the index of liability from histograms of arterial pressure by day (rest-time) and night (active-time).

Results: Streptozotocin did not change mean and SD of arterial pressure both in rest-time and active-time. SGLT2 inhibitor for 14 days reduced blood glucose by about 100 mg/dl (516 mg/dl to 423 mg/dl). Both of SGLT2 inhibitor and vehicle did not alter body weight and both of them almost equally increased urine volume, urinary sodium excretion and urinary noradrenaline excretion. Vehicle reduced mean arterial pressure a little bit both in rest (-5.2 mmHg, n=3) and active-time (-5.6 mmHg, n=3) but did not change SD of arterial pressure both in rest- and active-time. On the other hand, SGLT2 inhibitor reduced mean arterial pressure both in rest- (-14.7 mmHg, n=2) and active-time (-12.8 mmHg, n=2), and ameliorated SD of arterial pressure both in rest- (−7.7 mmHg to 6.0 mmHg, n=2) and active-time (6.6 mmHg to 5.5 mmHg, n=2).

Conclusions: SGLT2 inhibitor for 14 days ameliorates arterial pressure stability both in rest- and active-time without excess body weight loss and sympathoexcitation in streptozotocin-induced diabetic model rats.
Conclusions: The present results indicate independent relationships between uric acid levels and the new onset MetS in the Japanese general population. The uric acid level was an important predictor of the new onset MetS. Inhibition of an increase in uric acid levels may lead to an effective prevention of cardiovascular diseases through a reduction of the development of MetS. P4614 | BEDSIDE
Ivabradine therapy favorably modulates sympathetic overdrive and arterial stiffening in hypertensive patients with metabolic syndrome

Background/Introduction: Hypertension and metabolic syndrome are related to sympathetic overdrive and arterial stiffening, while there are no data whether ivabradine modulates sympathetic activity and vascular abnormalities in this setting.

Purpose: The aim of this study was to assess the effect of ivabradine on muscle sympathetic nerve activity (MSNA) and arterial stiffness in hypertensive patients with or without ivabradine (control group).

Methods: We studied 36 patients with essential hypertension (age: 56±10 years, 30 males, office blood pressure (BP): 148±92/14±11 mmHg) on antihypertensive therapy with a fixed combination of perindopril/amlopidine. Patients were randomized with a ratio 2:1 to ivabradine (5 mg twice daily) or no ivabradine (control group). Metabolic syndrome was defined according to the Adult Treatment Panel III criteria. In all participants at baseline and at 6 months follow-up arterial stiffness was evaluated on the basis of carotid to femoral pulse wave velocity (PWV), while sympathetic drive was assessed by MSNA estimations based on established methodology (microneurography).

Results: Patients on ivabradine (n=24) compared to controls (n=12) did not differ regarding baseline BP, creatinine, glucose and lipid profile (p>NS or all). There was no significant difference in the reduction of office BP between the two study groups (p=NS). However, hypertensive patients in the ivabradine group were characterized by a reduction in carotid to femoral PWV from 9.1±5.9 m/sec to 9.8±1.2 m/sec (p<0.001) and sympathetic nerve traffic as reflected by MSNA values from 86±22.5 bursts per 100 heart beats to 74±8±2.4 bursts per 100 heart beats (p=0.001) at 6 months. No significant changes in PWV and MSNA were observed in the control group (p=NS).

Conclusions: In hypertensive patients with metabolic syndrome, treatment with ivabradine reduces sympathetic activation and arterial stiffening as reflected by lower MSNA and PWV levels at 6 months follow-up. These findings suggest that ivabradine could exhibit additional therapeutic properties in the setting of dysmetabolic hypertension.
Bichat-Claude Bernard, Diabétologie Endocrinologie Nutrition, Paris, France;
Methods: To analyze the association between chronic metformin treatment and the Aim: patients undergoing percutaneous coronary intervention (PCI), associated with Contrast-induced nephropathy (CIN) is a frequent complication in Background: Contrast-induced nephropathy (CIN) is a frequent complication in percutaneous coronary intervention (PCI), associated with increased risk of renal failure, on CIN remains to be investigated. Aim: To analyze the association between chronic metformin treatment and the development of CIN after primary PCI for ST segment elevation myocardial infarction (STEMI).
Methods: 372 patients with diabetes mellitus (DM) treated with PCI <24h in 2 coronary care units (Paris-Bichat and Dijon Hospital, France) were included. Serum creatinine (Cr) was measured before and 48h after PCI. CIN was defined as an increase in Cr of 44μmol/L (0.5 mg/dL) or 25% over baseline after PCI. Since CIN was urgent, metformin could not be withheld prior to PCI but was usually stopped after PCI.
Results: Mean age was 66±11 y, and 25% were women. 64% had hypertension, 56% had DM duration >5 year, and 26% had prior coronary artery disease. Metformin and sulfonylurea were the most frequently used antidiabetic chronic treatments (40% for both), and 27% were on insulin therapy. The other antidiabetic medications, including glinide, glitazone, and acarbose were rarely used (3%, 2%, and 5%, respectively). Mean back to normal glycemic levels (STR). STR was defined as complete (0% to 25%), partial (25% to 75%), and none (75% to 100%).
Conclusion: Glucose fluctuation was related with myocardial damage after PCI in non-diabetic STEMI patients. Measurement of MAGE by CGMS is useful for risk stratification of STEMI patients undergoing emergent PCI, and glucose fluctuation may affect the microcirculatory disturbance.

P4617 | BEDSIDE
Glucose fluctuation for detection of myocardial damage risks after P4618 | BEDSIDE
Glucose fluctuation for detection of myocardial damage risks after percutaneous coronary intervention in non-diabetic ST-segment elevation myocardial infarction patients percutaneous coronary intervention in non-diabetic ST-segment elevation myocardial infarction patients
S. Oka, J. Deyama, K. Umetani, K. Sudo, S. Takahashi, A. Makino, K. Sano, M. Nakamura, Yamanashi Prefectural Central Hospital, Cardiology, Kofu, Japan
Background: Glucose fluctuation affects endothelial dysfunction and may promote atherothrombosis by increasing oxidative stress in diabetes mellitus patients, but it is unknown in non-diabetic patients. Thus, in this study we examined whether glucose fluctuation may provide information for myocardial damage risks after successful percutaneous coronary intervention (PCI) in non-diabetic ST-segment elevation myocardial infarction (STEMI) patients.
Methods: We researched glucose fluctuation with continuous glucose monitoring system (CGMS). CGMS was performed in consecutive 64 non-diabetic STEMI patients treated with emergent PCI and all of them were performed 75gOGTT at the same time. Glucose fluctuation was evaluated with mean amplitude of glycemic excursion (MAGE) from CGMS. Obtained coronary flow and myocardial damage after PCI were estimated by myocardial blush grade (MBG), ST segment resolution (STR), STR was defined as complete (>70%), partial (30% to 70%), or none (<30%). In subgroup study, patients were prospectively followed-up for 18 months or until the occurrence of one of the following major adverse cardiovascular events (MACEs): cardiac death, nonfatal myocardial infarction, unstable angina requiring coronary revascularization, or ischemic stroke.
Results: All the patients were performed emergent PCI on admission, and CGMS was performed on the day of PCI. MAGE was calculated by mean of glycemic excursion over 24h from admission. Patients were classified into 4 categories (the population-attributable fraction (PAF) in total = 51%) in DM, as this attribution was nearly double compared to the PAF in non-DM (27.3%).
Conclusion: MAGE affected the GLS in chronic phase in patients with anterior STEMI. GV may be one of the causes of LV remodeling.

P4619 | BEDSIDE
Glycemic variability is associated with left ventricular global systolic function in patients with anterior ST-segment elevation myocardial infarction
S. Kataoka, N. Iwashashi, M. Gohbara, E. Akiyama, N. Maejima, K. Tsukahara, K. Hibi, M. Kosuge, T. Ebina, K. Kimura. Yokohama City University, Cardiovascular Department, Yokohama, Japan
Background: Glycemic variability (GV) plays an important role in patients with ST-segment elevation myocardial infarction (STEMI). Speckle-tracking-based strain measurements of LV function is known for advanced image analysis technique. Previous reports demonstrated that global systolic longitudinal strain (GLS) predicts poor prognosis and cardiac death. However, the relationship between GV and GLS in patients with STEMI is remains unknown.
Methods: We investigated 52 patients (63 years, peak creatine phosphokinase (CK) was 3366U/L) with anterior STEMI who underwent primary reperfusion therapy. Mean GV, by measuring the arithmetic mean of the differences between consecutive peaks and nadirs if the differences were greater than 1 standard deviation. The mean amplitude of glycemic excursions (MAGE) was calculated as a marker of GV, by measuring the arithmetic mean of the differences between consecutive peaks and nadirs if the differences were greater than 1 standard deviation. We measured echocardiography using Vivid q (GE, Norway) at 6 months from onset. Strain imaging was analyzed using an off-line image analysis program (2D Cardiac Performance Analysis, TomTec Imaging Systems, Germany) and GLS was measured at apical 4ch and 2ch view.
Results: Mean value of GLS and MAGE were – 14.8±3.6%, and 39±19mg/dl. MAGE (=0.37, p=0.01) and peak CK (r=0.37, p=0.01) were positively correlated with GLS. Multivariate analysis showed MAGE was independently associated with GLS (β=0.07, p=0.01).

P4617 | BEDSIDE
Glycemic variability is associated with left ventricular global systolic function in patients with anterior ST-segment elevation myocardial infarction
S. Kataoka, N. Iwashashi, M. Gohbara, E. Akiyama, N. Maejima, K. Tsukahara, K. Hibi, M. Kosuge, T. Ebina, K. Kimura. Yokohama City University, Cardiovascular Department, Yokohama, Japan
Background: Glycemic variability (GV) plays an important role in patients with anterior ST-segment elevation myocardial infarction (STEMI). GV may be one of the causes of LV remodeling.
Results: Mean value of GLS and MAGE were – 14.8±3.6%, and 39±19mg/dl. MAGE (=0.37, p=0.01) and peak CK (r=0.37, p=0.01) were positively correlated with GLS. Multivariate analysis showed MAGE was independently associated with GLS (β=0.07, p=0.01).

P4616 | BEDSIDE
Metformin and contrast-induced nephropathy in diabetic patients treated with primary percutaneous coronary intervention for ST segment elevation myocardial infarction and a multicentre study
M. Zeller1, M. Labalette-Bart2, J.-M. Julliard3, L. Feldman3, G. Steg3, Y. Cottrin4, R. Roussel3, 1University of Burgundy, INSERM U866, Dijon, France; 2Hospital Bichat-Claude Bernard, Diabétologie Endocrinologie Nutrition, Paris, France; 3Hospital Bichat-Claude Bernard, Cardiologie, Paris, France; 4University Hospital Center, Department of Cardiology, Dijon, France
Background: Contrast-induced nephropathy (CIN) is a frequent complication in patients with acute coronary syndromes (ACS), especially during percutaneous coronary intervention (PCI). Although the association between long-term metformin treatment prior to primary PCI had no significant impact on CIN. Larger studies are needed to confirm these findings.
Method: We researched glucose fluctuation with continuous glucose monitoring system (CGMS). CGMS was performed in consecutive 64 non-diabetic STEMI patients treated with emergent PCI and all of them were performed 75gOGTT at the same time. Glucose fluctuation was evaluated with mean amplitude of glycemic excursion (MAGE) from CGMS. Obtained coronary flow and myocardial damage after PCI were estimated by myocardial blush grade (MBG), ST segment resolution (STR), STR was defined as complete (>70%), partial (30% to 70%), or none (<30%). In subgroup study, patients were prospectively followed-up for 18 months or until the occurrence of one of the following major adverse cardiovascular events (MACEs): cardiac death, nonfatal myocardial infarction, unstable angina requiring coronary revascularization, or ischemic stroke.
Results: All the patients were performed emergent PCI on admission, and CGMS was performed on the day of PCI. MAGE was calculated by mean of glycemic excursion over 24h from admission. Patients were classified into 4 categories (the population-attributable fraction (PAF) in total = 51%) in DM, as this attribution was nearly double compared to the PAF in non-DM (27.3%).
Conclusion: MAGE affected the GLS in chronic phase in patients with anterior STEMI. GV may be one of the causes of LV remodeling.

P4616 | BEDSIDE
Waist circumference is associated with elevated blood pressure in children with normal body mass index: a cross-sectional evaluation of 3,417 schoolchildren
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The childhood prevalence of obesity became a major problem of public health. Conditions associated with high body mass index (BMI), such as hypertension,
have emerged in younger groups. Although waist circumference (WC) is a marker of cardiovascular risk in adults, it is unclear whether this index is associated with cardiovascular risk factors in children, especially when the BMI is normal.

**Objective:** To evaluate the association between WC and elevated blood pressure (BP) in children within normal BMI range.

**Methods:** Cross-sectional evaluation of students between 6 and 11 years. The WC was categorized by quartile for each age group (6–7, 7–8, 8–9, 9–10, 10–11). Normal BP was defined as values <90th percentile for gender, height, and age. Levels above this range were considered elevated.

**Results:** Of the 5,037 children initially assessed, 404 (8%) were excluded for being overweight or obese (overweight: 374, 7.4%; obesity: 842, 16.7%). 3,417 children were evaluated. The prevalence of overweight was 10.7%. In children with WC in the lowest quartile, the prevalence of overweight BP was 8.1%.

The increased LV mass/volume ratio was due to a greater increase in LV mass to LV end-diastolic volume. In multivariate analysis, BMI z-score and systolic blood pressure were independent determinants of LV mass-to-volume ratio (R2 = 0.28). MPI was significantly associated with LV mass-to-volume ratio in the school and adolescents groups (r = 0.22 and 0.16, p < 0.01, respectively), but this association was not significant in the infants and preschool children groups.

**Conclusion:** In infancy, higher BMI is associated with concentric LV hypertrophy; however, LV functional change is not present yet. Concentric LV remodeling plus LV functional change begins to appear in school children. Our data support prevention of obesity in early childhood because higher BMI is responsible for significant change in LV geometry in early life.

### P4621 | BEDSIDE

**Obesity and overweight in female and male patients with atrial fibrillation: insights from the EURObservational Research Programme on Atrial Fibrillation (EORP-AF) Pilot Registry**


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**Background:** The impact of overweight and obese terms in prognosis implications and adverse events in patients with atrial fibrillation (AF) is still uncertain. Prevention of AF in infancy outcomes at 1-year follow-up of AF patients enrolled in the EORP-AF Registry, according to BMI (kg/m2), focusing on patients with normal BMI (defined as 18.5 to ≤25kg/m2), overweight (25 to <30kg/m2) and obesity (≥30kg/m2).

**Results:** Amongst 2540 EORP AF patients with 1 year follow-up data available, 720 (28%) had normal BMI, 1084 (43%) were overweight and 736 (29%) were obese. The proportion of female patients was 39% overall, with 42% with normal BMI, 33% overweight and 44% obese (p < 0.0001). Obese patients were younger and with higher prevalence of diabetes and hypertension (p < 0.0001). One-year outcomes of normal, overweight and obese patients are shown by gender in the Table.

**Conclusions:** Among AF patients, overweight and obesity are common and are associated with one-year differences in outcomes. In female patients an increased BMI is associated with lower all-cause mortality and stroke, in line with the so called “obesity paradox”. In male patients, obesity was associated with more bleeding.

### P4622 | BEDSIDE

**Obesity and overweight in female and male patients with atrial fibrillation: insights from the EURObservational Research Programme on Atrial Fibrillation (EORP-AF) Pilot Registry**

C. Larocco1, I. Diemenger2, M.I. Popescu3, L.H. Rasmussen4, G. Sinagra5, L. Tavazzi6, A.P. Maggioni7, G.Y.H. Lip8 on behalf of EORP AF.

1Cardiology, University of Modena and Reggio Emilia, Modena, Italy; 2European Society of Cardiology, EORP AF Research Programme, Sophia Antipolis, France; 3Institute of Cardiology, Univ. of Bologna, Bologna, Italy; 4University of Medicine of Oradea, Cardiology, Oradea, Romania; 5Aalborg University Hospital, Thrombosis Research Unit, Aalborg, Denmark; 6University of Trieste, Cardiologie, Trieste, Italy; 7Maria Cecilia Hospital, Cardiology, Cotignola, Italy; 8Queen Elizabeth Hospital Birmingham, Center of Cardiovascular Sciences, Birmingham, United Kingdom

**Background:** Obesity-related left ventricular (LV) hypertrophy is an independent risk factor for cardiovascular morbidity and mortality in adults. Increased LV mass is also observed in obese children, however, there is little information when LV structural change begins to appear. To clarify this, we examined the relationship between body mass index (BMI) z-score and LV mass-to-volume ratio from infancy to adolescence.

**Methods:** Echocardiography with tissue Doppler imaging was performed in 1056 subjects aged 4 months to 20 years. Subjects were divided into 4 age groups: infants group, 0–11 months (n=212); preschool children group, 1 to 6 years (n=281); school children group, 7 to 12 years (n=438); and adolescents group, 13 to 20 years (n=169). LV end-diastolic volume and LV mass were measured and LV mass-to-volume ratio was calculated. Using tissue Doppler imaging, myocardial performance index (MPI) and isovolumetric relaxation time (IRT) were calculated.

**Results:** In the total study population, there were significant relationships between BMI z-score and systolic blood pressure (r = 0.38, p < 0.01), heart rate (r = 0.12, p < 0.01), LV mass-to-volume ratio (r = 0.40, p < 0.01), IRT (r = 0.14, p < 0.01), and MPI (r = 0.22, p < 0.01). Within each group, LV mass-to-volume ratio increased significantly with BMI z-score (infants, r = 0.20; preschool children, r = 0.43; school children, r = 0.37; and adolescents, r = 0.30, p < 0.01, respectively).

### Table.

<table>
<thead>
<tr>
<th>BMI (kg/m2)</th>
<th>Normal</th>
<th>Overweight</th>
<th>Obesity</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>18.5 to &lt;25</td>
<td>25 to 30</td>
<td>≥30</td>
<td></td>
</tr>
<tr>
<td>Female patients (N=987)</td>
<td>301</td>
<td>360</td>
<td>326</td>
<td>0.0228</td>
</tr>
<tr>
<td>All-cause death</td>
<td>29 (9.3%)</td>
<td>19 (3.5%)</td>
<td>14 (4.3%)</td>
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</tr>
<tr>
<td>CV death</td>
<td>11 (3.8%)</td>
<td>13 (3.7%)</td>
<td>6 (2.2%)</td>
<td>0.2887</td>
</tr>
<tr>
<td>Any TE</td>
<td>10 (3.9%)</td>
<td>14 (4.5%)</td>
<td>6 (2.2%)</td>
<td>0.0639[a]</td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td>6 (2.3%)</td>
<td>4 (1.3%)</td>
<td>0</td>
<td>0.5938[a]</td>
</tr>
<tr>
<td>Bleeding</td>
<td>1 (0.4%)</td>
<td>4 (1.3%)</td>
<td>3 (1.1%)</td>
<td></td>
</tr>
<tr>
<td>Male patients (N=1553)</td>
<td>419</td>
<td>724</td>
<td>410</td>
<td></td>
</tr>
<tr>
<td>All-cause death</td>
<td>29 (6.8%)</td>
<td>42 (5.8%)</td>
<td>25 (6.1%)</td>
<td>0.7479</td>
</tr>
<tr>
<td>CV death</td>
<td>15 (3.6%)</td>
<td>12 (1.7%)</td>
<td>11 (2.7%)</td>
<td>0.1247</td>
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<tr>
<td>Any TE</td>
<td>14 (3.7%)</td>
<td>31 (4.8%)</td>
<td>12 (3.4%)</td>
<td>0.5043</td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td>5 (1.3%)</td>
<td>3 (0.5%)</td>
<td>4 (1.1%)</td>
<td>0.7033[a]</td>
</tr>
<tr>
<td>Bleeding</td>
<td>2 (0.5%)</td>
<td>5 (0.8%)</td>
<td>9 (2.5%)</td>
<td>0.0354[a]</td>
</tr>
</tbody>
</table>

Legend: Data shown as N pts (%). *p* or Fisher exact test [a] was used for binary variables. CV = cardiovascular; Any TE = stroke, TIA, ACS, coronary intervention, cardiac arrest, peripheral embolism and pulmonary embolism.

**Conclusions:** Among AF patients, overweight and obesity are common and are associated with one-year differences in outcomes. In female patients an increased BMI is associated with lower all-cause mortality and stroke, in line with the so called “obesity paradox”. In male patients, obesity was associated with more bleeding.

### P4623 | BEDSIDE

**Obesity and overweight in female and male patients with atrial fibrillation: insights from the EURObservational Research Programme on Atrial Fibrillation (EORP-AF) Pilot Registry**

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**Background:** Cardiovascular disease is reported to have origins in childhood. Prevention of obesity in early childhood because higher BMI is responsible for significant change in LV geometry in early life.

**Methods:** This study included 190 Australians aged 7–15 years at baseline in 1985 and aged 36–46 years at follow-up in 2015, as part of a nation-wide prospective study. Anthropometry, blood pressure, blood biochemistry and physical fitness were measured both at baseline and follow-up. Cardiovascular (left atrial volume index (LAVI) and left ventricular mass index (LVM)) and function (left ventricular global longitudinal strain (GLS)) were measured by 2D and 3D echo in 2D. Cut-offs for defining abnormal values of LAVI (34ml/m2), 2D LVM (men 115g/m2, women 95g/m2), 3D LVM (men 97g/m2, women 90g/m2) and GLS (−18%) were used.

**Results:** Both childhood waist circumference and body mass index were corre-
lateral with LAVI (r=0.20 p=0.01 and r=0.15 p<0.05 respectively) and LVMi (r=0.30 p<0.001 and i=0.17 p<0.05 respectively) in adulthood, but were not correlated with GLS. One standard deviation (by age and sex) increase in childhood waist circumference was associated with greater risk of diastolic left atrium (RR=1.52 [95% CI: 1.11, 2.10]) and hypertrophic left ventricle (RR=1.49 [95% CI: 1.15, 1.92]) independently of current adiposity, but were not associated with abnormal GLS. These adverse relationships with adult cardiac structure were marginally reduced after adjusting for adult cardiovascular risk factors such as blood pressure, glucose, insulin and lipids.

Conclusions: Obesity in childhood is independently associated with enlarged left atrium and ventricle, but not with abnormal GLS, in adulthood. This might be due to some compensatory mechanisms that preserve cardiac function.

P4623 | BEDSIDE

Systolic blood pressure is strongly related to indices of obesity in children

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Objective: Obesity is a well-known cause of hypertension in adults. We hypothesized that it is strongly related to blood pressure in children.

Methods: Blood pressure data on 1981 participants aged 8–19 yrs (1007 boys, 974 girls, mean age 13.0±3.5 yrs) in the United States National Health and Nutrition Examination Survey (NHANES) 2011–2 were analysed. The National Center for Health Statistics Research Ethics Review Board approved the protocol. Certified personnel measured blood pressure. Lifestyle information was obtained using questionnaires.

Results: Systolic and diastolic blood pressure (SBP, DBP) correlated with waist circumference (WC) (r=0.41 and 0.21 respectively, p<0.001), and to a lesser extent, BMI (r=0.40 and 0.19 respectively, p<0.001). SBP correlated with WC more strongly in boys than girls (r=0.47 and 0.36 respectively, p<0.001). The slope of the regression of SBP on WC was the same. 0.2 mmHg/cm (p<0.001), for age groups 8–11, 12–15 and 16–19 yrs. There was no significant association between SBP or DBP with amount of sleep, amount or rigour of physical exercise, hours of television viewing or hours at the computer. In a general linear model, WC, age and gender explained 28% (26% in boys and 16% in girls) of the variance in SBP.

Conclusions: The size of the effect of abdominal obesity on blood pressure in children is large and is found in children as young as 8 years old. Addressing obesity in childhood may help to prevent the development of hypertension later in life.

P4624 | BEDSIDE

The effect of BMI on statin-induced diabetes mellitus

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Purpose: To assess the effect of body weight on statin-induced diabetes mellitus (DM).

Methods: The effect of statin therapy on the incidence of DM, during a five year period between 2010–2014, was assessed retrospectively among 351,917 sub- jects aged 40–70 years old without DM or coronary heart disease at baseline. 15.8% of the study population was treated with statins, 89.6% of whom were pre- scribed low-intensity dose regimens and comprised the study group in the present report. Outcomes were evaluated according to level of adherence to statins and analyses were stratified by baseline body mass index (BMI) levels.

Results: 14,221 (4.0%) new cases of DM were recorded. As expected, the in- cidence of DM was higher among obese patients irrespective of statintherapy status. Statin therapy increased the risk of DM at all BMI values. However, the excess risk of DM was highest in subjects with normal BMI through- out the 5-year study period [Risk Ratio (RR) = 6.04/2.35 = 2.56], and lowest in obese persons (RR = 25.71/18.41 = 1.4), p<0.001; FAI, r=0.36 95% CI (-0.50,-0.21), P-trend=0.018; PLR, values were lower in the 4th quartile than in the lower three quartiles (median 4.5, IQR2.6–7.3 vs 4.9, IQR 2.8–8.3, p=0.018); likewise, PLR values were lower in the lower quartile than in the lower three quartiles (median 127, IQR 85–185 vs 141, IQR 95–216, p<0.001). There were no significant differences in CK peak and LV ejection fraction between the two groups.

Conclusions: Acute STEMI treated with primary PCI is associated with a milder inflammatory response in markedly overweight and obese patients compared with patients with lower weight. This mechanism may contribute to the obesity paradox showing better long-term survival among these patients.

P4625 | BEDSIDE

Fatter is better? The obesity paradox and inflammation in ST elevation myocardial infarction patients

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Background: Several observations suggest that overweight and obese patients (pts) have a better prognosis in many diseases, including acute coronary syn- dromes. One of the proposed explanations of this “obesity paradox”, is that a chronic inflammatory status may play a protective role in acute inflammatory clinical conditions.

Purpose: The aim of our study was to evaluate the presence of the obesity para- dox in a large single-center ST elevation Myocardial Infarction (STEMI) population and to analyze the relationship between body mass index (BMI) and two estab- lished acute inflammatory indexes: Neutrophil to Lymphocyte Ratio (NLR) and Platelet to Lymphocyte Ratio (PLR).

Methods: We studied consecutive STEMI pts treated with primary percutaneous coronary intervention (PCI) at our Institution. They were stratified in BMI quartiles, while NLR and PLR were calculated on blood samples collected on admission; Kaplan-Meier curves with log-rank test were used to investigate long-term cardio- vascular mortality.

Results: Among the 1940 patients enrolled, the mean BMI was 26.4±4.4 kg/m². Patients in the upper quartile showed BMI values -26.9 kg/m². All-cause mortal- ity during a five year follow-up was an average follow-up of 774 days was 5.6% in the upper quartile pts and 9.4% in the remaining pts (p<0.023). NLR values were lower in the upper quartile than in lower quartiles pts (median 4.5, IQR2.6–7.3 vs 4.9, IQR 2.8–8.3, p<0.018); likewise, PLR values were lower in the 4th quartile than in the lower three quartiles (median 127, IQR 85–185 vs 141, IQR 95–216, p<0.001). There were no significant differences in CK peak and LV ejection fraction between the two groups.

Conclusions: The University of Hong Kong, Li Ka Shing Faculty of Medicine, Hong Kong, Hong Kong SAR People’s Republic of China; 2The University of Hong Kong, Department of Medicine, Hong Kong, Hong Kong SAR People’s Republic of China
Higher levels of SHBG were associated with a decrease in A/G fat ratio independently of body mass index, glucose, insulin and C-reactive protein (compared to the 1st tertile, 3rd tertile: p<0.005-0.001, P-trend=0.02). Conclusion: Endogenous sex hormone levels may lead to changes in body composition in postmenopausal women.

PREMATURE AGEING: WHAT DO WE KNOW?

P4627 | BEDSIDE
Premature cardiac ageing in South Asians: the ethnic-echocardiographic heart of England screening study (E-ECHOES)
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Background: People of South Asian origin (SAs) have increased cardiovascular morbidity, but underlying mechanisms are poorly understood. Ageing is the key predictor of deterioration in diastolic function, which can be assessed by echocardiography using E/e' ratio as a surrogate of left ventricular (LV) filling pressure.

Aims: To assess the prevalence of premature cardiac ageing in SAs participating in the Ethnic-Echocardiographic Heart of England Screening Study (E-ECHOES), a community based epidemiological screening study.

Methods: We studied 4540 subjects aged 45 years or older: 2880 SAs and 1660 African Caribbeans (ACs). All participants underwent detailed echocardiography, including LV ejection fraction (LVEF), average septal-lateral E/e', LV mass index (LVMI). These 4540 subjects excluded individuals with conditions known to affect utility of E/e' as an estimate of LV filling pressure: moderate-severe aortic or mitral valve disease, significant cardiac dysynchrony (QRS >140 sec) and subjects with missing data in variables used in regression model below.

Results: When compared to ACs, SAs were younger (median 61 [IQR 50–72] vs 56 [51–66] years), had lower LVMi (117 [93–143] vs 103 [85–125] g/m²), systolic BP (143 [131–157] vs 138 [126–152] mmHg), diastolic BP (82 [75–90] vs 81 [74–88] mmHg) and BMI (29 [26–33] vs 28 [25–31] kg/m²), as well as lower prevalence of hypertension (57% vs 44%) and smoking (44 vs 23%) (p<0.001 for all), AC and SA had similar low rates of reduced LVEF (<55% in both groups). Despite SAs having more favourable profile of factors known to predispose to diastolic dysfunction, E/e' was non-significantly different from ACs (8.0 [6.3–10.2] vs 8.0 [6.5–9.9], p=0.85).

In a multivariable linear regression model including age, gender, ethnicity, BP, heart rate, BMI, waist circumference, LVMi, history of smoking, hypertension, coronary artery disease, diabetes, chronic pulmonary obstructive disease, SA origin was independently associated with higher E/e' (regression coefficient ± standard error 0.66±0.10; p<0.001, adjusted R-squared for the model 0.21, p<0.001). E/e' was consistently higher in SAs across all age groups tested. Further analysis showed significant interactions between ethnicity and age with SAs having significantly steeper age-dependent increase in E/e' compared to ACs (Figure).

Conclusion: Premature cardiac ageing is evident in SAs and may contribute to high cardiovascular morbidity in this ethnic group.

P4628 | BEDSIDE
Augmentation index by volume plethysmography as a measure of wave reflection: distribution, reference values and its clinical utility in the general population
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Background: Augmentation index (AIx), as assessed by peripheral arterial tone (PAT) signal technology, may represent an operator-independent and reliable method of the assessment of wave reflection. However, no reference values for this method have been reported so far.

Methods: We report the age- and sex-specific reference values and major determinants of AIx and assess its clinical utility.

Methods: For the present analysis, data from the population-based Gutenberg Health Study, including 15,010 subjects aged 35–74 years were analyzed. AIx was assessed by plethysmography with radial arterial pulse volume changes (EndoPAT, Itamar). After exclusion of subjects with missing values for AIx due to technical and logistic reasons, the study sample comprised 11,250 subjects. During an average follow-up of 5.7 years 331 deaths due to all-causes occurred.

Results: Age- and sex-specific reference values were reported with markedly higher AIx among females. A non-linear increase in AIx with aging was observed with a plateau-building after age 55 years in women and 60 years in men. Multivariable linear regression analysis indicated female sex, smoking (both positively and well as height, heart rate and obesity (inversely) as independent predictors of PAT-derived AIx. Age in both sexes and diastolic blood pressure in males were related to AIx only in younger subjects (≤55 years).

Conclusion: Survival was worse for higher tertiles of AIx; this effect was more prominent in men than in women. In multivariable Cox regression analysis, an increase of AIx by one standard deviation (SD) was associated with 33% higher risk for all-cause mortality in men and 25% increased risk in women after adjustment for age, height, heart rate and traditional CV risk factors. Additional adjustment for prior CVD (i.e. myocardial infarction, coronary artery disease, stroke, congestive heart failure or peripheral artery disease) did not change results significantly in men (HR 1.31, 95% CI 1.10–1.56, p=0.0028), whereas in women the association became slightly stronger with a HR of 1.32 (95% CI: 1.05–1.65, p=0.016). Reclassification analysis showed a very moderate improvement of the prediction of all-cause mortality by AIx beyond well-established CV risk measures (height, heart rate and conventional Framingham risk factors); net reclassification improvement was 6.12% in men and 4.6% in women; integrated discrimination improvement was 0.004 in men and 0.004 in women.

Conclusion: Age- and sex-specific reference values for AIx and its major determinants were reported. In addition, AIx was also found to be a strong predictor of all-cause mortality, independently of cardiovascular risk factors and prevalent CVD. Although this finding did not add clinically-relevant additional information beyond established markers for risk prediction, AIx represents an interesting surrogate marker of biological aging that deserves further research.

P4629 | BEDSIDE
Expansion of immunosenescent T cell fraction in chronic kidney disease patients: exploring new pathogenic mechanisms of increased arterial stiffness
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Background: Chronic kidney disease (CKD) is associated with increased arterial stiffness, which is a well-known predictor of future cardiovascular events. However, the underlying mechanism of arterial stiffening in CKD is not well known. Accelerated immune aging, characterized by expansion of immunosenescent T cell fraction might be involved in the pathogenesis of arterial stiffening in CKD.

Purpose: We aimed to evaluate the relationship between arterial stiffness and immunosenescent T cell (CD8+CD57+ or CD8+CD28- T cell) fraction in patients with CKD.

Methods: Four hundred and twenty-nine consecutive hypertensive patients with CKD (266 male, mean age 61±10 years) who registered in Cardiovascular and Metabolic Disease Etiology Research Center - High Risk Cohort (CMERC-HI, NCT02030781) were enrolled. Arterial stiffness was evaluated by pulse wave ve-
lyocytic (PWV) and the frequency of CD57+ or CD28- senescent T cells in peripheral blood lymphocytes were examined by multicolor flow cytometry.

**Results:** Immunosenescent T cell fraction showed significantly increased tendency according to CKD stages (CD8+CD57+ T cell fraction, p<0.001: 40.8±16.4% in stage 1, 47.5±17.0% in stage 2, 48.3±16.0% in stage 3, 51.9±19.3% in stage 4, 52.0±18.0% in stage 5, CD8+CD28- T cell fraction, p<0.001: 46.8±17.9% in stage 1, 50.4±19.7% in stage 2, 50.7±17.7% in stage 3, 60.2±19.3% in stage 4, 60.3±16.5% in stage 5). Multivariate analysis revealed that CD8+CD57+ T cell fraction is independently associated with PWV even after adjustment with age, gender, body mass index, renal function and systolic blood pressure (p<0.102, p=0.038).

**Conclusion:** In CKD patients, CD8+CD57+ T cell fraction are expanded and independently associated with increased arterial stiffness. These findings may explain the role of immunosenescence in the pathogenesis of accelerated arterial stiffening in patients with CKD.

**Acknowledgment/Funding:** Basic Science Research Program through the NRF of Korea funded by the Ministry of Science, ICT & Future Planning (NRF-2015R1C1A1A02036645)

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**P4630 | BEDSIDE**

**Assessing metabolic and cardiovascular risk in survivors of childhood acute lymphoblastic leukemia: the contribution of integrated metabolic and vascular ultrasound indicators**

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**Background:** Acute lymphoblastic leukemia (ALL) is the most common cancer in childhood, with an annual incidence rate of 3.9 per 100,000 children. The introduction of multimodal risk-adjusted treatment and improvement of tailored therapy has resulted in a growing number of childhood leukemia survivors. The increased survival, however, is accompanied by health problems due to therapy sequelae and lifestyle changes. ALL survivors are at increased risk of metabolic and cardiovascular disease which are potentially life-threatening conditions.

**Purpose:** The present study aims to assess the metabolic and cardiovascular risk in children surviving ALL, and, in particular, to analyze the effectiveness of laboratory markers correlated with vascular ultrasound parameters in predicting cardiovascular risk in ALL children.

**Methods:** Ninety-one subjects, 54 cases and 37 controls, were enrolled in a case-control study. Inclusion criteria were: age 3 to 20 years; diagnosis of ALL: end of antineoplastic therapy since at least three months; complete remission of ALL. Exclusion criteria were: evidence of ALL; endocrine and/or metabolic disorders prior to ALL diagnosis; cardiovascular disorders prior to ALL diagnosis and genetic syndrome (patients with Down Syndrome were excluded). All patients underwent a general clinical examination and anthropometric measurements. We performed vascular ultrasound measurements to evaluate intima media thickness of common right and left carotids arteries (cIMT), the APAO (antero-posterior abductory parameter) and metabolic (glucose tolerance test: GTT) and haemostatic parameter. APAO measurements outlined a strong relationship with metabolic syndrome (patients with Down Syndrome were excluded). All patients underwent a general clinical examination and anthropometric measurements. We performed vascular ultrasound measurements to evaluate intima media thickness of common right and left carotids arteries (cIMT), the APAO (antero-posterior abductory parameter) and the FMD (flow-mediated vasodilatation) of brachial artery.

**Results:** The group of 54 ALL patients consisted of 35 females and 19 males, aged 4 to 19 years. The control group consisted of 17 males and 20 females, aged 3.7 to 16 years. Children with age ≥64 years. Twenty-five percent of patients were aged <55 years. Compared to older patients, those aged <55 years were more likely to be male (76% vs 62%), current smokers (48% vs 19%), have a body mass index (BMI) ≥30, 48% vs 34% and have high total cholesterol: HDL cholesterol ratios (>4.0, 70% vs 50%), all p<0.001. Sixteen percent of younger patients were diabetic; these patients were highly likely to have a BMI ≥30 (67%) or ≥40 (21%), and had higher median Hba1c than diabetic patients aged 55 or older (69mmol/mol vs 55mmol/mol). Mäori and Pacific Island patients were overrepresented in the younger age group and these patients had a very high risk factor burden with more prevalent diabetes, obesity, current smoking, and dyslipidaemia than other ethnic groups (Figure 1). Compared to older patients, those aged <55 years also had a higher proportion of ST elevation myocardial infarction (35% vs 28%) and single vessel disease (47% vs 37%) on angiography, both p<0.001.

**Conclusions:** A quarter of NZ patients admitted to hospital with first-time ACS are aged <55 years. These younger patients have a very high risk factor burden: half are current smokers, half have a BMI ≥30; and 16% have diabetes. NZ Mäori and Pacific Islanders are over-represented among young ACS patients and are thus important groups to target with primary CV disease prevention programmes.

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**P4632 | BENCH**

**Cardiac toxicity induced by high fat diet: a wild-type murine model**

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**Objective:** Long-term high fat diet (HFD) induces both cardiac remodeling and myocardial dysfunction in murine models. The aim was to assess the time course and mechanisms of metabolic and cardiac modifications induced by HFD in wild type (WT) mice during a 5-month follow-up.

**Methods:** Thirty-three WT mice (5 month-old) were subjected to HFD (60% fat, n=17) and Chow diet (CD, 13% fat, n=16). Thirty-three WT mice (5 month-old) were subjected to HFD (60% fat, n=17) and Chow diet (CD, 13% fat, n=16). Metabolic (glucose tolerance test: GTT) and echocardiographic data were collected at baseline and every 5 weeks for 20 weeks. Invasive hemodynamic data and myocardial samples were collected at 5 (n=8 HFD, n=7 CD) and 20 weeks. Echocardiographic data included left ventricular (LV) diameters and thickness, and systolic function using strain rate (SR).
Hemodynamic measurement under light anesthesia included aortic and LV pressures, and maximum and minimum dP/dt. Heart weight/tibia length (HW/TL) was calculated, histological assessment of cardiomyocyte/adipocyte sizes, interstitial fibrosis and apoptosis index (TUNEL method) were performed.

Results: During follow-up, body weight and glycemia levels were increased significantly higher in HFD than in CD mice, which were associated with an early adipose tissue remodeling. Despite no difference between both groups in blood pressure and LV mass at 5 weeks, an early LV dysfunction was observed in HFD mice by SR (HFD: 21±0.8% vs CD: 27±0.8%, P<0.001) and hemodynamic assessment (dP/dt max 8202±230 mmHg.s vs 11637±353 mmHg.s, P<0.05). During follow-up, both groups demonstrated a progressive systolic and diastolic LV dysfunction and remodeling including dilatation and hypertrophy, which were more severe in HFD mice. Compared to CD mice, the early LV impairment in HFD mice was associated with a higher cardiomyocyte apoptosis rate (0.95% vs. 0.02%, P<0.05), which worsen during follow-up.

Conclusion: HFD promoted early metabolic and cardiac dysfunctions, which seemed to be related to adipose and myocardial tissues accelerated remodeling.

P4635 | BENCH
Age-related cardiac dysfunction is linked to visceral adiposity
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Background: Ageing induces progressive myocardial dysfunction, contributing to cardiac morbidity and mortality. Ongoing experiments show that 1) visceral adipose tissue accumulates and remodels with ageing; 2) increased visceral adiposity promotes low-grade inflammation and furthermore several comorbidities, such as type II diabetes mellitus. Whether there is a link between visceral adiposity and age-related cardiac dysfunction is not yet known.

Purpose: We aimed to investigate the role of visceral adiposity in age-related cardiac dysfunction in a model of old mice undergoing epididymal fat pad removal (EWA Tectomy).

Methods: We compared cardiac in vivo haemodynamics and glucose intolerance (ITT) insuline (ITT) tolerance tests in 3 groups of Chow-fed C57BL/6 male mice (n=8–10/group): young (2–3 months old), aged sham and EWA Tectomy (12 months old). Animals were allowed to recover for 6 weeks after surgery before in vivo haemodynamics and sacrifice.

Results: EWA Tectomy mice confirmed a lower epididymal fat depot (young: 386±26, sham: 711±126, EWA Tectomy: 206±22 mg; p<0.01). In EWA Tectomy mice other white adipose tissue depots (inguinal and perirenal fat pads) showed a compensatory growth to the extent that total body adiposity index remained unaltered as compared with sham group (young: 25.1±1.7, sham: 42.9±4.6, EWA Tectomy: 43.9±4.0 mg/g body weight, p<0.001, young vs. both old groups: p<0.001, sham vs. EWA Tectomy: p=ns). Sham and EWA Tectomy mice had similar body weight.

Interestingly in vivo haemodynamic measurements demonstrated a rescue of cardiac function to the level of young mice in EWA Tectomy as compared with sham mice (dP/dtmax and dP/dtmin shown as figures, ***p<0.0001). Of note heart rate was similar among groups (young: 536±6, sham: 536±6.5, EWA Tectomy: 555±12 bpm; p=NS). Functional improvement by EWA Tectomy was accompanied by a reduction of age-related myocardial interstitial fibrosis. GGT and ITT were similar in sham and EWA Tectomy mice (AUC; GGT: young: 1133±76, sham: 1420±137, EWA Tectomy: 1399±112 mg/2hr, p=0.91 sham vs EWA Tectomy; ITT: young: 453±17, sham: 650.4±79, EWA Tectomy: 673±27 mg/2hr, p=0.74 sham vs EWA Tectomy).

Conclusion: Our results suggest a critical role of visceral adiposity in age-related cardiac dysfunction, seemingly unrelated to glucose metabolism. Reversibility of age-related cardiac dysfunction suggests a potential therapeutic option in targeting the visceral adipose tissue for protecting the ageing heart.

Acknowledgement/Funding: RUH CARMMA

P4636 | BENCH
Maternal infection complications and premature coronary heart disease in the offspring

Background/Introduction: MicroRNAs (miRNAs) are small non-coding RNAs that repress gene expression at the post transcriptional level binding to complementary sites located in 3’ untranslated region of their target gene miRNAs.

Hemodynamics and effect of EWA Tectomy

Conclusion: Our results suggest a critical role of visceral adiposity in age-related cardiac dysfunction, seemingly unrelated to glucose metabolism. Reversibility of age-related cardiac dysfunction suggests a potential therapeutic option in targeting the visceral adipose tissue for protecting the ageing heart.

Acknowledgement/Funding: RHU CARMMA

P4637 | BENCH
mIR299, 145, and 494 regulate human aortic smooth muscle cell aging via direct targeting of VEZF1

Background/Introduction: MicroRNAs (miRNAs) are small non-coding RNAs that repress gene expression at the post transcriptional level binding to complementary sites located in 3’ untranslated region of their target gene miRNAs.

Hemodynamics and effect of EWA Tectomy

Conclusion: Our results suggest a critical role of visceral adiposity in age-related cardiac dysfunction, seemingly unrelated to glucose metabolism. Reversibility of age-related cardiac dysfunction suggests a potential therapeutic option in targeting the visceral adipose tissue for protecting the ageing heart.

Acknowledgement/Funding: RHU CARMMA

P4638 | BENCH
Premature ageing: what do we know? 933

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Background: Pre-atherosclerotic vascular change starts in early life. Investigation on premature manifestation of atherosclerotic cardiovascular disease (CVD) in children with maternal pregnancy complications is of major importance and may have clinical implications. We aimed to investigate the association between maternal gestational problems with the occurrence of adult coronary heart disease in the offspring.

Methods: We conducted a population-based case-control study of 153 patients with a first acute coronary syndrome before age 56 years and 153 age- and sex-matched controls. History of maternal gestational complications (gestational hypertension, diabetes mellitus, pre-eclampsia, premature labour, low-birth weight, maternal infections and maternal depression) during pregnancy of participants was obtained together with the clinical data, laboratory measurements and other cardiovascular risk factors of the participants. Conditional logistic regression was performed to assess the association.
**MIRnas serve as key developmental regulators of post transcriptional gene expression and more than 1500 different miRNAs have been discovered in the human genome. They have therefore become interesting targets for the therapeutic strategies to chronic disease such as atherosclerosis. Recently, several studies have suggested that miRNAs related to cardiovascular disease, including atherosclerosis. However, vascular aging related miRNAs is not reported before.**

**Methods:** Human Aortic smooth muscle cells (hAoSMCs) were purchased from ATCC. hAoSMCs were cultured in SmBM medium (Lonza, Switzerland) supplemented with defined by the manufacturer. All cells were kept in humidified atmosphere (37°C and 95% CO2 in the air). Total RNA from hAoSMC cell was isolated using TRIzol reagent (Invitrogen,USA) according to the manufacturer’s instructions. About 1 ug of total RNA was using microRNA array, Affymetrix mouse miRNA 4.0 (mature). Complementary DNAs (cDNAs) were synthesized by adding purified RNA and oligo-dt primers to the invitrogen RT premix (Invitrogen,USA). cDNAs from miRNAs were synthesized using an Mir-X miRNA first strand Synthesis Kit (clontech, USA) according to the manufacturer’s instructions. Real-time quantitative PCR was performed using SYBR Green (Applied Biosystems, USA) according to the manufacturer’s protocol.

**Results:** The present invention is based on the finding that several miRNAs are differentially expressed in young hAoSMC cells (passage number 5) versus replicated senescence hAoSMC cells (passage number 9 and 13) (Fig. 1a). We were identifying senescence related miRNAs using the microRNA array based on the functional state of senescence cells, mir-145, mir-299, and mir-495 (Fig. 1b). The miRNAs are binding to putative target genes (VEZF1, Hey1, and GFPI3)’ UTR region and then the miRNAs will be regulating the putative target genes expression level in hAoSMC cells.

The VEZF1 (vascular endothelial zinc finger 1) gene was identified as a gene specifically expressed in vascular endothelial cells during early embryonic development. In this study, we reported that the VEZF1 was regulated a vascular cellular aging of human smooth muscle cells (hAoSMC). We found that VEZF1 expression is decreased in senescent hAoSMCs (Fig. 1c). To upstream regulators of VEZF1 during senescence, we screened for microRNAs. We found that the level of microRNAs, mir-145, mir-299, and mir-495 increased under cellular senescence in a hAoSMC. We demonstrate that for mir-145, mir-299, and mir-495 are able to decrease VEZF1 expression levels through binding to the VEZF1 transcripts (Fig. 1d).

**Conclusion(s):** Finally, our data demonstrate the VEZF1 regulates vascular cellular aging in hAoSMCs through mir-145, mir-299, and mir-495.

**P4637 | BEDSIDE**

**Testosterone deficiency in primary hypertension: an essential middle aged pathology triggered by vascular stiffness**


**Hippokration Hospital, University of Athens, 1st Department of Cardiology, Athens, Greece**

**Background:** There is increasing evidence of testosterone deficiency (TD) association with an adverse cardiovascular outcome. Middle aged male physiology is a determinant of peripheral wave reflections. Purpose: To investigate the influence of TD on cardiovascular performance in primary hypertension middle aged males.

**Methods:** 182 hypertensive middle aged males (57±9 years) underwent standard 2D echocardiography examination followed by 3D echo estimation of LV end-diastolic (EDV) and end-systolic volumes (ESV). Based on systolic blood pressure (SBP) and end-systolic blood pressure was calculated (ESP=0.9×SBP). LV elastance (Elv=ESP/ESV) and arterial elastance (Ea=ESP/SV) and ventricular-arterial coupling (Ea/Elv) were assessed. On 2D echo E/E’ ratio was measured assessing LV diastolic function. Vascular parameters were estimated by carotid-femoral pulse wave velocity (PWV=f) and augmentation index (AIx) both important determinants of Ea. TD was defined when total testosterone (TT) levels were <3.4 ng/ml.

**Results:** Compared to patients with normal TT levels, TD patients (n=54, 30%) had higher BMI, and a greater prevalence of diabetes (all P<0.05). They also had lower ejection fraction (EF), stroke volume (SV) and a higher Ea/Elv. TD was also associated with a higher E/E’ ratio, increased PWV=f and AIx (Table). The biomarkers for cardiovascular aging and cardiovascular risk factors.

**Conclusion:** In essential hypertension middle aged men, TD jeopardizes cardiac performance by affecting central and peripheral arterial stiffness parameters. This work assists clinical decision by identifying patients on altered cardiovascular status demanding more intensive follow up strategies in order to prevent further decline of their physiology.

**P4638 | BEDSIDE**

**The paradoxical association of platelet-to-lymphocyte ratio with coronary artery disease in high risk young and older patients**

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**Objective:** Thrombocytosis and inflammation are vital elements in the pathogenesis of atherosclerosis. The platelet-to-lymphocyte ratio (PLR) is a novel biomarker that combines these two parameters and has been shown to be associated with cardiovascular disease (CVD). Few studies have examined PLR and its relationship to angiographically demonstrated coronary artery disease (CAD).

**Hypothesis:** We hypothesized that PLR correlates with CAD in high-risk patients, and the relationship is affected by age.

**Methods:** Consecutive patients from the BRAVEHEART and MINACS cohorts referred for coronary angiogram at our institution were evaluated (n=822). Of these, 214 patients had normal coronary arteries on angiography and 608 patients had CAD, defined as ≥1 coronary vessels with ≥50% stenosis. Patients were stratified into groups based on the presence of CAD (Fig. 1c). To upstream regulators of VEZF1 during senescence, we screened for microRNAs. We found that the level of microRNAs, mir-145, mir-299, and mir-495 increased under cellular senescence in a hAoSMC. We demonstrate that for mir-145, mir-299, and mir-495 are able to decrease VEZF1 expression levels through binding to the VEZF1 transcripts (Fig. 1d).

**Conclusion:** There appears to be an age-related effect on the correlation between PLR and angiographically determined CAD. While high PLR was found to be an independent marker of CAD in older high risk patients, it was negatively correlated with CAD in younger patients. PLR is a widely available and inexpensive marker which could be used in highlighting patients at high risk for CAD. The role of the interaction of PLR and age with CAD warrants further study. Further studies are required to determine its clinical use in conjunction with conventional cardiac risk factors.
We hypothesized that 12 months of statin therapy increased telomerase activity in peripheral blood mononuclear cells (PBMC).

**Methods:** In a randomized, placebo-controlled study 100 hypercholesterolemic patients, aged 35–75 years, free of known cardiovascular diseases and diabetes mellitus type 2 received 20 mg of atorvastatin daily or placebo for 12 months. TA was measured by quantitative polymerase chain reaction.

**Results:** At study end 82 patients had sufficient PBMCs needed for longitudinal analysis. PBMC TA expressed as natural logarithms changed from 0.46±0.05 to 0.68±0.06 (p=0.004) in atorvastatin group and from 0.67±0.06 to 0.60±0.07 (p=0.477) in control group. In multiple regression analysis atorvastatin therapy was the only independent predictor (p=0.019) of the changes in TA independently of age, gender, lipids, c-reactive protein, glucose and blood pressure levels. Correlation analysis demonstrated that the increase in TA was significantly positively associated with SMDP and prevalence of subjects with the LTD lowest quartile (r=0.20, p=0.048) and significantly negatively associated with TA at baseline (r=−0.75, p<0.0001).

**Conclusions:** Atorvastatin therapy modulates TA primarily in patients with higher telomeres and lower TA, i.e. with inadequate tissue repair capacities. The modulation of TA can be recognized as an important pleiotropic effect of statins.

**P4640 | BEDSIDE**

**Comorbidity profile for out of hospital unexpected deaths varies by age**


**Background:** Out-of-hospital sudden unexpected death (OHSUD) is a common cause of death worldwide. While cardiovascular disease and its risk factors are common in OHSUD, the prevalence of these conditions among different age groups requires further understanding.

**Purpose:** We assessed the prevalence, by age group, of comorbidities in OHSUD victims.

**Methods:** We examined a retrospective cohort of 18–64 year old residents in an urban population (974,289) in North Carolina, US. 408 OHSUD cases were adjudicated for inclusion over 24 months. Comorbidities were determined from medical records and medical examiner reports. Using a 2-sided z-test, we compared comorbidities across three age groups: 18–44, 45–54, and 55–64.

**Results:** See table **Conclusions:** OHSUD victims ages 18–54 suffer from higher rates of obesity compared to the US population (prevalence ~35% for ages 20–59). More OHSUD victims also smoked than the US population (rate 20%). This high risk for OHSUD.

**P4642 | BENCH**

**Selective estrogen receptor modulator has cardioprotective effects based on better autonomic modulation in a model of menopausal rats**

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**Background:** The high risk of cardiovascular disease in post-menopausal women is linked to increased arterial pressure (AP). In this sense, estrogen therapy seems to improve heart function in rats undergoing oophorectomy. However, clinical studies have shown paradoxical effects, which the replacement of estrogen and progesterone have increased cardiovascular risk. Objective: To evaluate the effect of tamoxifen, a selective estrogen receptor modulator, on hemodynamic parameters (AP and heart rate, HR) and in autonomic modulation of the heart in a model of menopausal rats.

**Methods:** For this purpose, 18 Wistar rats (200–220g) were divided into 3 groups (n=6 each): control females (C), ovariectomized control (OC) and ovariectomized treated with tamoxifen (OT). After 8-week protocol, the animals were cannulated in the carotid artery for direct AP registration (2 KHz, CODAS) and cardiovascular autonomic modulation was evaluated. The statistical test Anova One Way was applied for comparison of data, followed by post-hoc Student Newman-Keuls, p<0.05.

**Results:** The ovariectomized rats treated with tamoxifen had reduced mean AP (C:116±1.20; OC:112±3.17; OT:99±7.05mmHg), systolic AP (C:133±0.29; OC:129±2.77; OT:114±7.56 mmHg) and diastolic AP (C:96±9.51; OC:92±2.95; OT:84±0.50 mmHg) in relation to control females. Furthermore, the OT group showed resting bradycardia in comparison to ovariectomized control rats (C:75±7.57; OC:385±17.96; OT:350±7.75 bpm), associated with an increase in the pulse interval (PI, C:168±5.26; OC:158±5.70; OT:181±4.79ms) and the variance of PI (C:46.6±7.35; OC:33.8±14.00; OT:194±61.89ms) (vs. C and OC). The OT group also presented higher values of parasympathetic modulation compared to the other studied groups, as root mean square of successive differences between adjacent NNs (RMSDSS, C:8.03±0.32; OC:6.61±1.61; OT:15.66±1.52ms) and the high frequency band of PI (HF-PI, C:14.50±1.12; OC:9.31±1.94; OT:35.80±9.45ms). Regarding the variance of SAP, treatment with tamoxifen could restore the increase in this variable that occurred in OC group (C:14.19±0.49 and OT:14.55±1.57 vs. OC:18.45±1.11 mmHg2). The reduction in SAP was correlated with an increase in parasympathetic modulation, evidenced by: HF-PI band (R2=0.663; p<0.0013), RMSDSS (R2=0.781; p<0.0001) and standard deviation of SAP (R2=0.781; p<0.0001). Furthermore, the low frequency band of SAP, a parameter which shows vascular sympathetic modulation, was positively correlated with SAP (R2=0.557, p<0.008).

**Conclusion:** The results suggest that tamoxifen induces a reduction of SAP not only by production of local factors, as NO, but also due a better autonomic modulation and increased parasympathetic modulation. This study indicate that the cardioprotective effects of estrogen are dependent on their receptors and tamoxifen may be promising for cardioprotection in postmenopausal period.
Background: Physiological changes associated with aging lead to a decrease in the function of various organ systems. Given that aging also increases mortality risk as a function of time, it is important to understand precisely the anatomic and physiological changes attributed to the normal aging process.

Purpose: This present study was to clarify age-related changes in 13 clinical parameters and their relations to common complex diseases in Japanese individuals.

Methods: Study subjects comprised 6027 community-dwelling individuals who were recruited to a population-based longitudinal genetic epidemiological study. Body mass index and waist circumference increased with age up to 50 years and then decreased thereafter in men, whereas both parameters increased linearly with age in women. The prevalence of obesity was highest (41.1%) in men aged 40 to 49 years, after which it decreased with age. The prevalence of obesity in women increased with age up to 32.2% in those aged ≥70 years. Systolic and mean blood pressure as well as pulse pressure increased linearly with age in both men and women. Proteinuria and albuminuria concentrations were higher with age up to 60 years and then decreased. The prevalence of hypertension increased with age up to 69.9% or 68.5% at age ≥70 years in men and women, respectively. Fasting plasma glucose level, blood hemoglobin A1c content, and the prevalence of type 2 diabetes mellitus increased gradually with age in both men and women. The serum triglyceride concentration increased with age up to 50 years and decreased thereafter in men, whereas it increased linearly with age in women. The prevalence of hypertriglyceridemia increased to a peak of 56.8% at age 50 to 59 years in men and decreased thereafter, whereas in women increased variance with age up to 34.9% at ≥70 years. The serum HDL-cholesterol concentration increased slightly with age up to 50 years and decreased thereafter in men, whereas it increased linearly with age in women. The prevalence of hyper-HDL-cholesterolemia increased with age up to 53.4% at ≥50 to 59 years in men and up to 63.9% at ≥60 to 69 years in women, and it decreased thereafter in both genders. The serum creatinine concentration and the estimated glomerular filtration rate increased or decreased linearly with age, respectively. The prevalence of chronic kidney disease was increased with age up to 45.1% or 39.6% at ≥70 years in men and women, respectively.

Conclusion: Our results thus indicate that 13 clinical parameters as well as the prevalence of obesity, hypertension, type 2 diabetes mellitus, dyslipidemia, and chronic kidney disease were significantly related to age.

Results:

- Older compared to younger group had lower office and 24-h diastolic BP (90.8±8 vs 96.9±9 mmHg and 74.7±8 vs 83.9±8 mmHg, respectively; p<0.0001 for both), and greater left ventricular mass index (114.3±15 vs 105.2±11 g/m², p<0.05) but did not differ regarding sex, body mass index and metabolic profile (p>NS).
- Moreover, older compared to younger patients exhibited increased levels of hs-CRP (3.2±0.7 vs 2.1±0.7 mg/l, p<0.05), ACR (36.5±12 vs 22.6±7 mg/g, p<0.05) and PWV (8.8±1.5 vs 7.9±1.2 m/sec, p<0.001). In the entire population, age was associated with hs-CRP (r=0.120, p<0.001), ACR (r=0.221, p<0.001) and PWV (r=0.399, p<0.0001), while it was negatively related to 24-h diastolic BP (r=−0.319, p<0.0001).
- Furthermore, hs-CRP was correlated with body mass index (r=0.281, p<0.0001) and PWV (r=0.233, p<0.05).

In multiple regression analysis, age and hs-CRP were independent predictors of both PWV and ACR (p<0.05). Analysis of covariance revealed that hs-CRP, ACR and PWV concentrations were significantly different between groups after adjusting for confounders (p<0.05 for all).

Conclusions: Hypertensive patients of more than 60 years of age are characterized by increased levels of hs-CRP, ACR and PWV, whereas the main determinants of early renal dysfunction and arterial stiffness are age and low-grade inflammation. These findings provide an insight into the accelerated atherosclerotic mechanisms of cardiovascular aging.

P4645 | BEDSIDE Coronaries age in a complex fashion

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Background: Age, diabetes and hypertension are conventional risk factors for coronary artery disease. Conventional belief suggests that they may also play a role in determining the complexity of coronary artery disease. Evidence proving this however scarce. This study aims to provide objective evidence of relative strategy was analyzed in study with respect to age, diabetes mellitus and hypertension, the common risk factors for coronary artery disease as determined by SYNTAX score.

Methods: Retrospective analysis of 792 patients who underwent coronary angiography in the period of January 2013 to December 2014 was carried out and mean SYNTAX scores were calculated for each age group. The effect of age, diabetes mellitus and hypertension on SYNTAX score was analyzed by a multivariate (linear regression) analysis.

Results: Out of the 792 patients analyzed, 244 (30.7%) patients had diabetes mellitus and 149 (18.70%) patients had hypertension. The mean SYNTAX scores of patients show a rising trend with increasing age, scores of patients above the age of 70 years being significantly more than those below 70 years of age (as depicted in the table). Logistic regression analysis was carried out and by considering three groups depending on SYNTAX score (i.e. SYNTAX score <23, 23–32 and >32), it is observed that there exists significant relationship between age and SYNTAX score (p<0.01). The existence of relationship between DM and SYNTAX score is not supported (p=0.834). Further existence of relationship between HTN and SYNTAX score also is not supported (p=0.736).

Comparison of SYNTAX scores of ≤70 years vs >70 years age groups

<table>
<thead>
<tr>
<th>Age</th>
<th>Mean</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;70 (n=600)</td>
<td>12.35</td>
<td>0.0027</td>
</tr>
<tr>
<td>&gt;70 (n=299)</td>
<td>14.64</td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: SYNTAX score is which a score measuring the complexity of coronary artery disease and guiding and planning the appropriate revascularization strategy was analyzed in study with respect to age, diabetes mellitus and hypertension, the common risk factors for coronary artery disease. Against all expectations, diabetes mellitus and hypertension showed no significant correlation with rising SYNTAX score and only rising age was shown to have a significant correlation with increasing SYNTAX score in a multivariate analysis.
who did not experience an acute coronary event, subjects who developed an event were older (P<0.008) and more frequently had hypertension (P=0.01) and TD (48% vs 22%, P<0.001). The prevalence of diabetes, hypercholesterolemia and smoking was not different between groups. The unadjusted outcomes (acute coronary events) by baseline TT level (patients with TD vs subjects with TT above in the cut-off point for the biochemical definition of TD) are shown in figure (Kaplan-Meier analysis). There was a significantly higher rate of acute coronary events in males with TD compared to patients with normal TT concentration [adjusted hazard ratio: 1.35 (95% CI, 1.10–1.62; P=0.028)] during the study follow-up.

**Conclusions:** The present study shows that total testosterone concentration below 3.5 mg/ml is associated with an increased risk of acute coronary events in men without CV disease. Low testosterone levels in middle-aged men should prompt investigation and intervention for CV risk factors.

**ARE WE BETTER AT MANAGING CARDIOVASCULAR DISEASE IN THE ELDERLY?**

**P4647 | BEDSIDE**

Does GRACE score overestimate mortality risk in elderly patients with ACS?  

**Background:** GRACE index is a validated prognostic score for patients with Acute Coronary Syndrome, used for risk stratification and decision making. Nevertheless, people over 75 years were underrepresented in the registries used for the validation of GRACE score, which can entail an excessive weight of age in overall risk estimation. Our objective was to assess the relationship between GRACE index score and 6 months mortality in this population.

**Methods:** Consecutive patients ≥75 years admitted with ACS were included in this prospective, multicenter and observational registry. GRACE index was calculated upon admission, following the cohort throughout 6 months. Main endpoint was mortality at 6 months.

**Results:** A total of 218 patients were included, with a mean GRACE score of 147.63 (SD 22.23) and a total of 156 (71.5%) patients over 140 points. 6 months mortality among the population was 3.2% (n=7). Among dead patients, mean GRACE index was 147.11 (SD 22.15), while mean GRACE index among alive patients was 163.14 (SD 20.63, p=0.06), being over 140 in both subgroups.

**Conclusion:** For patients above 75 years, GRACE score might overestimate mortality risk in Acute Coronary Syndrome. It seems appropriate to further evaluate new scores for this population or to consider the adjustment of the existing ones.

**P4648 | BEDSIDE**

Comparison of outcomes in patients <85 versus >85 years of age undergoing transcatheter aortic valve-implantation  

**Objective:** The impact of age on baseline characteristics and outcomes in patients with severe aortic stenosis who undergo transcatheter aortic valve implantation (TAVI) has not been thoroughly investigated. The aim of our study was to describe the baseline characteristics of TAVI patients aged <85 and >85 years and to evaluate these outcomes in the elderly.  

**Methods:** Patients with severe and symptomatic aortic stenosis (effective orifice area [EOA]≤1 cm²), who were scheduled for TAVI with a self-expanding valve at the University Hospital Ramon y Cajal de Madrid, were included in the study. The primary clinical end-point occurred in 41 patients (26.1%) during a follow-up period of 26.8±20.7 months. Patients were divided into 2 groups: patients aged <85 years (n=120) and patients aged ≥85 years (n=120). Women comprised 59.5% of the older group and 52.5% of the younger age group. Baseline clinical profile, including EuroSCORE index (<85: 26.1±10.8, p=0.02) and NYHA classification (<IV: 85: 6.7% versus <85: 18.9%, p<0.01) was different between groups. Preprocedural aortic valve area was similar in both age groups (<85: 0.617±0.16 versus <85: 0.566±0.14, p=0.09). Mean preprocedural ejection fraction was similar between groups (<85: 50.7±8.8 versus <85: 50.4±6.1±0.3 ммг/л, p=0.87). Mean preprocedural pulmonary artery systolic pressure was similar between groups (<85: 42.9±11.3 versus <85: 43.6±11.5 ммг/л, p=0.74). The mean age of patients that reached the primary clinical end-point was similar between groups (<85: 79.8±6.4 versus <85: 50.7±8.8, p=0.91).

**Conclusions:** In conclusion, among patients who undergo transcatheter TAVI, older patients (<85 years) experience similar benefits and outcomes when compared to younger patients.

**P4649 | BENCH**

Short and medium-term outcomes after primary percutaneous coronary intervention in an Asian elderly population  
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**Background:** With advancing age being traditionally associated with worse outcomes following percutaneous coronary intervention (PCI), it is critical to understand the predictors of outcomes after primary PCI in the very elderly. Such data is lacking, especially in an ageing Asian population.

**Methods:** We studied the clinical and sociocultural correlates of mortality and morbidity outcomes up to 1 year in very elderly Asian patients who have undergone primary PCI for ST-elevation myocardial infarction (STEMI). Data was analysed using the General Structural Equation model and variables selected for its clinical and social significance.

**Results:** From 2004 to 2015, 142 patients aged ≥85 years (range 80–95, 54% women, 74% Chinese, 16% Malay, 7% Indian) underwent primary PCI for STEMI. Median door-to-balloon time was 70 minutes and procedural success rate was 97%. 12 patients (9%) developed bleeding complications of Bleeding Academic Research Consortium (BARC) class ≥3, and 33 patients (24%) had contrast-induced nephropathy. Mortality was 15% (n=22) at 30-day and 25% (n=36) at 1-year follow-up. Time to death at 1-year had both clinical and social predictors. Patients with pre-existing chronic kidney disease had 4 times higher risk towards 1-year death (95% CI, 1.37–13.93, p=0.01), after adjusting for other clinical variables (table). Higher LVEF post-STEMI was associated with lower risk of mortality hazard ratio, 0.92; 95% CI 0.89–0.96; p=0.01). Patients who stayed with family had significantly lower hazard of death at 1-year than those who did not stay with family (hazard ratio, 0.11; 95% CI, 0.03–0.44; p<0.01).

**Predictors of time to death at 1 year**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Adjusted hazard ratio</th>
<th>95% Confidence interval</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Co-morbidities</td>
<td>Chronic kidney disease</td>
<td>4.36</td>
<td>1.37–13.93</td>
</tr>
<tr>
<td></td>
<td>Prior coronary artery disease</td>
<td>2.57</td>
<td>0.93–7.05</td>
</tr>
<tr>
<td></td>
<td>Staying with family</td>
<td>0.11</td>
<td>0.03–0.44</td>
</tr>
<tr>
<td></td>
<td>Kilp class</td>
<td>2 reference</td>
<td>reference</td>
</tr>
<tr>
<td></td>
<td>Door-to-balloon time</td>
<td>0.98</td>
<td>0.96–1.00</td>
</tr>
<tr>
<td></td>
<td>Single reference</td>
<td>reference</td>
<td>reference</td>
</tr>
<tr>
<td></td>
<td>Door 0.76</td>
<td>0.18–3.10</td>
<td>0.70</td>
</tr>
<tr>
<td></td>
<td>Triplet 0.96</td>
<td>0.33–2.78</td>
<td>0.94</td>
</tr>
<tr>
<td>Complications</td>
<td>Contrast-induced nephropathy</td>
<td>2.83</td>
<td>0.85–9.42</td>
</tr>
<tr>
<td></td>
<td>Bleeding of BARC ≥3</td>
<td>4.84</td>
<td>0.54-43.8</td>
</tr>
<tr>
<td></td>
<td>LVEF post-STEMI</td>
<td>0.92</td>
<td>0.89–0.96</td>
</tr>
</tbody>
</table>

BARC: Bleeding Academic Research Consortium; VEF: left ventricular ejection fraction.

**Conclusion:** Amongst Asian elderly patients with STEMI, primary PCI is a feasible treatment option, with high success rate and reasonable survival outcome enhanced by prior family support. Greater understanding of these predictors have important implications for therapeutic decisions.
Prevalence of ACHD in elderly

Conclusion: In Greece, CHD patients older than 60 years were mostly females, had mild CHD, were more commonly symptomatic, underwent fewer surgeries and were more frequently under cardiac medical therapy.

Acknowledgement/Funding: Hellenic Cardiological Society

P4651 | BEDSIDE
Comparison of magnetic resonance imaging and acoustocerebrographic signals in the assessment of focal microangiopathic lesions in patients with atrial fibrillation


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Background: Acoustocerebrography (ACG) is a novel, noninvasive, transcranial ultrasound method processing the set of data variables acquired from the transmission of multispectral ultrasound signals propagating through the brain tissue. The data include: broadband absorption coefficient, frequency dependent attenuation, speed of sound and tissue elasticity. ACG could potentially help to diagnose early stages of brain changes. ACG and Magnetic Resonance Imaging (MRI) results were compared in a clinical study assessment of focal white matter lesions (WML) in the brains of patients with asymptomatic atrial fibrillation (AAF).

Methods: The clinical study included 55 patients with AAF; the study population (WML) in the brains of patients with asymptomatic atrial fibrillation (AAF).

Figure 1. Density distribution of two most discriminative acoustocerebrographic variables: AlphaQuc_75.3 and QuasiC_50.4. The colors represent the groups of lesions: L0 – blue, L30 – red.

The points L0, L30 represent the medians of the variables. The contour lines represent color intensity from most typical (the strongest intensity) up to less typical data (the weakest intensity). Each contour contain the same number of data.

Results: The ACG method could clearly differentiate a group of WML patients with 0 to 4 lesions (L0) and a group of patients with 30 and more lesions (L30). Fisher’s Exact Test shows that this correlation is highly significant (p<0.001) (Fig. 1).

Conclusions: ACG is a new, effective method for detecting WML in patients with AAF. The ACG measurement methodology may become increasingly useful to diagnose and to stratify patients with AAF in order to individualize their treatment and maybe significantly reduce their risk of stroke.

Acknowledgement/Funding: MW, AD, PK are supporting the fundamental research on the ACG with EFPRE Grant No.100190912/990.301573.3.1.

P4652 | BEDSIDE
Comparison of equations that use cystatin C and creatinine levels for estimating glomerular filtration ratio in elderly Japanese patients with chronic heart failure

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Introduction: The average age of patients with chronic heart failure has been increasing with the aging of the population. Most patients have impaired renal function. Our aim was to evaluate the clinical utility of cystatin C for estimating renal function in elderly heart failure patients.

Purpose: We aimed to compare several calculation methods that use cystatin C (CysC) and creatinine levels for estimating glomerular filtration ratio (eGFR).

Methods: One hundred hospitalised male patients (mean age: 76 years) were enrolled in a study. We measured 24-hour creatinine clearance (24-hr Ccr), serum CysC levels, and serum creatinine levels (Cr). eGFR was calculated with the following methods using the plasma clearance of CysC and Cr: the Cockcroft-Gault equation (CLCr), the Japanese version of the Modification of Diet in Renal Disease equation (eGFR), and the CysC-based equation (GFRCyS). We investigated the correlation between 24-hr Ccr and the results calculated using these equations. The study population was divided into two groups according to their serum brain natriuretic peptide (BNP) levels. We regarded the patients with BNP values >100 pg/ml as having chronic heart failure (CHF).

Results: The mean Cr level was 0.94±0.34 mg/dl; CysC level, 1.11±0.32 mg/dl; and 24-hr Ccr, 67±28 ml/min. In the CHF group (n=51), >50% of the patients had chronic renal diseases (eGFR <60 ml/min). In the non-CHF group (n=49), the correlation coefficient values (r) between 24-hr Ccr and eGFR, CLCr, or GFRCyS were 0.60, 0.58, and 0.70, respectively. In the CHF group, the r values were 0.64, 0.69, and 0.84, respectively. A Z test revealed that GFRCyS more statistically significantly correlated with 24-hr Ccr than with eGFR in both groups (P<0.01).

Conclusion: Measurement of CysC level was useful for estimating the renal function of elderly patients with low muscle volume. Especially in the patients with CHF, measurement of CysC level was more useful for evaluating renal function than creatinine level.

P4653 | BEDSIDE
Dosing and tolerability of ivabradine in the LIVE: LIFE study, an evaluation of ivabradine given to older patients with heart failure 24-hr Ccr, 67±28 ml/min. In the non-CHF group (n=49), the correlation coefficient values (r) between 24-hr Ccr and eGFR, CLCr, or GFRCyS were 0.60, 0.58, and 0.70, respectively. In the CHF group, the r values were 0.64, 0.69, and 0.84, respectively. A Z test revealed that GFRCyS more statistically significantly correlated with 24-hr Ccr than with eGFR in both groups (P<0.01).

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mained on ivabradine (mean dose 8.8mg/day). 84% of patients and 84% of physi-
cians assessed tolerability of ivabradine treatment as "somewhat well" or better.

<table>
<thead>
<tr>
<th>Dosing and tolerability of ivabradine</th>
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<tr>
<td>Ivabradine dose</td>
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<td>N</td>
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<td>2.5mg bd, n (%)</td>
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<td>5mg bd, n (%)</td>
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<tr>
<td>7.5mg bd, n (%)</td>
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<td>Not taking, n (%)</td>
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Conclusion: These contemporary prospective data from an elderly UK CHF pop-
ulation with multiple co-morbidities on polypharmacy, demonstrate improvement in clinical variables with good tolerability of ivabradine and low incidence of side effects.

Acknowledgement/Funding: LIVE:LIFE is funded by Servier UK Ltd

P4654 | BENCH
Underuse of more potent P2Y12 antagonists in elderly patients, despite having worse response to clopidogrel compared to younger patients

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Background: Elderly patients with an acute coronary syndrome (ACS) have worse prognosis than younger patient, which may be due, in part, to a poor response to antiplatelet therapy, especially clopidogrel. Despite being a high-risk subgroup, elderly patients are less likely to receive evidence-based therapies such as more potent antiplatelet agents, particularly ticagrelor. In fact, clopido-
grel is still widely used in this population in a real-world scenario.

Purpose: To assess the use of P2Y12 antagonists in elderly patients in a real-
world registry and the impact of age on platelet reactivity in ACS patients receiving dual antiplatelet therapy.

Methods: Prospective, multicentre, observational, pharmacodynamic study con-
ducted in a Spanish population of ACS patients undergoing percutaneous coro-
nary intervention (PCI) and treated with dual antiplatelet therapy including as-
pirin and a P2Y12 inhibitor. Elderly was defined as age ≥75 years. Platelet func-
tion tests were performed the morning after the PCI and included: 1) VerifyNow P2Y12 assay, expressed as P2Y12 reaction units (PRU), with high on-treatment platelet reactivity (HTPR) defined as PRU >208; and 2) VASP analysis, expressed as platelet reactivity index (PRI), with HTPR defined as PRI >50%.

Results: Results of the first 211 patients included in this national registry are presented. Forty-three patients (20.6%) were ≥75 years. The proportion of pa-
tients treated with clopidogrel was higher among elderly patients compared to younger subjects (72.1% vs. 27.7%; P < 0.001). Only 12 patients older than 75 years were treated with ticagrelor and none of them with prasugrel. Elderly pa-
tients treated with clopidogrel had significantly higher platelet reactivity compared to younger patients (189.6 ±16.52 vs. 146.3 ±13.34 PRU; p = 0.045, Figure). The proportion of clopidogrel-treated patients with HTPR was also numerically higher among elderly patients (43.3% vs. 23.9%; p = 0.075). There were no differences in platelet reactivity among elderly compared to younger patients treated with tica-
grelor (44.5 ±15.7 vs. 49.9 ±24 PRU; p = 0.750). No elderly patient treated with ticagrelor had HTPR. Similar results were observed with VASP analysis.

Conclusions: Elderly ACS patients have worse response to clopidogrel than younger subjects. However, a very low proportion of aged patients are treated with potent P2Y12 antagonists (ticagrelor) in a real-world registry.

P4655 | BEDSIDE
Age predicts initiation of and persistence with P2Y12 inhibitor treatment after acute coronary syndrome - results from a nationwide retrospective cohort in Finland

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Background: Secondary preventive drug therapy following acute coronary syn-
drome (ACS) is recommended to reduce the risk of new cardiovascular events in all age groups. However, there are limited contemporary data on the associa-
tion of age with the initiation of and persistence with secondary preventive drug therapy, especially the use of P2Y12 inhibitors.

Purpose: To describe ACS patients aged ≥75 and ≥75 years, and eventual dif-
fferences in initiation of and persistence with secondary preventive drugs in an outpatient setting.

Methods: This observational cohort study linked patient-level data from differ-
ent nationwide registers in Finland. The patients were hospitalized for unstable angina pectoris or acute myocardial infarction (MI) in 2009–2013. Differences be-
tween the two age groups were tested with Pearson’s chi-squared test. Sensitivity analyses were performed with logistic regression and Cox model.

Results: The study included 54,416 patients: 29,372 (54%) of them were ≥75 years old and 25,044 (46%) ≥75 years old. Women were represented more of-
ten in the older population (55% vs. 27%, P < 0.001). The ACS event was more often ST-elevation MI (33% vs. 19%, P < 0.001) and invasively treated in patients ≥75 years than in the older group (PCI related to ACS: 47% vs. 20%, P < 0.001). Rates of comorbidities increased with age (Table). The proportion of patients fill-
ing prescription for P2Y12 inhibitors lower is greater for P2Y12 inhibitor ≥75% vs.
< 61%, P < 0.001. Persistence with P2Y12 inhibitors further decreased with ad-
vanced age, and less than 50% of patients aged ≥75 years completed 6 months of therapy. Moreover, the proportion of patients having statin (77% vs. 52%), beta-blocker (77% vs. 63%) and ACE inhibitor/ARB (61% vs. 47%) at discharge decreased with age (P < 0.001 for all).

Conclusions: The proportion of patients undergoing any invasive treatment and initiating post-event P2Y12 inhibitors decreased to well below half of the popula-
tion before the age of 75 years. Patients over 75 years of age had more underlying diseases at baseline and lower persistence with P2Y12 inhibitors than younger patients. Age was independently associated with a lower initiation of and persis-
tence with P2Y12 inhibitor use.

Acknowledgement/Funding: The study was fully sponsored by AstraZeneca Nordic Baltic.

P4656 | BEDSIDE
Comparison of pharmacological treatment alone versus treatment combined with implantable cardioverter-defibrillator therapy in patients over 75 years

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Introduction: Implantable cardioverter-defibrillator (ICD) therapy has been shown to reduce mortality in high risk patients, both for primary and secondary prevention of sudden cardiac death. However, the benefit of the ICD in the elderly is still a matter of debate due to controversial results of observational studies and the lack of randomized trials in patients of this age group.

Purpose: To assess the role of ICD therapy in patients aged ≥75 years.

Methods: From January 2008 to July 2014 we have recruited prospectively 802 patients aged ≥75 years that had a left ventricular ejection fraction (LVEF) ≤35%. From this group we identified 365 patients with a class I or IIa recommendation for ICD implantation at inclusion or during follow-up. Based on the presence or at-
tending cardiologists’ decisions, 92 patients received an ICD. In order to avoid potential confounding factors, we performed a propensity-score matched analy-
sis. Patients-matching was performed in a 1:1 ratio with the nearest neighbor method.

Results: 126 patients were included in our study (63 with ICD). The mean age of the study population was 79.1±3.1 years and 86.5% were males. As com-
pared with the medical therapy group, the ICD patients had a lower percentage of chronic obstructive pulmonary disease (19.0% vs. 38.1%, p < 0.05), and showed higher use of beta-blockers (BB) (87.1 vs 71.0%, p < 0.05). Other treatments were otherwise similar in both groups. There were not significant differences in relation with age, etiology or other comorbidities between ICD group and non-ICD
group. During the follow-up of 39.2±22.4 months, total mortality was 46.0% and cardiovascular events (death or hospitalization because of ventricular tachycardia or heart failure) occurred in 66.7% of the patients. After a multivariate Cox proportional hazard analysis, only BB therapy was shown to be an independent protective variable with respect to total mortality (HR 0.4 (0.2–0.7)). ICD therapy did not produce an improvement in mortality or hospitalization rate.

Conclusion: According to our results, the use of ICD did not demonstrate any benefit compared with medical therapy. Well-designed randomized controlled studies in patients over 75 years are needed to ascertain the value of ICD therapy.
upward trend in hospital admissions due to HF in comparison to other cardiovas-
cular diseases.

P4661 | BEDSIDE
Age-related differences in the management of acute coronary syndromes
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Introduction: The risk of acute coronary syndrome (ACS) increases with age. Several studies show that the elderly are less likely to receive invasive manage-
ment and evidence-based therapies, although the associated benefits are main-
tained at older ages. The aim of this study was to assess the relation between age and management with an invasive approach and with secondary-prevention therapies, taking into account the functional status of the patients.
Methods: Within a prospective cohort study of consecutive patients admitted to two tertiary hospitals with acute ACS, between August 2013 and December 2014, we evaluated patients whose functional status, assessed through the Barthel index scale (BIS), was available at baseline. Data were obtained through face-to-face interviews and medical records review.
Results: Of 1437 patients, 425 (29.6%) were aged 75 years and over. The proportion of patients discharged with aspirin was 95%, adenosine diphosphate recep-
tor inhibitors 97%, dual anti-platelet agents 92%, statins 91%, beta-blockers 80%, and ACE-inhibitors/ARB 80%. Older patients were significantly less likely to undergo invasive management (OR=0.10, 95% confidence interval (95% CI)=0.04–0.24), even after adjustment for BIS (OR=0.12, 95% CI: 0.05–0.30), and independently of the ACS type.
Conclusions: Although the vast majority of ACS patients were managed invasively and discharged on evidence-based secondary preventive medications, elderly patients were still less likely to be treated with these recommended therapies. Other factors not functional status might explain this inequality.

P4662 | BEDSIDE
Trends in characteristics and outcomes of elderly patients presenting with acute myocardial infarction
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Background: Most developed countries are experiencing an ageing population. Current guideline based therapy for acute myocardial infarction is mostly based on trials which excluded elderly patients. We sought to determine if there has been an improvement in outcomes for elderly patients presenting with acute myocardial infarction over an 18 year period.
Purpose: To assess the trend in outcomes from acute myocardial infarction in patients aged 75 years and over in a large health district.
Methods: The Hunter Area Cardiac and Stroke Outcomes Unit prospectively identifies all admissions to the Hunter New England health district with acute myocardial infarction. All patients were included in the database if they had an ICD 10 code of I21 or an ICD 9 code of 410 on discharge from any Hunter New England Health hospital during the admission dates of 1 January 1996 to 31 De-
Results: We identified 5548 patients aged 75 years and over presenting with acute myocardial infarction between 1996 and 2013. The mean age increased from 79.7 years in the first 6-year period to 83.5 years in the final 6-year period (p<0.001). In-hospital mortality decreased significantly from 20.6% in the first period to 11.7% in the last period (p<0.001). There was also a dramatic decline in 28 day (p<0.001) and 6 month (p<0.001) mortality. The proportion of patients receiving in-hospital PCI increased from 1.2% to 16.1% (p<0.001).
Conclusions: Surgeon variation for elderly patients has improved significantly over the study period. A greater proportion of patients re-
ceived in hospital PCI, however the absolute numbers were still low.

P4663 | BEDSIDE
Primary angioplasty program in the elderly: differential characteristics of a high risk population
Background: Patients aged 75 years or older are a subgroup of high risk in the management of acute myocardial infarction. They present special considerations in terms of symptoms, associated comorbidities, risk of complications and manage-
ment.
Objective: Our purpose is to analyze the differential characteristics of elderly patients in a primary percutaneous coronary intervention (PCI) program.
Methods: Prospective clinical observational registry study including 518 consec-
utive patients with suspected ST-segment elevation myocardial infarction (STEMI) who underwent emergency coronary angiography during the year 2014. We performed a comparative analysis of the elderly population (>75 years old) versus those aged 74 years or younger.
Results: Elderly patients (N=116, 22%) had similar delay times from symptom onset to first medical contact (FMC) to those aged 74 years or younger (93 vs 78 minutes; p=0.44). Nevertheless, elderly patients had longer FMC - to - PCI-team alert and FMC - to - reperfusion times compared with younger patients (40 vs 31 minutes (P=0.014) and 135 vs 123 minutes (P=0.005) respectively). Pretreatment rate with dual antiplatelet therapy among elderly patients was similar to that of younger patients (80% vs 73%; p=0.14) although clopidogrel was preferred over prasugrel (NAA) (83% vs 45%; p=0.003). Radial access was elective in both groups, but more frequent in younger patients (72% vs. 86%; p<0.001). The prevalence of multivessel disease was higher in elderly patients (55% vs 42%; p=0.021) and they had higher hospitalization (6 days; p<0.001). Mortality was similar (0.10 vs. p=0.001). Incidence of MACE after 1 year follow up tended to be higher in elderly patients, but did not reach statistical significance (13% vs 8%; p=0.12). On the other hand, elderly patients had higher haemorrhage rates (9% vs 4%, P=0.046).
Conclusions: Elderly patients present greater delays in primary angioplasty pro-
gram activation leading to longer FMC-to-reperfusion and total ischaemic times. Short and mid-term prognosis are similar to those of younger patients although they present significantly higher bleeding rates.

VALVULAR DISEASE
P4664 | BEDSIDE
Clinical profile and prognosis of acute heart failure complicating severe aortic stenosis: Insights from the CURRENT AS Registry
K. Nagao1, T. Morimoto2, T. Taniguchi3, R. Sakata3, T. Kimura4 on behalf of CURRENT AS Registry Investigators. 1 Osaka Red Cross Hospital, Osaka, Japan; 2 Hyogo College of Medicine, Clinical Epidemiology, Hyogo, Japan; 3 Kyoto University, Graduate School of Medicine, Kyoto, Japan
Background: Patients with severe aortic stenosis (AS) often present with acute heart failure (AHF), which is a clinical challenge and has a high mortality.
Purpose: The present study sought to clarify the clinical profile and prognosis of AHF complicating severe AS.
Methods: CURRENT AS Registry is a retrospective multicenter registry enrolling consecutive patients with severe AS defined by echocardiographic criteria. Entire patients were categorized into the 3 groups; no heart failure (HF), chronic HF (CHF) and AHF according to the symptom of HF and necessity for in-hospital management at the time of index echocardiography. Clinical outcomes at 5-year were compared among the 3 groups.
Results: Of 3815 patients, 2212 (58%), 813 (21%) and 790 (21%) patients were categorized into no HF, CHF and AHF groups, respectively. Median follow-up was 1361 days with 90% follow-up rate at 2 years. The cumulative 5-year incidence of all-cause death, aortic valve-related death and HF hospitalization in No HF, CHF and AHF groups were 37.1%, 41.8% and 61.8%, p<0.001; 9%, 13% and 30.7%, p<0.001; 13.7%, 23.4% and 38.8%, p<0.001, respectively. The cumulative 5-year incidence of surgical aortic valve replacement (AVR) or transcatheter aortic valve implantation in No HF, CHF and AHF groups were 55.4%, 69.6% and 48.2%, p<0.001, respectively. By using a multivariate proportional hazards model, AHF was an independent predictor of all-cause mortality (adjusted hazard ratio, 1.67 vs no HF; p<0.001), while CHF was not (adjusted hazard ratio, 1.10 vs no HF; p=0.21). Of note, even among the patients for whom AVR was initially planned, AHF was associated with high 5-year mortality rate (No HF; 17.3%, CHF; 25.2%, AHF; 33%, p<0.001, respectively).
Conclusions: In this observational registry of severe AS patients, AHF was as-
associated with a dismal prognosis with extremely high mortality rate, which could not be fully reversed by AVR after AHF. Early AVR strategy before emergence of AHF should be warranted to improve the clinical outcomes of patients with severe AS.

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Conclusion: It can be speculated that the dabigatran may inhibit the effects of thrombin at levels encountered in vivo within aortic stenotic valves and lead to sclerosis of aortic valve fibrocalcification in humans.

Acknowledgement/Funding: National Science Centre (2013/11/B/NZ5/00157 to EW)

Discussion and conclusion

The prevalence and main correlates of right ventricular dysfunction in patients with severe aortic stenosis and preserved left ventricular ejection fraction


Background: Right ventricular (RV) systolic dysfunction is a predictor of cardiovascular mortality in many cardiovascular diseases. Data regarding the prevalence and determinants of RV dysfunction in patients (pts) with severe aortic stenosis (AS) is still scarce. Moreover, RV function is not routinely taken into consideration in the preoperative risk assessment in this clinical setting.

Aim: To evaluate the prevalence and correlates of RV systolic dysfunction in pts with severe AS and preserved left ventricular ejection fraction (LVEF).

Method: We prospectively studied 218 consecutive pts (65 ±11 yrs, 58% men) with severe AS ( indexed aortic valve area, AVAi < 1.3 cm²/m²) and preserved LVEF (>50%), in sinus rhythm, without coronary artery disease or more than mild aortic or mitral regurgitation. Clinical assessment and a complete echocardiogram were performed in all pts. Patients meeting at least one of the following criteria: tricuspid annular plane systolic excursion (TAPSE) <17 mm, RV free wall systolic longitudinal strain (2D speckle-tracking echocardiography) ≤−21%, TDI-derived tricuspid lateral annular peak systolic velocity (TIS) <9.5 cm/s and RV fractional area change (FAC) ≤−35% were defined as having RV systolic dysfunction, as recommended by current guidelines.

Results: In 50% of pts, severe AS was associated with LV dysfunction (LVEF <50%), in sinus rhythm, without coronary artery disease or more than mild aortic or mitral regurgitation. Clinical assessment and a complete echocardiogram were performed in all pts. Patients meeting at least one of the following criteria: tricuspid annular plane systolic excursion (TAPSE) <17 mm, RV free wall systolic longitudinal strain (2D speckle-tracking echocardiography) ≤−21%, TDI-derived tricuspid lateral annular peak systolic velocity (TIS) <9.5 cm/s and RV fractional area change (FAC) ≤−35% were defined as having RV systolic dysfunction, as recommended by current guidelines.

Conclusions: Patients with permanent pacemaker immediately after TAVI did not have a higher risk for late mortality, however, this subgroup of patients could have increased the risk of developing heart failure in the medium to long term.
Systolic longitudinal strain of the RV free wall was significantly correlated to LV mass index (p=0.005) and RV diameter (p=0.04). Decreased TS' was associated to a more impaired LV longitudinal function as expressed by LV global strain (p=0.02) and septal S (p=0.004), while both TAPSE and TS' were inversely correlated with septal E/e' ratio (p=0.002, and p=0.02 respectively). We found no correlation between RV function parameters and systolic pulmonary arterial pressure.

Conclusion: In the present study, RV dysfunction was common in pts with isolated severe AS and preserved LVEF and was mainly related to LV remodeling and longitudinal dysfunction. All these findings may be accounted for by ventricular interdependence. An accurate routine evaluation of RV function and its correlates must be taken into consideration when assessing the preoperative risk in pts with severe AS.

Acknowledgement: Funding: CNCS – UEFISCDI grant, project number PN-II-ID-PCE-2012-4-0560 (contract 21/2013)

P4669 | BEDSIDE
Effect of body mass index on clinical outcomes and all-cause mortality in elderly patients undergoing transcatheter aortic valve replacement
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Objective: To assess the effect of body mass index (BMI) on clinical outcomes and mid-term all-cause mortality in elderly patients with severe aortic stenosis after transcatheter aortic valve replacement.

Methods: A retrospective observational cohort study of consecutive patients who underwent TAVR between 2008 and 2015 at our university medical center was conducted. Baseline characteristics and clinical outcomes were compared between 3 patients groups stratified according to the WHO-classification of BMI (18.5–24.9 kg/m², 25.0–30.0 kg/m², >30.0 kg/m²), peri-procedural complications according to VARC-2 were assessed and all-cause mortality was evaluated by the BMI group. Cox proportional hazard regression model was used to estimate hazard ratio and 95% confidence intervals for an association between BMI and all-cause mortality.

Results: Four hundred and twenty-eight consecutive patients who underwent TAVR were stratified according to BMI: 42.3% (n=181) normal weight (18.5–24.9 kg/m²), 36.9% (n=158) overweight (25.0–30.0 kg/m²), and 20.6% (n=88) obese (>30.0 kg/m²). After a median follow-up of 19.6 [interquartile range: 7.5–34.2] months, normal weight patients (BMI: 18.5–24.9 kg/m²) showed an increased rate of all-cause mortality when compared with overweight and obese groups (38.6% vs. 21.6% and 28.0%, p<0.005). As a continuous variable, BMI was predictive of mortality when adjusted for Logistic EuroSCORE, hypertension, diabetes mellitus, smoking status, and the occurrence of major complications. For every kg/m² increase in BMI, the hazard of risk-adjusted mortality was 5% lower (Hazard Ratio: 0.95; 95% CI 0.91–0.998, p=0.040).

Conclusions: After transcatheter aortic valve replacement patients with overweight and obesity showed lower all-cause mortality, as compared with normal weight equivalents.

P4670 | BEDSIDE
Continuity equation in paradoxical low flow severe aortic stenosis: can we only trust left ventricular outflow tract measurements?
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Background: Paradoxical low-flow severe aortic stenosis (PLFAS) is a controversial entity, as reliance on mean pressure gradient (MPG) may underestimate stenosis severity. On the other hand, grading of stenosis severity by aortic valve area (AVA) may overrate stenosis severity. These discordant evidence causes uncertainty about the actual severity of the stenosis in these cases. The aim of this study was to evaluate the aortic valve area in patients with PLFAS by means of continuity equation applied on the right ventricular outflow tract (RVOT) as an alternative position.

Methods: Sixty-seven patients with severe aortic stenosis were evaluated using 2D transthoracic echocardiography. Patients were divided in two groups, based on the measured transaortic gradients. The first group was designated as normal flow-high gradient (NFHGAS), while the second group was designated as paradoxical low-flow (PLFAS – defined by the presence in the transthoracic echocardiography of aortic valve area<1 cm², mean ventricular gradient>40 mmHg, ejection fraction<50% and SV of <-35 ml/m²). In both groups continuity equation was applied on the left ventricular outflow tract (LVOT) first and subsequently on the RVOT, as an alternative position.

Results: Mean age of patients was 71±9 years (38 male). The NFHGAS group (mean MPG 49±5 mmHg) consisted of 36 patients, while the PLFAS group consisted of 31 patients exhibiting (mean MPG 30±4 mmHg), p<0.05. The left ventricular ejection fraction was similar between groups (55±5 vs. 54±3%, respectively, p=N.S.). Applying the continuity equation on LVOT and then on RVOT, mean AVA was calculated at 0.67±0.1 and 0.67±0.01 cm² (p=N.S.), respectively for the NFHGAS group. For the PLFAS group, the respective values were significantly different; 0.69±0.1 cm² and 0.78±0.14 cm² (p=0.0003). The correlation between the two methods was higher in NFHGAS patients (r=0.76), while there was a significant weaker correlation in PLFAS cases (r=0.49).

Conclusion: The best agreement between the two methods of continuity equation was observed in patients with NFHGAS. In contrast, the lower agreement observed in patients with PLFAS, which may be attributed to structural remodeling and hernomdromic alterations in LVOT, should lead us to further explore the most accurate way of diagnostic approach.

P4671 | BEDSIDE
Benefit of pre- and intensified post-procedural physiotherapy in patients with symptomatic aortic stenosis undergoing transcatheter aortic valve implantation (4P-TAVI) study
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Background: Percutaneous transcatheter techniques emerge in the treatment of high risk patients with aortic stenosis. The objective of this study is to demonstrate that pre-procedural and intensified post-procedural physiotherapy is associated with a better functional and clinical outcome.

Methods: This is a prospective study of 51 patients randomized in two groups. While patients in group A (control group: 24 patients, age: 83±6,6 years, 46% male) did not receive physiotherapy prior transcatheter aortic valve implantation (TAVI), group B (intervention group: 27 patients, age 82,5±6,2 years, 44% male) participated in intensive preinterventional physiotherapy which comprises inspiratory muscle training (IMT: 4x5minutes/day) and a minimum of 30 minutes of walking below the threshold of subjective exhaustion. After TAVI, the participants of both groups A and B get individual therapy with supervision of a physiotherapist (group B: 2x30 minutes/day, group A: 1x30 minutes/day). After TAVI 30 and 90 days Follow-up (FU) included clinical examination and standardized functional and psychological tests.

Results: Patients in the interventional group had a 5 days shorter mean hospital stay (p<0.05), a lower rate of postoperative pulmonary complications score 3 months after TAVI (PPC-Score: 0.07±0.26 vs. 0.8±1.3, p<0.05) and a lower NYHA value 3 months after TAVI (NYHA: 1±0,4 vs. 2.2±0,7, p<0.05). Mortality, rehospitalisation rate and psychological status was not different between groups.

Conclusion: Intensified preinterventional physiotherapy seems to have positive effects on clinical outcome 90 days after TAVI. These preliminary results of the 4P TAVI study should be regarded as hypothesis generating. Longer follow up and higher numbers of subjects are needed to confirm these interim results.
P4672 | BEDSIDE

Impact of Concomitant Mitral Regurgitation on Non-Invasive Evaluation of Severe Aortic Stenosis


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Objectives: Non-invasive assessment of aortic stenosis (AS) is based on mean transvalvular gradients (MPG), Doppler-derived flow velocity (vmax) and aortic valve area (AVA). Treatment is recommended if MPG is >40 mmHg or vmax >4.0 m/s. The purpose of the present in-vitro study was to analyse the impact of systemic hemodynamic variables (e.g. stroke volume (SV), heart rate, peripheral vascular resistance SVR, arterial compliance) and concomitant mitral regurgitation on non-invasive measurement of MPG and vmax in severe AS.

Methods and results: A pulsatile mock circulatory model was set up to study valve function with ejection pressure ranging from 0–300 mmHg, SV from 30 to 100 ml, and heart rates from 40 to 100 bpm. In the model, patients with high-long term mortality despite an “event-free” procedure and might help to identify futile patients.

Conclusions: An “event-free” TAVI procedure could be achieved in patients with less morbidity. However, an STS-score >8 characterizes patients with high risk for mortality during TAVI. Systematic analysis of inter-dependence of aortic MPG and vmax from concomitant moderate or severe MR, systemic vascular resistance (SVR) and systemic compliance (C) was performed using Doppler ultrasound and direct pressure measurements.

In absence of severe MR, a given stepwise increase of SV and decrease of aortic VA resulted in a proportional increase of aortic MPG. When moderate and severe MR were introduced into the model, the forward stroke volume significantly decreased (70.9±1.1 ml vs 60.8±1.6 ml vs 47.4±1.1 ml; p<0.02) while mitral regurgitant volume increased proportionally. This was associated with a reduction of aortic MPG (57.1±9.4 mmHg vs 48.6±13.8 mmHg; p=0.035) and vaxm (5.09±0.4 m/s vs 4.91±0.7 m/s vs 3.75±0.5 m/s; p<0.001), while calculated aortic VA remained unchanged (without MR: VA=5.03±0.04 cm²; with MR: VA=5.02±0.05 cm²; p=0.932).

In a single center registry of consecutive patients undergoing TAVI, we investigated the impact of moderate or severe MR on cardiovascular (CV) mortality at 2 years stratified according to MR etiology as assessed by transesophageal echocardiography. Baseline characteristics, echocardiographic parameters, and procedural data were prospectively collected in a web-based database. All patients underwent telephone follow-up by means of a standardized questionnaire; adverse events were adjudicated by an independent clinical event committee. Categorical data are expressed as frequencies and percentages and compared using the chi-square test or Fisher’s exact test. Survival is estimated using the Kaplan-Meier method. All analyses were adjusted for differences in baseline characteristics. The registry has been approved by the local ethics committee.

Results: Among 603 patients (mean age 82.5±6.7 years, 55% female) with severe AS undergoing transcatheter aortic valve implantation (TAVI), the incisional rates were 4.4% for severe MR and 454 patients had no or mild MR. Functional (FM) and degenerative mitral regurgitation (DMR) was documented in 53 (36%) and 96 (64%) patients, respectively. Compared to patients without MR, patients with FM or DMR had significantly higher STS and EuroSCORE (FM vs no MR: STS 8.8±5.5/ES 5.4±4.0, p<0.001; DMR vs no MR: STS 8.8±5.5/ES 5.4±4.0, p<0.001). Left ventricular ejection fraction was significantly lower in patients with FM (33±13%) and DMR (51±15%) compared to patients with no MR (57±13% (p<0.001). At 2 years, patients with FM and DMR had a significantly higher crude rate of mortality (30.2% vs. 16.2% in patients with no MR (p=0.001). A similar pattern was observed for all-cause mortality. In adjusted analyses, DMR was as...
sociated with an increased risk of CV mortality throughout 2 years of follow-up (adjusted HR 2.59, 95% CI 1.64–4.08, p = 0.001); a similar trend with a weaker signal though was observed for patients with FMR (HR 1.78, 95% 0.99–3.19, p = 0.053) (Figure 1).

Conclusions: Patients with severe, symptomatic AS undergoing TAVI complicated by moderate or severe MR portend impaired prognosis. Particularly, patients with DMR are at increased risk for CV mortality during long-term follow-up.

P4676 | BEDSIDE
Adverse effects of electrical dyssynchrony on left ventricle and left atrial reverse remodeling and prognosis after aortic valve replacement
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Background: Electrical dyssynchrony (ED) is an important contributing mechanism in the progression of heart failure and of left ventricular (LV) remodeling. In patients undergoing aortic valve replacement (AVR), ED might occur not only in the course of LV remodeling due to severe aortic valve disease but also due to damage to the conduction system during AVR.

Purpose: We hypothesized that ED would interfere with LV and left atrial (LA) reverse remodeling and affect prognosis in patients undergoing AVR.

Methods: A total of 411 consecutive patients (57% male, 64±11 years, 67% aortic stenosis, 13% concomitant coronary artery bypass surgery) who underwent surgical AVR between 2010 and 2015 in a single tertiary center were retrospectively analyzed. The patients were grouped according to the presence of ED [Group 1 (n=382, 93%); no ED, Group 2 (n=29, 7%); ED]. ED was defined as a pre-existing or new-onset left ventricular bundle branch block (LBBB) and electrical pacing rhythm by permanent pacemaker after AVR. LV and left atrial structure and function were assessed preoperatively and function were assessed preoperatively, and after 1-year follow-up. The primary endpoint was a composite of re-hospitalization for heart failure and all-cause mortality.

Results: Baseline characteristic, LV chamber size, ejection fraction, and LV volume index (LAVI) were comparable between patient groups, except for significantly older in group 2. Group 2 showed lower ejection fraction (58±15 vs. 64±9%, p=0.044), lower relative wall thickness (0.39±0.08 vs. 0.43±0.08, p=0.015), higher LAVI (41±17 vs. 33±13mL/m², p=0.025), and higher E/E’ (19.3±9.0 vs. 14.5±6.6, p=0.009) than group 1 at 1-year after AVR. LV reverse remodeling assessed by changes in LV end-systolic volume relative to baseline (∆LVEDV), or LV performance improvement (∆LVEF) and LA reverse remodeling assessed by ∆LAVI was lower in group 2. During a median follow-up of 39 months, 29 (7.9%) patients in group 1 and 6 (20.7%) patients of group 2 occurred adverse clinical events (p=0.031).

Conclusions: ED after AVR negatively affected the recovery of LV systolic and diastolic function, and clinical outcome.

P4677 | BEDSIDE
Outcome of interventional treatment for access site complications in transmemorial aortic valve implantation

Aims: The most frequent complications of transmemorial aortic valve implantation (TAVI) are vascular access site complications. Vessel dissections from perforations or insufficient closure can be treated with balloon angioplasty and sometimes require stent implantation. To address this risk in our institution, we routinely insert an elastic iliosaphic 5F “security sheath” distally of the TAVI sheath in the superficial femoral artery. In this study, we examined short- and mid-term efficacy, safety and sustainability of emergency procedures via this additional access site.

Methods: We conducted a retrospective database analysis including all 472 patients that received TAVI from 2011 until 2015. To facilitate detection of late vascular access site complications, we conducted a structured telephone interview.

Results: During that analysed time, 472 patients underwent TAVI. More than 90% of our patients were treated with the Sapien bioprostheses with sheath diameters ranging from 14 to 18F. Access site closure was undertaken using the Proglide device. Vascular access site complications that required balloon angioplasty or stent implantation occurred in 11% (angioplasty n=27 (7%) and stent implantation n=26 (5%) of our patients). Stenting was performed with GoreTex-covered (Fluency plus) or uncovered (Lilistent) stents (Bard). Mean follow-up was 368 days (14–1124). Technical success rate for the vascular intervention was 96%. Of all treated patients, only one required surgical repair (0.2%). To facilitate detection of late vascular access site complications, we conducted a structured telephone interview. Of 53 patients with vascular access site complications, 14 patients had died, 4 did not consent to the interview and 9 were lost to follow-up or were not able to answer the questions. None of the 26 patients that consented to the interview had a new diagnosis of perfusion deficit or peripheral artery disease and none was diagnosed with symptoms of claudication. Self-reported walking distance improved in 20 of 26 patients and increased from 579±336m to 1885±674m, p<0.001. Patients with a reduced walking distance following access site complications were not limited by claudication, but by various other comorbidities.

Conclusion: Treatment of vascular access site complications during TAVI with balloon angioplasty (with or without stenting) via an electrically covered iliosaphic sheath is safe and effective. During short- and mid-term follow-up these interventions were associated with low complication rates and good clinical outcome.

P4678 | BEDSIDE
Outcome of acute and chronic renal injury in patients undergoing MitraClip implantation: retrospective data analysis from two German high-volume centers
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Objectives: In patients (pts) suffering from relevant mitral regurgitation (MR), MitraClip (MC) implantation represents an alternative treatment strategy. If open-heart surgery cannot be performed. Kidney injury is associated with increased rates of mortality and morbidity in pts suffering from heart failure. We sought to assess the long-term outcome of acute kidney injury (AKI) and chronic kidney disease (CKD) after MC implantation.

Methods and results: Between 09/2008 to 11/2013, 674 pts (74±8±9 years, 38.1% females) were treated for MR 3+/4+ by MC implantation (success rate 92.4%, functional MR 66.4%) at the university centers Göttingen (n=210) and Hamburg (n=464). Significant baseline differences concerning LVEF (p<0.001), heart rate (p<0.001), severity of MR at baseline (p<0.001), stroke (p<0.001), pulmonary hypertension (p<0.001), and renal function (p=0.026) and success rate (p=0.008). According to VARC criteria, AKI was defined according to increasing creatinine values within 48 hours after procedure compared to prehospital data in 521 pts (AKIN 0=405 pts, 1=100 pts, 2=14 pts, 3=2 pts). Stroke, ESKD, logEuroSCORE, NYHA class IV and NT-proBNP levels were significant higher in AKIN class 1 to 3 compared to AKIN 0. Neither objective physical capability, expressed by 6-minute-walking distance nor quality of life did differ between the groups. Total procedure time, radiation time and procedural success rate were similar. In Kaplan-Meier analysis, the highest mortality rate was seen for AKIN 2&3 (p<0.0001) and in univariate Cox regression analysis for mortality the Hazard ratio (HR) for AKIN 1 was 2.41 (p<0.001) and 2.98 for AKIN 2&3 (p=0.0015) compared to AKIN 0. This association remained significant even after multivariate adjustment (age, gender, body mass index, logEuroSCORE, atrial fibrillation and LVEF<30%) (HR=2.33; p<0.001 for AKIN 1 and HR=3.10, p<0.0021 for AKIN 2&3). Similar data were observed in Kaplan-Meier analysis for rerehabilitation for heart failure (p=0.008). The HR was 1.52 (p=0.023) for AKIN
P4679 | BEDSIDE
Long term predictors of recurrent mitral regurgitation after mitral valve repair evaluated by three dimensional transesophageal echocardiography

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Purpose: The tendency of recurrent MR.

Methods: The Japan Society for the Promotion of Science

Results: Baseline ST-2 levels were associated with successful MR reduction (MR reduction ≥2 grades: 851.9 pg/mL [IQR: 438.5 vs. 1108.1] vs. MR reduction <2 grades: 1728.0 pg/mL [IQR: 1051.3 vs. 1930.1; p=0.001]). In addition, low ST-2 baseline values were predictive for successful reduction of MR severity after PMVR (AUC: 0.782 [0.612–0.9]; p=0.004).

Conclusions: ST-2 is associated with enhanced myocardial pressure and volume overload, increased wall stress, and fibrotic alterations in MR. In this study, low baseline ST-2 levels were predictive of therapeutic success in high-risk patients undergoing PMVR. Accordingly, high-risk patients with severe heart failure and elevated ST-2 levels might not benefit from PMVR.

P4680 | BEDSIDE
Predictors of natriuretic peptide non-response in patients underwent MitraClip

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Background: Mitraclip implantation has rapidly become as an alternative therapeutic option for patients with severe symptomatic mitral regurgitation (MR) who are not amenable to MV surgery. Heart failure is complicated with most of candidates for mitraclip and we previously reported that increasing N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels reflecting severe heart failure were associated with worse outcomes of patients undergoing MC. However, the response of NT-pro BNP levels after mitracle is still incompletely understood and predictors of NT-pro BNP nonresponders have not been studied.

Methods: Among 136 consecutive patients successfully treated with mitraclip there were 55 patients (41%) were responders, whereas 55 patients (47%) were nonresponders. Gender and age were comparable between two groups. Diabetes mellitus (51% vs. 25%, p=0.003) and atrial fibrillation (67% vs. 49%, p=0.049) were more common in nonresponders. MR grade at baseline and at hospital discharge was not different. Patients with base line New York Heart Association class IV was more common in responders. Baseline NT-pro BNP levels were higher in responders (7.775±7.043 vs. 4.278±3.578 pg/mL; p=0.001). Left ventricular ejection fraction was comparable. Right ventricular systolic dysfunction (RVSD) defined as tricuspid annular plane systolic excursion (TAPSE) <15 mm was more common in nonresponders (41% vs. 18%; p=0.008). Multi BNP logistic regression test revealed that diabetes mellitus (odds ratio (OR) 2.966, p=0.014), RVSD (OR 3.948, p=0.006), and baseline NT-pro BNP >5000 pg/mL (OR 2.04, p=0.001) were independent predictors of nonresponders after mitraclip procedure. All-cause death tended to be less common in responders of NT-pro BNP (20% vs. 31%, p=0.163).

Conclusion: NT-pro BNP levels significantly decreased after mitraclip in the chronic phase. Presence of diabetes mellitus and RVSD were predictors of NT-pro BNP nonresponse. We need to carefully observe patients with diabetes mellitus and RVSD as these may be considered high-risk subjects for sustained heart failure after mitraclip. Response of NT-pro BNP might be associated with long-term survival after MiraClip.

Acknowledgement/Funding: The Japan Society for the promotion of Science.

P4682 | BEDSIDE
Relationship of oxidative stress markers and mitral valve chorda tendinea rupture


Background: Percutaneous mitral valve repair (PMVR) is an interventional treatment option in patients with severe mitral regurgitation (MR) who have a high risk for open-heart surgery. Although PMVR is safe and feasible, there is limited information about predictors of clinical outcome and procedural success. ST-2, a predictor of recurrent MR.
gurgitation with CTR group compared to both rheumatic severe mitral regurgitation group without CTR and healthy controls (11.7±3.15, 8.3 vs 6.6±5.5, p=0.038 and 11.7±3.15, 8.3 vs 5.6±3.10, p=0.019, respectively). Calculated OSI was also significantly higher in severe mitral regurgitation with CTR group compared to rheumatic severe MR without CTR and healthy controls (0.50±0.61 vs 0.31±0.24, p=0.026 and 0.50±0.61 vs 0.27±0.15, p=0.023, respectively). There was no relationship between IL-6, TNF-αpha and severe mitral regurgitation with CTR.

Conclusion: We found for the first time, a significant association between oxidative stress markers and severe mitral regurgitation with CTR compared to mitral regurgitation without CTR. This association was independent from inflammation markers. According to our findings, heightened oxidative stress could play an important role in the pathogenesis of chorda tendinea rupture.

P4683 | BEDSIDE
Impact of atrial fibrillation on mitral valve repair with the mitrallip system: one-year outcomes from the GRASP registry
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Background: Atrial fibrillation (AF) is common in patients with mitral regurgitation (MR) referred for therapy. However, specific data on the impact of this condition on the outcomes after percutaneous mitral valve repair are limited.

Methods: Patients enrolled in the prospective Getting Reduction of Mitral insufficiency by Percutaneous Clip Implantation (GRASP) who were eligible at one-year follow-up were included in the present analysis. The primary efficacy endpoint was the composite of death, surgery for mitral valve dysfunction and grade 3+ or 4+ MR at one-year follow-up. Secondary endpoints were the components of the primary endpoint, re-hospitalization rates and functional NYHA class. Also echocardiographic parameters at baseline and one-year follow-up were assessed.

Results: A total of 180 patients were included: 111 (61.7%) without AF and 69 (38.3%) with AF. Thirty-three patients (18.3%) presented with degenerative MR and 147 patients (81.7%) with functional MR. Comparable clinical and echocardiographic baseline characteristics were observed between the two groups except for age, STS score and left atrial (LA) volume (worst in the AF group). All patients had a post-procedural residual MR ≤2+. At one-year follow-up, no significant differences were reported in terms of primary end-point (19.3% in patients with AF versus 29.9% in patients without AF, p=0.156). Secondary endpoints rates concerning the two groups are reported in Table 1. No statistically significant differences were observed. A positive correlation was observed between AF and re-hospitalization rates in patients with functional MR (p=0.043). At one-year follow-up, a significant reduction in left ventricular volumes was observed regardless of AF; no relevant changes were reported in LA volumes.

Conclusions: The mitrallip procedure was associated with low rates of adverse events in patients with AF, reporting one-year outcomes comparable to patients without AF.

Table 1. One-year outcomes in patients with or without AF

<table>
<thead>
<tr>
<th></th>
<th>No AF</th>
<th>AF</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>13.3%</td>
<td>10.7%</td>
<td>0.582</td>
</tr>
<tr>
<td>Surgery for mitral valve</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>MR 3+</td>
<td>19.2%</td>
<td>9.7%</td>
<td>0.139</td>
</tr>
<tr>
<td>Re-hospitalization</td>
<td>7.4%</td>
<td>18.1%</td>
<td>0.051</td>
</tr>
<tr>
<td>NYHA class 3</td>
<td>93.1%</td>
<td>82.4%</td>
<td>0.072</td>
</tr>
</tbody>
</table>

P4684 | BEDSIDE
Current profile of patients with recent infective endocarditis: insights from a large contemporary cohort
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Introduction: Patients surviving a first episode of infective endocarditis (IE) have a significantly worse survival, mainly due to late complications such as heart failure, higher risk of recurrence and increased need for valve surgery. The aim of this study was to analyze the current state of recurrent IE in a large contemporary cohort.

Methods: We analyzed 1335 consecutive episodes of IE recruited prospectively in three tertiary care centres between 1996 and 2015. Patients were categorized into two groups: group I (n=1228), patients with a single episode of IE, and group II (n=107), those with recurrent IE. Group II was subdivided into lla (n=86), reinfection, and llb (n=15). Reanalysis was performed compared to these two subgroups.

Results: The rate of recurrent IE was 8%, with no difference in incidence between the first and second decade of the study (1996–2005: 9%, 2006–2015: 7%, p 0.149). The median time until recurrence was 1077.5 days [IQR 339–2027] in the reinfection group and 84.5 days [IQR 55–130] in the relapse group. Patients with reinfecions were younger (58.0 vs 63.8 years, p<0.001) and more commonly male (76% vs 65%, p=0.045), compared to those with a single episode. Intravenous drug users (IVDU) and prosthetic valve carriers were present in the reinfection group more than twice as frequently (11% vs 5%, p=0.019, and 68% vs 31%, p<0.001, respectively). In patients with this group had less embolic complications and required less cardiac surgery, with similar in-hospital mortality (table 1). There was no difference in microbiological etiology between groups.

Conclusion: The rate of recurrent IE in our population was similar in both decades of the study. Patients with reinfecions were more commonly male, prosthetic valve carriers, and had a history of IVDU. This patients had fewer embolic complications. Relapse group had the highest incidence of periannular complications and mortality.

P4685 | BEDSIDE
Increase in activated dendritic cells infiltrating into endocardium in the left atrium of rheumatic heart disease
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Background: Left atrial (LA) structural remodeling develops according to the disease severity of mitral valve and the presence of atrial fibrillation in rheumatic heart disease (RHD). Inflammatory lesions are found in LA in patients with RHD, suggesting a direct role of cell-mediated immunity in the pathogenesis of LA remodeling. Dendritic cells (DCs) are the major antigen-presenting cells and known as crucial modulators of innate and adaptive immunity.

Methods: Autopsy specimens were taken from the consecutive series of RHD patients with chronic rheumatic valvular disease (CRVD) subjects from 2002 to 2014 (RHD group, n=5) and from age-, sex- and LA dimension-matched non-RHD controls (control group, n=5). Immunohistochemical analysis was performed using antibodies to CD11c, CD209, and CD80 as markers of myeloid DCs, migratory active DCs, and mature DCs, respectively. Additionally, infiltrated inflammatory cells including T lymphocytes (CD3), M1 (CD68; pro-inflammatory profile) and M2 (CD163; pro-resolution profile) macrophages, and tenasin-C, one of the extracellular matrix (ECM) proteins which appears during ECM remodeling and inflammatory response, were examined.

Result: To clarify the impact of DCs on the inflammatory process in RHD, we sought to identify and quantify endomyocardial infiltration of DCs into the LA using human autopsied samples.

Methods: Autopsy specimens were taken from the consecutive series of RHD patients with chronic rheumatic valvular disease (CRVD) subjects from 2002 to 2014 (RHD group, n=5) and from age-, sex- and LA dimension-matched non-RHD controls (control group, n=5). Immunohistochemical analysis was performed using antibodies to CD11c, CD209, and CD80 as markers of myeloid DCs, migratory active DCs, and mature DCs, respectively. Additionally, infiltrated inflammatory cells including T lymphocytes (CD3), M1 (CD68; pro-inflammatory profile) and M2 (CD163; pro-resolution profile) macrophages, and tenasin-C, one of the extracellular matrix (ECM) proteins which appears during ECM remodeling and inflammatory response, were examined.

Result: Baseline heart rhythm was atrial fibrillation in all patients in both RHD and the control groups. LA dimension of the control group was larger compared to RHD group (572 vs 56±11 mm, p=0.67). The numbers of infiltrated T lymphocytes (173±91 vs 2±11 /mm², p=0.009), M1 macrophages (106±47 vs 0±1.02 /mm², p=0.007), M2 macrophages (88±27 vs 14±18 /mm², p=0.009), myeloid DCs (18±14 vs 1±1 /mm², p=0.03) and migratory active DCs (78±27 vs 5±5 /mm², p=0.09) and infiltrating mature DCs (12±16 vs 0±7 /mm², p=0.05) were significantly higher in RHD group compared with the control group. Tenasin-C positive area fraction was significantly higher than control (11.2±4.4 vs 1.1±0.8%, p=0.004). Furthermore, there were correlation between tenasin-C area and other immunohistochemical staining (CD68, CD163, CD209 and CD11c, in which the most strongly correlated with was CD163 (R²=0.71, p=0.0019).

Conclusion: Increase in migrated activated DCs and other inflammatory cells in LA was associated with ECM remodeling, which may affect persistent
inflammatory process in RHD. Tenascin-C might be set as the maker of inflammatory profile.

**P4686 | BEDSIDE**

Tricuspid regurgitation has marked negative survival implications for elderly patients with left heart valve disease

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Background: Tricuspid regurgitation (TR) is recognized as a common valvular lesion with important clinical and prognostic significance. Data are available for large patient groups, but its specific effects in the elderly are relatively unknown. This study therefore compared the impact of TR on survival in elderly patient and younger patients with concomitant left valve disease (LVD).

Methods: Cases were sequential retrospectively reviewed from an echocardiographic imaging database. LVD was defined as moderate or severe mitral or aortic valve disease (stenosis or regurgitation), and elderly defined as >75 years. Four patient groups were created, Elderly (E) and Non-elderly (NE), subdivided into those with (TR) and without (nTR) tricuspid regurgitation. Clinical data including atrial fibrillation, LV ejection fraction and death were tabulated. Followup was achieved for a mean 596 days. The Cardiac event was defined as all cause death and hospitalization caused by heart failure.

Results: TR prevalence among the non-elderly (n=227) and elderly groups (n=267) was 29.1% and 41.2% respectively (p<0.01). Ejection fraction did not differ among the four groups. Atrial fibrillation (AF) was more prevalent in patients with TR, regardless of age group (p<0.05). Fifty-eight (14%) patients died during follow up. The all cause death and Cardiac event as estimated by Kaplan-Meier analysis was considerably worse in elderly patients with TR compared with other groups (Log-rank test, p<0.001). Multivariate analysis revealed that TR, lower EF and NYHA (II,III,IV) were independent risk factors of cardiac event for one year among elderly patients.

Conclusions: TR prevalence in elderly patients with LVD is significantly higher than non-elderly, and the elderly patients are associated with substantially worse prognosis. TR status should be taken seriously when considering intervention for aortic or mitral disease in the elderly. Whether TR repair will moderate this adverse prognosis remains to be seen.

**P4687 | BEDSIDE**

High sensitivity troponin T in risk stratification in patients undergoing valve surgery

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Background: Several studies have reported that elevated high sensitivity troponin T (hs TnT) is associated with poor outcomes in patients with myocardial infarction, heart failure or nonischemic dilated cardiomyopathy. The relationship between hs TnT and the prognosis for patients with valvular disease after cardiac surgery was studied in a small number works and it is not entirely clear.

Purpose: The aim of the study was to investigate the prognostic value of hs TnT in patients undergoing valve replacement or repair of the valve/valves. Serum levels of hs TnT were measured 24 h before valve surgery. The primary endpoint at the 30-day follow up or until the patient was discharged from the hospital was death from all causes. Univariate analysis followed by multivariate regression analysis were performed.

Results: The primary endpoint occurred in 17 patients. At univariate analysis coronary artery disease (OR 2.805; 95% CI 1.010–7.791; p=0.04), diabetes mellitus (OR 3.285; 95% CI 1.195–9.023; p=0.02), red blood cell count (OR 0.112; 95% CI 0.041–0.306; p<0.0001), hemoglobin level (OR 0.518; 95% CI 0.379–0.706; p<0.0001), hematocrit (OR 0.793; 95% CI 0.710–0.895; p<0.0001), glomerular filtration rate (OR 0.972; 95% CI 0.944–1.001; p=0.035), creatinine (OR 1.017 95% CI 1.000–1.033; p=0.005) and hs TnT (OR 1.335; 95% CI 1.102–1.602; p<0.02) were associated with the occurrence of the death. At multivariate analysis hs TnT (OR 1.303; 95% CI 1.098–1.606; p=0.03) remained independent predictor of the primary endpoint. ROC analysis determined a cut-off value of hs TnT for the prediction of the occurrence of the primary endpoint at 29.8 ng/l. Figure 1 depicts Kaplan–Meier event-free survival curves for primary endpoint according to the cut-off value of hs TnT.

Conclusions: Elevated hs TnT is associated with a worse outcome following cardiac surgery repair or replacement. hs TnT may be helpful in patients with a higher risk for postoperative complications requiring more attention while being qualified for cardiac surgery.

**P4688 | BEDSIDE**

The safety and efficacy of etanercept on cardiac functions and lipid profile in patients with active rheumatoid arthritis

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Objective: Patients with rheumatoid arthritis (RA) are known to be at increased cardiovascular risk. Etanercept is a tumor necrosis factor α (TNF-α) blocking agent that has been successfully used in the treatment of RA. We sought to assess the effects of etanercept on cardiac functions and lipid profile in RA patients with through a systematic review of the literature.

Methods: Sixteen patients with active RA were recruited to the study prospectively. Etanercept was administered subcutaneously twice a week for 6 months. Clinical and laboratory predictors of RA activity and lipid profile were evaluated at baseline and at 6 months. The systolic and diastolic function parameters of the left ventricle were obtained by echocardiographic examination and included mitral inflow Doppler and tissue Doppler imaging.

Results: Sixteen patients (13 women; median age, 48 years [range, 27–69 years]) completed the study. hs TnT completed the Syntax Score and Health Assessment Questionnaire scores were significantly reduced by treatment (6.35 to 4.45 [P<0.001] and 2.0 to 0.75 [P=0.005], respectively). Diastolic dysfunction was detected in 6 patients (37.5%) (3 in grade 1 and 3 in grade 2) by mitral inflow Doppler and the tissue Doppler parameters before the treatment. No significant change in diastolic dysfunction was observed during follow-up (5/16 to 5/16, P=0.164). In addition, there were also no significant differences in the left ventricular ejection fraction (65.8–66.9, P=0.164) and lipid profiles after 6 months of etanercept treatment.

Conclusions: Etanercept treatment was safe for use as regards cardiac functions and lipid profiles and effective on RA parameters during 6-month follow-up in patients with active RA.

**P4689 | BEDSIDE**

Role of multi detector computed tomographic angiography (MDCTA) for the evaluation of prosthetic valve function after successful thrombolysis of stuck valve


Background: Patients of prosthetic valve thrombosis (PVT) after thrombolysis may continue to have residual prosthetic obstruction and/or dysfunction which can serve as a nidus for the recurrence of PVT. Echocardiographic and cinefluoroscopy (CF) examination may not unequivocally establish the residual dysfunction and morphological cause for the persistent obstruction.

Purpose: We have prospectively evaluated whether the multi detector computed tomographic angiography (MDCTA) provides additional information about anatomical substrate for functional abnormalities.

Methods: Consecutive patients presenting with PVT who underwent successful thrombolysis were prospectively studied. All patients underwent detailed clinical evaluation, trans-thoracic as well as trans-oesophageal echocardiography, CF and MDCTA evaluation. Their comparative diagnostic value in the evaluation of prosthetic valve function was evaluated with special emphasis on detection of residual obstruction and to identify the cause for the prosthetic valve dysfunction.

Results: During the study period, a total of 16 patients underwent successful thrombolysis for PVT (8 male, mean age 38.07±10.14 years). Nine had mitral valve replacement and other 7 had mitral & aortic valve replacement. All these had been presented with mitral PVT. All had been implanted with bileaflet valves except for 1 who had TTK–Chitra valve. Mean duration between valve replacement surgery and PVT was 40.7±30.7 weeks. Echocardiogram showed restricted leaflets in 9 patients despite decreased gradients. Two patients had evidence of thrombus while in one patient true pannus was present. CF and MDCTA showed restricted leaflet excursion as measured by opening and closing angles in 12 patients. In CF, right anterior oblique with cranial or caudal angulation projection was found to be most useful for visualizing leaflet motion. In MDCTA, morpholog-
Valvular disease / Acute pulmonary embolism 949

3.9%, p=1.0) or closure device failure (L-MB 1.9%; H-MB: 2.8%; p=0.43).

no significant differences concerning the incidences of stroke (L-MB: 4.1%; H-MB: 5.2%; p=0.35).

923 patients (pts) received TF-AVI at our centre between 03/2012 to 09/2014. We determined peak CK-MB release within the first 72 h after implantation.

Methods: We identified and quantified 760 proteins in MPs during the estrogen surge of IVF. One sample during down regulation (DR) of estrogen by a gonadotropin releasing hormone (GnRH) agonist and one sample during high level stimulation (HLS) of estrogen achieved by bilec stimulating hormone (FSH). Platelet-poor plasma aliquots were stored at -80°C. LC MS/MS analysis: Sam-

tomography & cinefluoroscopy and can help in better man-
agement decisions.

Acknowledgement/Funding: Supported by grants provided by the Stockholm County Council (ALF project) and the Swedish Heart and Lung Foundation

Conclusion: We could show in a large monocentric cohort that patients with a CK-MB release above the 75th percentile exhibit a significantly higher 30-day-mortality compared to patients with lesser peak CK-MB values despite similar baseline characteristics.

P4690 | BEDSIDE

Predictive value of creatine kinase-myocardial band after transcatheter aortic valve implantation

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Introduction: A transient elevation in myocardial biomarkers after transcatheter aortic valve implantation (TF-AVI) is observed often, although its significance remains unclear. We examined patient characteristics and procedural outcomes after TF-AVI in dependence of peak creatine kinase-myocardial band (CK-MB) release after implantation.

Methods: 923 patients (pts) received TF-AVI at our centre between 03/2012 and 09/2014. We determined peak CK-MB release within the first 72 h after implantation in 877 pts (95.0%). The 75th percentile of CK-MB in these pts was 0.35±0.41 μ/l. According to this threshold, pts were divided into two groups (high CK-MB (H-MB) and low CK-MB (L-MB) with postprocedural CK-MB below the 75th percentile). Baseline characteristics compared between the groups were presence of coronary artery disease (CAD), arterial hypertension, diabetes mellitus and lung disease as defined by the Society of Thoracic Surgeons-Predicted Risk of Mortality (STS-PROM) score. STS-PROM and logistic EURO-Score were compared as well.

We examined 30-day-survival as well as the incidence of myocardial infarction (MI), stroke, bleeding, renal failure, access site complications and closure device failure as defined by the Valve Academic Research Consortium –2 (VARC-2). We also compared the incidence of moderate or high paravalvular regurgitation on day 10 after TF-AVI.

Results: There were no significant differences between both groups concerning the baseline characteristics age (L-MB 79.9±5.7 years; H-MB 80.1±5.4 years, p=0.59), incidence of CAD (L-MB 47.8%; H-MB: 49.8%; p=0.64), hyper tension (L-MB 94.6%; H-MB 96.7%; p=0.27), diabetes (L-MB 47.0%; H-MB 42.3%; p=0.24), and lung disease (L-MB 31.4%, H-MB 29.4%; p=0.61). There was also no significant difference in procedural risk (STSPROM: L-MB 6.7±5.1%; H-MB: 7.0±5.2%; p=0.18; logEURO-Score: L-MB: 15.8±11.5%; H-MB 17.2±12.7%; p=0.15).

However, 30-d-survival in pts with postprocedural CK-MB below the 75th percentile was significantly higher than in the H-MB group (L-MB: 98.0%, H-MB: 90.7%; p=0.01). We also saw a significantly higher incidence in bleeding in the H-MB group (28.7% vs. 39.7%, p=0.01) as well as renal failure (10.0% vs. 23.3%, p=0.01) and access site complications (25.7% vs. 38.6%, p=0.01). There were no significant differences concerning the incidences of stroke (L-MB: 4.1%; H-MB: 3.9%, p=0.1) or closure device failure (L-MB 1.9%; H-MB: 2.8%; p=0.43).

Conclusion: Even after successful thrombolysis for PVT, most of the prosthetic valves continue to have residual dysfunction which can serve as a nidus for the future recurrence of PVT. MDCTA imaging can provide information about prosthetic valve function, structural substrate for recurrence of PVT more precisely beyond that provided by echocardiography & cinefluoroscopy and can help in better man-
agement decisions.

P4691 | BEDSIDE

The micro particle proteome in women during in vitro fertilization - potential clues to the pathophysiology of the increased incidence of pulmonary embolism

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Introduction: Women conceived by in vitro fertilization (IVF) have a sevenfold increased incidence of potentially fatal pulmonary embolism during the first trimester of their pregnancy. Hemostatic variables in plasma have been shown to be slightly altered but within normal limits. Cell mediated hemostasis is difficult to study in vivo. However, whole blood coagulation can be studied with flow cytometry.

Methods: Venous blood samples were drawn from 31 women (median age 33 years), during IVF. One sample during down regulation (DR) of estrogen by a gonadotropin releasing hormone (GnRH) agonist and one sample during high level stimulation (HLS) of estrogen achieved by blicle stimulating hormone (FSH). Platelet-poor plasma aliquots were stored at -80°C. LC MS/MS analysis: Sam-

tomography & cinefluoroscopy and can help in better man-
agement decisions.

Acknowledgement/Funding: Supported by grants provided by the Stockholm County Council (ALF project) and the Swedish Heart and Lung Foundation

Conclusion: Even after successful thrombolysis for PVT, most of the prosthetic valves continue to have residual dysfunction which can serve as a nidus for the future recurrence of PVT. MDCTA imaging can provide information about prosthetic valve function, structural substrate for recurrence of PVT more precisely beyond that provided by echocardiography & cinefluoroscopy and can help in better man-
agement decisions.

P4692 | BEDSIDE

Risk factors for pulmonary embolism mortality in patients with and without congestive heart failure

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Background: Determining appropriate treatment for acute pulmonary embolism (PE) is a challenging clinical task, and is becoming more complex with the emergence of catheter-based therapies. Analyses of the effects of co-morbidities on survival after PE could aid in risk stratification and further inform treatment decisions.

Purpose: This analysis sought to identify risk factors (RFs) for in-hospital mortality (fatal PE) in populations with and without known congestive heart failure (CHF and no-CHF groups).

Methods: Fatal PE was defined as in-hospital mortality during index admission for PE. Data was from Healthcare Cost and Utilization Project State Inpatient Databases including all PE admissions in New York, Florida, and California from 2003–2011. Variables were binary (ICH-9 codes) and pre-defined co-morbidity variables. Logistic regression was used to find RFs for fatal PE in CHF and no-CHF. Variables were included in multivariable analysis if p<0.20 in univariable analysis.
Results: Of 284,654 admissions for PE, 28,288 had CHF and 256,366 did not have CHF. Incidence of fatal PE for CHF (4.279; 15.1%) was twice that of no-CHF (17.432; 6.8%). Notably, acute right heart failure was a significant RF for fatal PE in the CHF group only (CHF: OR 1.9, 95% CI 1.4–2.8; no-CHF: 1.0, 0.7–1.6). RFs present in both groups included hypotension (CHF: 1.8, 1.6–2.1; no-CHF: 2.8, 2.6–2.9), renal failure (CHF: 1.3, 1.2–1.4; no-CHF: 1.7, 1.6–1.8), and metastatic cancer (CHF: 2.4, 2.1–2.7; no-CHF: 2.9, 2.8–3.0).

Conclusions: Hypotension and metastatic cancer were the strongest RFs for mortality in both CHF and no-CHF. The higher risk of fatal PE in CHF patients presenting with acute right heart failure supports investigation of more aggressive approaches to PE treatment in this high-risk population.

P4694 | BEDSIDE
Right heart thrombi in pulmonary embolism
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Background: There is a lack of comprehensive data on the prevalence, predictors and prognostic significance of right heart thrombi (RHT) in pulmonary embolism (PE).

Methods and results: In this prospective cohort study of patients with acute PE identified from the RIETE registry, we assessed the prevalence and predictors of RHT, and the association between the presence of RHT and the outcomes of all-cause mortality, pulmonary embolism (PE)-related mortality, VTE recurrence, and major bleeding through 30 days after initiation of PE treatment. Of 12,441 patients with acute PE and complete baseline echocardiographic data, 2.6% (325/12,441; 95% confidence interval [CI], 2.3% to 2.9%) had RHT. The following increased the risk of RHT: younger age (odds ratio [OR], 1.01 per year), previous bleeding (OR, 2.56), congestive heart failure (OR, 2.06), cancer (OR, 1.46), syncope (OR, 1.83), systolic blood pressure (<110 mm Hg [OR, 1.97]), and arterial oxyhemoglobin saturation <90% (OR, 1.58). Patients with RHT at the time of PE diagnosis were significantly more likely to die from any cause (adjusted OR, 2.50; 95% CI, 1.62 to 3.84; P < 0.001) (Table 1) and from PE (adjusted OR 4.29; 95% CI, 2.45 to 7.48; P < 0.001) during follow-up. RHT was associated with an increase in the risk of symptomatic VTE recurrence during follow-up (1.8% versus 0.7%, P = 0.04). Major bleeding was similar in patients with and without RHT. We found a significant interaction between the type of treatment (anticoagulation versus thrombolysis or surgery), the severity of PE (low-, intermediate- and high-risk) and the prognostic effect of RHT.

Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>CHF</th>
<th>No-CHF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Acute right heart failure</td>
<td>1.9</td>
<td>1.9</td>
</tr>
<tr>
<td>Deep vein thrombosis</td>
<td>0.7</td>
<td>0.7</td>
</tr>
<tr>
<td>Hypotension</td>
<td>1.8</td>
<td>1.8</td>
</tr>
<tr>
<td>Metastatic cancer</td>
<td>2.4</td>
<td>2.4</td>
</tr>
<tr>
<td>Periperal vascular disease</td>
<td>1.1</td>
<td>1.1</td>
</tr>
<tr>
<td>Renal failure</td>
<td>1.3</td>
<td>1.3</td>
</tr>
<tr>
<td>Acute decompenated heart failure</td>
<td>0.7</td>
<td>0.7</td>
</tr>
<tr>
<td>Liver disease</td>
<td>1.4</td>
<td>1.4</td>
</tr>
<tr>
<td>OR: Odds ratio; CI: confidence interval;</td>
<td>p-value</td>
<td>p-value</td>
</tr>
</tbody>
</table>

Conclusions: In patients presenting with acute symptomatic PE, RHT is relatively infrequent. Patients with RHT had a worse outcome when compared to those without RHT.

P4695 | BEDSIDE
Elevated levels of interleukin 6 at the time of acute pulmonary embolism diagnosis are associated with short- and long-term adverse outcomes
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Background: Little is known about the association between inflammatory response at the time of diagnosis of acute pulmonary embolism (PE) and adverse outcomes.

The main aims of our study were 1) to compare the levels of inflammatory biomarkers interleukin 6 (IL-6), C reactive protein (CRP) and procalcitonin between patients with confirmed symptomatic PE and healthy controls, and 2) studying their association with adverse outcomes in PE patients.

Results: We prospectively studied 286 unselected PE patients included in a single-centre cohort study (median age: 70, interquartile range [IQR]: 54–77 years; females: 55.9%) and 448 young healthy adults with no concomitant inflammation.
P4696 | BEDSIDE
Validation of the modified FAST score for risk stratification of normotensive patients with pulmonary embolism
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1University Medical Center, Center for Thrombosis and Hemostasis, Mainz, Germany; 2University of Perugia, Internal and Cardiovascular Medicine–Stroke Unit, Perugia, Italy; 3San Carlo Hospital, Department of Cardiology, Milan, Italy; 4Chante – Campus Virchow-Klinikum (CVK), Department of Cardiology, Berlin, Germany

Background/Introduction: Recent studies demonstrate an improved prognostic performance of the ESC 2014 algorithm for risk stratification of patients with pulmonary embolism (PE) compared to the ESC 2008 algorithm. Additionally, the modified FAST (based on a positive troponin test, syncope and tachycardia) and the Bova score appear especially helpful to identify normotensive PE patients at highest risk of PE-related complications.

Purpose: To externally validate the prognostic performance of the modified FAST score compared to other scores for risk stratification.

Methods: Normotensive patients with confirmed PE included in the observational multicentre Italian Pulmonary Embolism Registry (IPER) between January 2006 and November 2010 were studied. Patients without an echocardiogram or troponin test on admission were excluded from analysis.

Results: Overall, 868 normotensive PE patients (mean age: 70.1 [IQR, 63–81]; males: 55.2%) were included in the analysis. During the in-hospital stay, 27 patients (3.1%) had clinical worsening that required at least one of the following: i) i.v. catecholamine infusion, ii) endotracheal intubation, or iii) cardiopulmonary resuscitation. Additionally, 32 patients (3.7%) died and 12 deaths (1.4%) were related to PE.

Conclusions: The 2014 ESC guideline algorithm classified one third of patients in each risk class while the Bova and especially the modified FAST score classified more patients in low-risk classes. The percentage of patients with clinical worsening was highest in the intermediate-high-risk classes of the ESC 2014 algorithm (5.7%) and the modified FAST score (5.3%) while the Bova score failed to identify patients at highest risk (intermediate-low [4.7%] and intermediate-high-class risk [4.5%]). Accordingly, patients classified as intermediate-high-risk by the use of the ESC 2014 algorithm (compared to low- and intermediate-low-risk; OR, 3.13 [1.4–6.8]; p=0.004) and modified FAST score (compared to low-risk; OR, 2.82 [1.3–6.2]; p=0.009) had a higher risk of clinical worsening compared to the patients classified by the use of the Bova score (compared to low- and intermediate-low-risk; OR, 1.65 [1.3–6.1]; p=0.263). Using continuous risk classes, the c-index for prediction of clinical worsening was higher for the ESC 2014 algorithm and the modified FAST score (AUC, 0.67 [0.59–0.76]) each) compared to the Bova score (AUC, 0.63 [0.53–0.73]). Regardless of the score or algorithm used, less than 1% of all patients classified in low-risk classes died due to PE.

Conclusions: We were able to externally validate the usefulness of the modified FAST score for risk stratification of acute normotensive PE in a large multicentre cohort. While the ESC 2014 algorithm and the modified FAST score accurately stratified PE patients in different risk classes, the Bova score failed to identify patients at highest risk who need monitoring and possibly rescue reperfusion therapy.

P4697 | BEDSIDE
The predictive value of high sensitivity-troponin T velocity for short term and long term mortality of acute pulmonary embolism
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Background/Introduction: Troponin elevation in non-coronary conditions remains a challenge for identifying patients at increased risk of adverse outcomes. 

Purpose: We aimed to determine if troponin velocity would be helpful in early identification of patients with pulmonary embolism (PE) who are at increased risk of mortality.

Methods: In a prospective study of 109 normotensive patients with confirmed acute PE by pulmonary computed tomography angiography at a cardiac tertiary center between February 2013 and August 2014, high sensitivity troponin T (hs-cTnT) measurement was carried out at presentation and 6 hours later. The primary endpoint was all-cause mortality during the first 30-day, and the secondary endpoint included long-term all-cause mortality. We compared the association of first hs-cTnT level, peak level of hs-cTnT and troponin change velocity with outcome.

Results: Mean age of the study patients was 64.89±16.56 years. Men accounted for 47.7% (n=52). Overall 30-day mortality was 11% (n=12). In univariate analysis, troponin change velocity equal or above 1.003 ng/L/h (Area under the curve of 0.67, Sensitivity of 75% and specificity of 68% (95% CI: 0.506–0.844) was strongly associated with 30-day (p=0.008) and also long-term mortality (p=0.011). In multivariate analysis, after adjustment for simple pulmonary embolism severity index (sPESI), significant association was proved between troponin change velocity above the defined cut-off and 30-day mortality, OR=5.464 (95% CI: 1.354–22.052), p=0.017.

The median follow-up was 15.97 (range: 15.10–16.83) months. During the follow-up period, 18 (16.51%) patients died. Adjustment for right ventricular dysfunction and sex, also revealed significant association between higher troponin change velocity and long-term mortality. HR: 2.822 (95% CI: 1.052–7.570), p=0.039.

Association of high sensitivity troponin

<table>
<thead>
<tr>
<th>Unadjusted OR (95% CI)</th>
<th>p value</th>
<th>Adjusted OR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Troponin change velocity ≥ 1 ng/L/h</td>
<td>6.387 (1.616–25.251)</td>
<td>0.008</td>
<td>5.464 (1.354–22.052)</td>
</tr>
<tr>
<td>Troponin change velocity ≥ 1 ng/L/h</td>
<td>3.419 (1.319–8.861)</td>
<td>0.011</td>
<td>2.822 (1.052–7.570)</td>
</tr>
</tbody>
</table>

Adjusted for simple pulmonary embolism severity index (sPESI), Adjusted for right ventricular dysfunction and sex.

Conclusion: Our principal conclusion is that the troponin change velocity provide superior prognostic value over baseline hs-cTnT for both 30-day and long-term mortality in acute pulmonary embolism.

P4698 | BEDSIDE
A validated improved risk prediction model for in-hospital death during acute presentation with pulmonary embolism
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1Concord Repatriation General Hospital, University of Sydney, Sydney, Australia; 2South Australian Health and Medical Research Institute, Adelaide, Australia

Introduction: Pulmonary embolism (PE) is a major cause of death. Hypoxaemia and metabolic acidosis are both predictors of adverse PE outcome. Hypoxaemia may reflect neurohormonal activation after acute PE whereas low bicarbonate may occur as a result of metabolic acidosis from systemic hyperper
fusión, and from metabolic compensation following hyperventilation related respiratory alkalosis as a response to hypoxia. At hospital present there are no predictive models for in-hospital mortality after acute PE.

**Purpose:** We hypothesized that combining serum sodium and bicarbonate levels with the simplified Pulmonary Embolism Severity Index (sPESI) would improve acute mortality risk prediction.

**Methods:** From a confirmed acute PE database of 1,426 consecutive patients admitted to a tertiary-referral center (2000–2012), 1,378 patients had day-1 serum sodium and bicarbonate assessed. Patients presenting in the odd and even years constituted the derivation and validation cohorts respectively. Risk stratification for in-hospital death was performed using multivariable logistic regression modelling. The performance of each model in predicting in-hospital death was compared using the area under the receiver operating characteristic curve (ROC) and C-statistic. Using population-wide data linkage, we compared our cohort's mortality to all other patients admitted with PE state-wide.

**Results:** The derivation (n=693) and validation cohorts (n=733) did not differ significantly with respect to baseline characteristics and clinical parameters at presentation. In-hospital mortality was 3.6% in the derivation cohort. Low sodium (<135 mmol/L) and bicarbonate (<24 mmol/L) were present in 13.1% and 40.2% of patients respectively. The independent predictors of in-hospital death in the derivation cohort were sPESI (OR 1.75; 95% CI 1.13–2.70), day-1 sodium (OR 0.83; 95% CI 0.76–0.90) and day-1 bicarbonate (OR 0.87; 95% CI 0.77–0.98). Adding day-1 sodium and bicarbonate to sPESI significantly increased the C-statistic for predicting in-hospital death in the derivation cohort (0.71 to 0.86, P=0.049), with similar results observed in the validation cohort (C-statistic 0.85) (Figure 1). The new model was associated with a net reclassification improvement of 61.3% (P=0.0007), and an integrated discrimination improvement of 6.7% (P=0.001). Age and sex-adjusted all-cause mortality following acute PE in our cohort and rest of the state of New South Wales (n=36,195) was very similar (OR 1.04; 95% CI 0.96–1.14, P=0.34).

**Conclusion:** A risk model combining serum sodium and bicarbonate to the sPESI significantly improves the prediction of in-hospital mortality after acute PE. Decisions to allocate intensive in-patient monitoring could be facilitated by the accurate prediction of in-hospital mortality.

PG4700 | BEDSIDE

Pocket-size imaging devices in the initial assessment of patients with suspected pulmonary embolism

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**Background:** Since the clinical symptoms of pulmonary embolism (PE) are non-specific, this severe and life-threatening condition can be initially misdiagnosed. Pocket-size imaging devices (PSID), perceived as ultraportable diagnostic tools can enhance the prompt physical examination with the basic elements of imaging diagnostics.

**Purpose:** We hypothesize, that in patients (pts) with suspected pulmonary embolism (PE) augmentation of initial bedside assessment with four-point compression venous ultrasonography (CUS) and right ventricular size assessment with the use of PSID equipped with linear probe can improve the diagnostic process.

**Methods:** 63 pts (32 men, mean age 68±14 years) with suspected PE underwent clinical assessment in the ER environment on the basis of Wells and revised Geneva score. Subsequently physical examination was supplemented with CUS and RV measurements in long axis parasternal and 4-chamber apical (basal and mid diameter) view. Final diagnosis was established in accordance with the algorithms recommended by ESC guidelines.

**Results:** The mean time of CUS and RV size assessment was 5.3 minute and was universally accepted by the patients as a part of clinical examination. PE was confirmed in 13 pts (21%), 9 pts (14%) had the deep venous thrombosis (1 proximal, 8 distal) detected in CUS. In 40 pts (63% including 12 with confirmed PE) RV enlargement was recorded in at least 1 measurement. According to the three-category Wells rule the clinical risk of PE was calculated as low in 54 pts (among which 6 were ultimately diagnosed with PE), as intermediate in 8 pts (6 cases of PE), as high in 1pt (PE confirmed). In compliance with revised Geneva score 38 pts had low clinical risk of PE (in 6pts PE was finally confirmed), 24 pts intermediate (8 cases of PE); 1pt-high (PE confirmed). Depending on the criteria of the positive test (CUS and RV size assessment) results following data was obtained. If the condition of test positivity was both DVT diagnosis established in CUS and RV enlargement detection, the positive predictive value was 100%, the negative predictive value 93%, specificity 99%, sensitivity 69%. When either RV enlargement or DVT detected in CUS were sufficient to consider test result as positive the negative predictive value increased to 98%, however the positive predictive value was 29%. The values of specificity and sensitivity altered to 42% and 92% respectively.

**Conclusion:** PSID’s limited imaging capabilities prove sufficient to perform basic ultrasonographic screening in cases of suspected PE with promising diagnostic value. Despite the well-acknowledged role of the PE clinical risk assessment scores the diagnostic process may benefit from the addition of basic ultrasonographic techniques in terms of accuracy.

**Background/Introduction:** Computer tomographic pulmonary angiography (CTPA) scan is the gold standard imaging modality to diagnose pulmonary embolism. Current ESC guidelines risk-stratify PE patients into 3 risk categories (high, intermediate and low) to guide clinical management. Intermediate risk patients are characterised by the presence of radiographic or biomarkers of right heart strain (RHS), warrant more intensive patient monitoring and are more likely to develop pulmonary hypertension. Patients treated with anticoagulation therapy are more likely to develop severe right heart strain (RHS) if they do not receive adequate anticoagulation therapy.

**Methods:** To elucidate the gender differences in APE patients treated in the cardiothoracic care of patients, which consists of 71 multicenter CCUs. The registry database of 1049 patients with APE treated at the Tokyo CCU network from 2010 to 2013 were collected for analysis.

**Results:** This study included 468 men (44.6%) and 581 women (55.4%). The women were older than men (67.8±16.2 vs. 60.5±15.7 years, P<0.001) and the proportion of nosocomial cases was higher in the women than men (21.7% vs. 14.5%, P<0.01). As regarding symptoms, dyspnea (64.4% vs. 59.2%, P<0.09) and consciousness disturbance (7.4% vs. 3.7%, P<0.01) were more frequent and chest pain (14.3% vs. 19.1%, P<0.04) was less frequent in the women than men. Pulmonary arterial systolic pressure (52.2±20.6mmHg vs. 48.0±21.3mmHg, P<0.02) and the serum BNP level (196.5±548.6 pg/mL vs. 107.6±24.3±304.0 pg/mL, P<0.001) were higher in the women than men. The women, rather than the men, had the higher proportions of severe cases with massive and collapse types (13.9% vs. 8.3%, P<0.005). The usage rate of inferior vena cava filters (IVC) was lower in women (16.3% vs. 29.0% in the men) with in-hospital APE related mortality tended to be higher in the women than the men. (5.3% vs 3.2%, P=0.09).

**Conclusion:** This cohort study demonstrated that female APE patients were older and severer than male APE patients, which resulted in the poorer prognosis.
to have adverse clinical outcomes. Failure to report the presence of RSH on CTPA represents a missed opportunity to identify PE patients at greater risk of decom- pensation and results in delayed risk stratification.

**Purpose:** To validate the effectiveness of a quality improvement intervention to standardize reporting of RSH parameters on all CTPA reports.

**Methods:** Consecutive patients with PE treated at an academic medical centre in Singapore from 2013 to 2015 were recruited. A quality improvement intervention was performed on the 1st May 2015. All radiologists reporting CTPA were trained to measure 4 measures of RSH namely abnormal position of the interventricular septum, inferior vena cava contrast reflux, right ventricle diameter to left ventricle diameter ratio on axial sections and 4-chamber views and mean pulmonary artery dimensions. Standardized reporting of CTPA including all parameters of RSH was strongly encouraged. CTPA reports were audited to determine whether intervention increased the inclusion of RSH parameters in CTPA reports, the des- ignated primary endpoint. Secondary endpoints include length of stay and 30 day all-cause mortality.

**Results:** 1889 CTPA was requested between 1st Jan 2013 to 31st Oct 2015 due to clinical suspicion of PE. 263 CTPA were positive for PE, of which 205 and 58 reports were done prior to and after the intervention respectively. RSH was visible in 31.2% of positive scans. 48.8% (100 out of 205) reports prior to the intervention and only 15.5% (9 out of 58) reports after the intervention did not measure RSH parameters. (p<0.01) Patients in whom RSH was not assessed during CTPA reporting had longer lengths of stay (24.2±27.8 versus 20.5±30.8 days, p=0.18) and increased risk of 30 day all-cause mortality, although these did not reach statistical significance. (14.3% versus 8.4%, p=0.13)

**Conclusion(s):** Standardized reporting of CTPA incorporating RSH parameters results in earlier identification of intermediate-high risk PE patients and is associated with shorter hospitalisations and improved survival.

P4704 | BEDSIDE

**Association of disease prevalence and failure rate in diagnostic management studies in suspected pulmonary embolism: towards a new tailored standard for future studies**

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**Introduction:** Traditionally, the accepted failure rate of pulmonary embolism (PE) diagnostic studies is <2.7%, based on a meta-analysis of pulmonary angiography studies performed in the 1990’s. However, the disease prevalence in PE studies has decreased considerably over the past decade and differs between geographical regions. Considering Bayes’ theorem, this should imply that the failure rate margin of contemporary diagnostic tests or algorithms should be lowered as well. We set out to evaluate the association of PE prevalence and diagnostic failure rate in prior studies in order to set a new standard for future studies.

**Methods:** We selected all high-quality diagnostic studies in acute PE from 1990 on, that included consecutive patients who were followed for at least three months and were subjected to a appropriate diagnostic standard, i.e. (an algorithm consisting of) a validated clinical diagnosis rule combined with a highly sensitive D-dimer test, multi-slice CT pulmonary-angiography, ventilation/perfusion scintigraphy in accordance to the PIOPED criteria, and/or conventional pulmonary angiography.

**Results:** Fifty studies including 28,848 patients were included, with a mean baseline PE prevalence of 23.3% (95% CI 20.5–26.1, range 0.28–44.5%). The reference line computed by linear regression analysis adjusted for study sample size of the graph plotting failure rate against PE prevalence corresponded to a mean sensitivity of 99.6% across the studies (Figure 1). The background 3-month incidence of PE was 0.5%. The formula of the upper 95% confidence interval of the reference line is “1.85+ 0.0041*prevalence”.

**Conclusion:** We propose that future PE diagnostic studies should incorporate the deviation of RSH as reference standard, in order to assess the minimum diagnostic accuracy of new diagnostic tests or algorithms and thus customize their power analysis to the expected PE prevalence in the studied cohort.
simplified Geneva score was 0.52 (95% CI 0.39–0.65); 0.53 (95% CI 0.4–0.68); 0.54 (95% CI 0.41–0.67); 0.56 (95% CI 0.43–0.69) respectively. In multivariable logistic regression analysis the following factors were found to be the independent predictors of PE: pain on lower limb (OR 5.64; 95% CI 1.35–23.3; p=0.018), or wave in V1 lead (OR 3.65; 95% CI 1.39–9.93; p=0.008), D-dimer level ≥3.3 mld/dl (OR 5.13; 95% CI 1.84–14.28; p=0.002), LVEDD <4.8 cm (OR 7.12; 95% CI 1.21–41.5; p=0.03), LAD <4.3 cm (OR 9.28; 95% CI 1.74–49.58; p=0.009) TAPSE <1.3 cm (OR 3.54; 95% CI 1.42–8.79; p=0.007). On this basis the new model for PE probability assessment was developed (PEP-HF score) with appropriate scoring given to the above-mentioned factors. For the cut-off value >11 pts the AUC, PPV and NPV for this model were 0.92; 93.1% and 83.0% respectively, whereas for the cut-off value <10 pts PPV and NPV were 63.0% and 92.9% respectively. More than 35% of studied population had PEP-HF <10 pts, indicating no presence of PE and suggesting withdrawal from performing angio-CT scan, with acceptable 7% risk of diagnostic error.

Conclusions: Neither Wells score nor does Geneva score have sufficient predictive value for correct assessment of PE probability in ADHF patients. The new PEP-HF score enables the identification of high as well as low PE probability patients and is especially useful among ADHF patients with elevated D-dimers level precluding PE exclusion without performing additional imaging tests.

P4706 | BEDSIDE
Cardiac MRI findings in the N215S mutation subtype in Anderson Fabry Disease
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Introduction: The N215S mutation is thought to result in later-onset disease in Anderson Fabry (AFD), with higher residual enzyme activity, a predominantly cardiac phenotype, and lower FOS-MSI severity scores. This study aimed to examine the difference in CMR findings in patients with the N215S mutation, compared to an otherwise genetically mixed AFD cohort.

Methods: 14 patients with the N215S mutation (8 female, 6 male), and 14 age and gender matched patients with non-N215S AFD mutations underwent CMR at 1.5T (Siemens Magnetom Aera), following a standard clinical protocol including T1 mapping (Siemens MOLLI WIP 448). LV mass was determined from the short axis stack (CMR Tools). Mean native T1 value was determined from the average of a ROI selected in the mid-wall of the basal and mid-short axis slice, which was then corrected for heart rate. Global longitudinal (GLS) was derived from 4-chamber SSFP cine images, using dedicated CMR feature tracking software.

Results: Considering the cohort as a whole, no difference was seen in LV mass or volumetrics, strain parameters or native T1 between N215S and non-N215S genotypes.

Females with the N215S mutation displayed a trend towards lower indexed LV mass (50.6±17.6 vs 51.5±16.2) and higher T1 values (985.7±64.0 vs 948.9±37.5ms), but with a higher degree of variability, and not reaching statistical significance. Less females in this group received ERT (p=0.021).

Conversely, males displayed significantly lower T1 values (901.8±25.0 vs 951.3±62.1ms, p=0.046), with a trend towards higher indexed LV mass (112.2±26.9 vs 74.1±25.7) and worse GLS (−18.3±6.7 vs −17.4±5.9).

Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>N215S (n=11)</th>
<th>Non-N215S (n=21)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>n=6</td>
<td>n=5</td>
<td>0.296</td>
</tr>
<tr>
<td>Females</td>
<td>n=8</td>
<td>n=16</td>
<td>0.04</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>120.4±12.3</td>
<td>123.5±11.3</td>
<td>0.635</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>72.0±6.5</td>
<td>74.8±5.5</td>
<td>0.451</td>
</tr>
<tr>
<td>LV mass/BSA (g/m²)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>50.6±17.6</td>
<td>51.5±16.2</td>
<td>0.911</td>
</tr>
<tr>
<td>Females</td>
<td>51.2±17.6</td>
<td>50.6±17.6</td>
<td>0.911</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>60.2±5.6</td>
<td>63.8±5.1</td>
<td>0.262</td>
</tr>
<tr>
<td>Females</td>
<td>60.5±5.1</td>
<td>63.8±5.1</td>
<td>0.262</td>
</tr>
</tbody>
</table>

Conclusion: Characterisation of the N215S mutation disease-subtype is important. Males seem to display a more severe cardiac phenotype, despite it previously being considered to cause overall milder disease. This may have implications for staging and prognostication, and therapeutic decisions.

P4707 | BEDSIDE
Risk factors for mortality in patients with left ventricular non-compaction
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Introduction: Left ventricular non-compaction (LVNC) is a relatively rare cardiomyopathy with phenotype and prognosis very variable.

Purpose: To determine risk factors for mortality in patients with diagnosis of LVNC. The sample comprised 86 patients with LVNC, 57% of male gender and a mean age of 51±19 years. Most of the patients were diagnosed by echocardiographic criteria (80%); Chin criteria in 31%; Stollerberger criteria in 78% and Jenni criteria in 96%. Approximately 74% of patients diagnosed by transthoracic echocardiogram made CMR-C for confirmation of the diagnosis. The mean ejection fraction (EF) was 48%. 25% of patients had EF <35%. The Holter monitoring

Discussion: The PLR, as a simple, inexpensive and available marker of inflammation and pro-thrombotic status, seemed to be a novel predictor of in-hospital and long-term adverse outcomes in patients with acute PE.
detected atrial fibrillation (AF) in 12% of patients, supraventricular tachycardia in 15% and non-sustained ventricular tachycardia (VT) in 22% (without episodes of sustained VT). The mortality rate in this sample was 4.7%.

The mortality rate was associated to age (p=0.021) but not to sex (p=1.000), family history (p=1.000) or symptoms (dyspnea p=0.626, syncope p=0.100, palpitations p=1.000).

The presence of AF increased the risk of mortality (p=0.009). There was no correlation between mortality and other EKG changes (atrioventricular block p=1.000), intraventricular conduction disturbances or ventricular arrhythmias (p=0.332), echocardiographic changes (EF p=0.250; diastolic dysfunction p=0.403) or CMR changes (presence of late enhancement p=0.065).

Mortality was also not correlated with occurrence of heart failure (p=1.000), thromboembolism (p=1.000) or arrhythmia (p=0.458).

Conclusion: In this multicenter study with 86 patients with LVNC mortality was associated to presence of atrial fibrillation (p=0.009) and most advanced age (p=0.021).

### P4708 | BEDSIDE

**Chronological changes in cardiac morphology and function and predictors of prognosis in light-chain amyloidosis; follow-up data by echocardiography**

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**Background:** There are few data regarding definitive diagnosis and its predictors of light-chain amyloidosis (AL). Follow-up data about echocardiographic parameters are also limited.

**Purpose:** The purpose of this study is to clarify chronological changes in cardiac morphology and function, prognosis and its predictors in AL patients.

**Methods:** We retrospectively investigated 44 consecutive patients who were diagnosed with AL between 1995 and 2014. Clinical background, prognosis, and existence of cardiac involvement were investigated. Moreover, patients with cardiac involvement were divided into two groups; patients who died within one year after diagnosis (group A) and patients who alive over one year (group B). In order to determine the predictors of prognosis, we compared clinical background and initial and follow-up echocardiographic parameters between the two groups.

**Results:** The mean age at diagnosis was 68±11 years old (29 males (66%)). The overall survival at 2 years and median survival time (MST) were 50.3% and 2.3±1.1 years. Freedom from cardiac death at 2 years and MST were 54.6% and 2.6±1.5 years. Cardiac involvement was detected in 36 (82%) patients (multiple myeloma in 14, AL in 22). Among these patients, the overall survival at 2 years and MST were 38.2% and 0.8±0.4 years, and freedom from cardiac death at 2 years and MST were 43.3% and 1.1±0.5 years. There were no differences in the survival at 2 years between patients with myeloma related and primary amyloidosis. (39.2% vs. 37.7%; p=0.95). Follow-up echocardiography was performed in 28 patients with cardiac involvement (13 in group A, 15 in group B) 3–12 months after diagnosis. There were no significant differences between group A and B in age, sex, vital signs, a QRS voltage in electrocardiogram, and echocardiographic parameters at diagnosis except diastolic wall thinning (DWS) (0.12±0.05 vs. 0.24±0.07; p=0.01, DWS may be a significant predictor of Group A). The prognosis of AL patients, especially with cardiac involvement, was very poor regardless of their background. DWS may be a significant predictor of prognosis. Narrowing of LV cavity and progressive diastolic dysfunction were revealed within one year after diagnosis in patients with poor prognosis.

### P4709 | BEDSIDE

**Clinical impact of segmental wall motion abnormalities in cardiac sarcoidosis**

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**Background:** Although there are some reports indicating that idiopathic dilated cardiomyopathy (IDCM) patients with the segmental left ventricular (LV) wall motion abnormalities (SWMA) have poor prognosis, characteristic feature and clinical impact of SWMA in cardiac sarcoidosis (CS) have not been well elucidated.

**Methods:** After excluding patients with complete left bundle branch block or cardiac pacemakers, we retrospectively evaluated left ventriculogram (LVG) in consecutive patients with new-onset CS (n=34) and IDCM (n=323). The LV wall motions were conventionally evaluated using the scoring into 4 degrees (0: normokinesis, 1: hypokinesis, 2: akinesis, 3: dyskinesis) on the 7 segments according to the Japanese Society of Cardiology. Moreover, LV wall motion abnormalities (SWMA) have poor prognosis, characteristic feature and clinical impact of SWMA in cardiac sarcoidosis (CS) have not been well elucidated.

**Results:** The overall survival at 2 years and median survival time (MST) were 50.3% and 1.1±0.5 years. There were no differences in the survival at 2 years between patients with myeloma related and primary amyloidosis. (39.2% vs. 37.7%; p=0.95). Follow-up echocardiography was performed in 28 patients with cardiac involvement (13 in group A, 15 in group B) 3–12 months after diagnosis. There were no significant differences between group A and B in age, sex, vital signs, a QRS voltage in electrocardiogram, and echocardiographic parameters at diagnosis except diastolic wall thinning (DWS) (0.12±0.05 vs. 0.24±0.07; p=0.01). At the follow-up echocardiography, left ventricular diastolic diameter (LVDD) was smaller, LV mass index (LVMI) was greater, and DWS was lower in group A than group B (LVDD: 37.4±5.5 vs 42.8±5.1mm; p=0.05, LVMI: 123.7±26.5 vs 154.0±41.7g/m²; p=0.04, DWS: 0.12±0.05 vs. 0.24±0.07; p=0.01). Moreover, LVDD, stroke volume index (SVI), and DWS significantly changed from initial diagnosis to follow-up echocardiography in group A compared with group B (ΔLVDD: -4.5±3.5 vs 0.2±2.3mm; p=0.01, ΔSVI: -11.5±6.9 vs -1.4±6.1ml/min/m²; p=0.01, ΔDWS: -0.07±0.07 vs. -0.01±0.06; p=0.02). On the other hand, LVMI did not change during follow-up in both groups (2.3±2.1 vs. 1.7±2.3); 0.24; 0.02. The presence of AF increased the risk of mortality (p=0.009). There was no correlation between mortality and other EKG changes (atrioventricular block p=1.000, intraventricular conduction disturbances or ventricular arrhythmias p=0.332), echocardiographic changes (EF p=0.250; diastolic dysfunction p=0.403) or CMR changes (presence of late enhancement p=0.065).

Mortality was also not correlated with occurrence of heart failure (p=1.000), thromboembolism (p=1.000) or arrhythmia (p=0.458).

**Conclusion:** PR deviation in Group A patients was a powerful indicator of Group A, and it suggested the essential etiology of TTC was inflammation.
survival curves demonstrated that the CS with SWMA had a lower event-free rate of the primary endpoints than those without (p = 0.018, log-rank test) (Figure2). Cox proportional hazards analysis demonstrated that the SWMA (Hazard ratio = 5.85, 95% confidence interval, 0.95–114.2; p = 0.05) together with NYHA functional class, III to IV was an independent predictor for the primary endpoints.

Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group I (n=37)</th>
<th>Group II (n=17)</th>
<th>Group III (n=28)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anulus height (mm)</td>
<td>11.6±1.2†</td>
<td>11.6±1.4‡</td>
<td>9.2±1.1†</td>
</tr>
<tr>
<td>Aorotomral angle (°)</td>
<td>107±7</td>
<td>104±6†</td>
<td>114±2</td>
</tr>
<tr>
<td>Tenting height of the leaflets (mm)</td>
<td>4.8±2.7</td>
<td>6.5±2.3‡</td>
<td>3.1±1.7</td>
</tr>
<tr>
<td>Anulus diameter (mm)</td>
<td>134.7±13.4</td>
<td>141±18†</td>
<td>125±17</td>
</tr>
<tr>
<td>Length of posterior leaflet at annulus plane (mm)</td>
<td>13.8±3.3‡</td>
<td>17.5±3.1</td>
<td>12.0±2.9</td>
</tr>
<tr>
<td>Area of posterior leaflet at annulus plane (mm²)</td>
<td>529±15</td>
<td>705±24‡</td>
<td>451±15</td>
</tr>
<tr>
<td>Ratio of anterior to posterior leaflet at annulus plane</td>
<td>1.4±0.4‡</td>
<td>1.7±0.3</td>
<td>2.4±0.7</td>
</tr>
</tbody>
</table>

*p = 0.05 Group I vs Control, †p = 0.05 Group II vs Control, ‡p = 0.05 Group I vs Group II.

Conclusion: The mitral valve in pts with HCM appears to have unique anatomic characteristics, such as larger anulus height and narrower aorotomral angle. Furthermore the anterior displacement of the coaptation line in pts with obstruction combined with a larger tenting height of the leaflets in the left ventricle in systole seems to contribute to the systolic traction of the anterior leaflet towards the interventricular septum that causes the LVOT obstruction. These primary changes of the mitral valve, as demonstrated by RT3DTEE, offer new data on the pathophysiology of the disease.

Figure 1 & 2

Conclusion: SWMA is located frequently in LV basal area, and is a significant predictor associated with a poor prognosis in CS patients.

P4714 | BEDSIDE
Mitral valve assessment in patients with hypertrophic cardiomyopathy using real time 3D transesophageal echocardiography. How much we still don’t know?

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Background: Adult human heart has the capacity to generate new cardiomyocytes that is markedly enhanced in acute heart failure of ischemic and non-ischemic origin and is attenuated with prolonged ventricular decompen-sation and aging. However, little is known about the regenerative potential of human heart in hypertrophic cardiomyopathy (HCM), a common genetic disorder occurring in ∼1 in 500 individuals worldwide.

Purpose: We sought to evaluate the regenerative capacity of human heart with HCM.

Methods: Endomyocardial biopsies from 10 patients with HCM (53±5 ys) were analyzed and compared with 10 aortic stenosis (58±6 ys) and 10 control hearts (55±7 ys). Cardiac progenitor cells (CPCs) were identified by c-kit immunostaining. Senescent cells were identified by the expression of the cell cycle inhibitor p16INK4a and cell death by hairpin 1 and 2. Replication of CPCs and cardiomyocytes were assessed by Ki67 and MCM5 labeling. Telomere length, cardiomycocyte cross-sectional area and myocardial fibrosis were also evaluated.

Results: HCM heart showed an increased number of p16INK4a positive CSCs and cardiomycocytes compared with aortic stenosis and control hearts. This was associated with an increase in cell death and a reduction in telomere length. Conversely, CSCs and cardiomycocyte proliferation was reduced compared with aortic stenosis hearts. The distribution of myocyte cross-sectional area in HCM patients showed that only a small fraction of cells was less than 150 μm², while the majority of cells were more than 400 μm².

Conclusion: Human HCM is characterized by premature senescence of CPCs and cardiomycocytes, and by a decline of regenerative potential that can contribute to the myocardial dysfunction occurring in the end stage of the disease. Cardiomycocyte proliferation does not play a major role in determining the HCM cardiac phenotype.

P4715 | BEDSIDE
Mitral valve assessment in patients with hypoplastic cardiomyopathy

Y. Kang, C. Chen, X.J. Chen, F. Wang, L.L. Li, Y.J. Liang, Q. Zhang. West China Hospital Sichuan University, Cardiology Department, Chengdu, China People's Republic

Background: Adaptive growth of mitral leaflet has recently been observed in animal models or patients with functional mitral regurgitation (FMR). However, there were only few in vivo studies that investigated the differential changes between anterior (AML) and posterior leaflets (PML).

Purpose: To observe whether the enlargement pattern of AML and PML was different and whether the ratio of mitral leaflet to apparatus change was related to the degree of FMR in patients with non-ischemic dilated cardiomyopathy (DCM).

Methods: This study prospectively enrolled 40 normal controls (Group I) and 113 patients with non-ischemic DCM (Group II: 43 patients with no or only mild FMR; Group III: 70 patients with more than mild FMR). By using two-dimensional (2D) echocardiography, the degree of mitral leaflet enlargement was reflected as the length of AML and PML measured at parasternal long-axis view (AML-lax, PML-lax) and the degree of mitral apparatus deformation was represented by tenting height (TH-lax) and mitral annular dimension (MAD-lax). Subsequently, the ratio of (AML-lax+PML-lax)/(TH-lax+MAD-lax) was calculated.

Results: Both AML and PML were elongated in Group II and Group III when compared with Group I (all p < 0.001) and the extent of elongation was greater in PML than in AML (62–92% vs. 25–29%). There was a further elongation of PML in Group III than in Group II. Despite elongated mitral leaflets in Group II and Group III, the (AML-lax+PML-lax)/(TH-lax+MAD-lax) was smaller in Group III, which appeared comparable between Group I and Group II. The ratio of AML-lax/(TH-lax+MAD-lax) was 1.03±0.10*< 0.05 Group I vs Group II. Despite elongated mitral leaflets in Group II and Group III, the (AML-lax+PML-lax)/(TH-lax+MAD-lax) was 1.03±0.10*< 0.05 Group I vs Group II, ¶p< 0.05 Group II vs Control, §p< 0.05 Group I vs Group II.

Conclusion: Both AML and PML were enlarged in non-ischemic DCM, but the extent and pattern were not identical between the two regions. Inadequate AML enlargement proportional to mitral apparatus remodeling more likely contributes to the pathogenesis of FMR.

Acknowledgement/Funding: The study was supported by a research grant from the National Natural Science Foundation of China (project number: 81470508).
P4714 | BEDSIDE 
Implementation of new oral anticoagulant agents in cardiomyopathy clinics

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Background: A significant proportion of patients with cardiomyopathies will develop atrial fibrillation (AF) and thromboembolic (TE) complications throughout their lifetime. New oral anticoagulant (NOAC) agents have demonstrated a better safety and efficacy profile compared to traditional vitamin K antagonists. CHADS scores do not apply to cardiomyopathies in particular to HCM.

Methods: All 2436 patients (aged 50±20 years, 63% males) consecutively evaluated at our cardiomyopathy clinic from 2003–2016. 1239 (51%) had Hypertrophic (HCM), 531 (14%) dilated (DCM), 10% (46%) arrhythmogenic (ACM), 11% (54%) isolated left ventricular non-compaction (LVNC), 23% (10%) Brugada (BR), 90% (33%) QT syndrome (LQTS), 121% (5) other CM/channelopathy. 478 (20%) of the total cohort had history of AF (mean age 60±14 years, 61% males). 250, 52%, permanent AF, 63, 13% persistent AF, 165, 35% paroxysmal AF. There was 26% of AF within HCM, 18% in DCM, 9% ACM, 4% in LVNC, 5% in BRs, 10% in LQTS, and 17% in other CM/channelopathy.

Mean age in AF patients ranged from 60±13 in HCM to 69±14 in DCM.

Anticoagulant was prospectively and retrospectively confirmed. In order to assess control of anticoagulation in patients on anti-vit-K antagonist (acenocoumarol), INR measurements were analyzed in 100 consecutive patients (a mean of 12 INR measurements were available per patient).

Results: 382 (15%) patients had received an anticoagulant agent at any time (a mean of 12 INR measurements were available per patient).

- In HCM, 4% in LVNC, 5% in BrS, 10% in LQTS, and 17% in other CM/channelopathy.
- 35% paroxysmal AF. There was 26% of AF within HCM, 18% in DCM, 9% ACM, 4% in LVNC, 5% in BRs, 10% in LQTS, and 17% in other CM/channelopathy.

Conclusion: Anticoagulant medication was prospectively and retrospectively confirmed. In order to assess control of anticoagulation in patients on anti-vit-K antagonist (acenocoumarol), INR measurements were analyzed in 100 consecutive patients (a mean of 12 INR measurements were available per patient).
Epidemiology and clinical profile of hypertrophic cardiomyopathy in an unselected regional Japanese cohort: Results from Kochi RYOMA Study

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Background: There have been very few studies on clinical features of hypertrophic cardiomyopathy (HCM) in a community-based patient cohort in Japan.

Purpose: The aim of this study was to provide detailed descriptions of the clinical features of HCM in an unselected regional Japanese population.

Methods: We established cardiomyopathy registration at Kochi Prefecture named Kochi RYOMA study consisting of 9 hospitals in 2004, and 302 patients with diagnosis of HCM were registered. Finally, 293 patients were followed.

Results: The ages at registration and at diagnosis were 63±14 (range: 7 to 88) and 56±16 (range: 6 to 87) years, respectively, and 197 patients (67%) were men. During follow-up period of 6.1±3.2 years, 44 patients died. In those patients, HCM-related deaths occurred in 25 patients (7.8% in whole HCM cohort) and annual mortality rate was 1.3%. Three distinctive modes of deaths were as follows: (1) sudden death (9 patients; age, 58±16 years); (2) heart failure death (11 patients; age, 72±13 years); and (3) embolic death (3 patients; age, 70±8 years).

In addition, 57 patients had HCM-related undeceased events including appropriate ICD discharges, heart failure admission and hospitalization for embolic events. Registration, 86 patients (29%) had documentation of paroxysmal or chronic atrial fibrillation (AF). Additional 31 patients (11%) showed new onset of AF during follow-up. AF was strongly associated with HCM-related events.

Conclusion: The prevalence and clinical features of HCM in the Kochi RYOMA study was older and the prevalence of AF was relatively higher compared with those in previous HCM studies in Western countries. Although annual mortality rate was reasonable, AF seemed to be an important factor for HCM-related morbidity.
P4721 | BEDSIDE

Reference values for cardiac Troponin I in pediatric age measured with a high sensitive platform


Purpose: The aim of this study is to determine the reference value for cardiac troponin I (cTnI) in healthy children. However, there are currently substantial gaps in our knowledge on the behaviour of circulating levels of cTnI in healthy children.

Methods: Blood samples were obtained from 381 healthy pediatric subjects [204 males, age 0.18–18 years mean (SD): 8.7 (6.6) y, including 36 neonates (<1 month), 57 infants (1–12 months), 65 toddlers (1–10 years), and 223 adolescents (10–18 years). Newborns had routine screening for genetic disorders, while infants, children and adolescents underwent blood sampling during follow-up after an intervening disease or endocrine work-up for normal variant of growth. The presence of any significant cardiac disease has been excluded by careful clinical examination and also by echocardiography, when necessary. cTnI was measured with a high sensitive method [limit of blank (LoB) and the limit of detection (LoD) were 1.3 and 1.9 ng/L, respectively].]

Results: Data of hs-cTnI levels in subject groups divided according to age are presented in Table. The percentages of healthy population with values equal or less than LoB and LOD values were 12% and 30%, respectively. When subjects were considered as a whole and subdivided by sex, circulating levels of hs-cTnI were 2.2±0.5 ng/L in males and 1.9±0.8 ng/L in females (p=0.03). At multivariate analysis using age and sex as independent variables, only age was associated with hs-cTnI plasma levels (age: -0.10±0.01, coefficients(SE). P<0.0001; sex: 0.10±0.08, P=ns).

Conclusion: Hs-cTnI plasma levels were highest in the first month of life with a progressive decline in the next years and was lower in female. These data suggest the existence of a physiological release of cardiac troponin I in healthy children.

P4722 | BEDSIDE

Left ventricular stiffness as assessed by diastolic wall strain late after repair of tetralogy of Fallot

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Background: Left ventricular (LV) remodeling related to myocardiob fibrosis and geometric eccentricity in patients after repair of tetralogy of Fallot (TOF) may have an adverse impact on LV stiffness.

Objective: We tested the hypothesis that left ventricular (LV) stiffness is altered late after TOF repair and is related to impairment of LV diastolic mechanics, severity of pulmonary regurgitation (PR), and right ventricular (RV) volume load.

Methods: Seventy-nine TOF patients aged 18.5±8.0 years and 80 healthy age-matched healthy controls were studied. Left ventricular diastolic myocardial stiffness was assessed by diastolic wall strain (DWS) as defined by (LVPW systole-LVPW diastole)/LVPW systole, where LVPW is LV posterior wall thickness. The average calibrated integrated backscatter (ibc), a marker of myocardiob fibrosis, of the ventricular septum and LVPW was determined. Doppler interrogation was performed to determine transmitral early velocity (E) and both RV s' and e' velocities (p=0.04 and p=0.03 respectively) were lower in MPS. LV GLS (-20.5±1.3% in MPS versus -21.3±1.9% in controls, p=0.20) did not differ significantly between the 2 groups. Transmural E/A ratio was lower (p=0.009) and E/e’ ratio was higher (p=0.06) in MPS. Among RV parameters, tricuspid annular plane systolic excursion (p=0.03) and both RV s’ and e’ velocities (p=0.04 and p=0.03 respectively) were lower in MPS. LV GLS (-20.5±1.3% in MPS versus -21.3±1.9% in controls, p=0.20) did not differ significantly between the 2 groups. GCS (-18.6±3.6% vs -22.1±5.7%, p=0.01). GRS (20.0±8.4% vs 27.4±6.5%, p=0.02), LV twisting (9.2±4.0° vs. 13.7±5.1°, p=0.01) and RV GLS (-21.3±6.3% vs. -25.7±3.2%, p<0.001) were lower in MPS than in controls. A subanalysis performed in patients with MPS, GLS, GRS, CGC, LV twisting and RV GLS did not differ significantly in patients treated or not treated with ERT.

Conclusions: Abnormalities of LV GCS, GRS and twisting are detectable in pediatric patients with MPS, independent on MPS type, when ejection fraction and GLS are still normal. RV GLS is also lower than in controls, in parallel with TAPSE and s' reduction. These abnormalities do not appear to be influenced by ERT. STE can be therefore useful for subclinical detection of myocardial damage in MPS.
Pediatric (aborted) sudden cardiac death: focus on cardiac etiologies and family history

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Introduction: Sudden cardiac death (SCD) in children accounts for almost 10% of total pediatric mortality. Studies on the etiology of (aborted) SCD < age of 40 years have shown a significant contribution of inheritable cardiac conditions (ICC). This knowledge stresses the importance of a thorough family history.

Purpose: To identify the distribution of cardiac etiologies and the cardiac family history in pediatric (aborted) SCD victims.

Methods: (Aborted) SCD victims <19 years were identified from a prospectively developed resuscitation database of a tertiary referral center between January 2002 until March 2015. (Aborted) SCD was defined as an out-of-hospital unexpected and abrupt loss of consciousness with loss of vital signs, resulting in death or, if successfully resuscitated, survival to hospital discharge, with a suspected cardiac etiology. Medical records were retrospectively reviewed on etiology of (aborted) SCD and family history.

Results: 93 (aborted) SCD victims were identified, median age 2.5 years (0.01–17.67 years; n=40–<1 year). 35% was diagnosed with (potential) ICC. In 57% the etiology remained unspecified. 8% was diagnosed with primary non-ICC (Table). 33% of patients diagnosed with potential ICC had a positive family history for potential ICC (Table). The family history was not reported in 49% of the unspecified cases. The family history in 22% of the unspecified cases with reported family history, was positive for potential ICC.

Conclusion: Over one third of pediatric (aborted) SCD was due to potential ICC and a significant proportion of these children had a positive cardiac family history at time of (aborted) SCD. In the majority of unspecified (aborted) SCD cases, no cardiac family history was reported. Societal and medical awareness of the importance of a positive cardiac family history might improve the identification of children at risk for SCD, as well as provide unsolved etiologies in (aborted) SCD victims.

Pediatric long-term outcome after surgical repair or palliation of congenital heart disease in low birth weight infants

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Background: Low birth weight (LBW) infants with congenital heart disease (CHD), represent a delicate population with reported high morbidity and mortality largely related to detrimental interplay between CHD, prematurity and patient frailty.

Purpose: Aim of the study was to evaluate the outcome of heart surgery in LBW infants with CHD and to detect the risk factors for mortality and morbidity.

Methods: This is a retrospective, single center study including consecutive infants with CHD and birth weight (BW) <2500 g, born from May 2004 to June 2014, who underwent corrective or palliative heart surgery. Infants with isolated patent ductus arteriosus were excluded. Standard statistics were used to compute among group demographic and procedural variables comparison. Survival was analysed using Kaplan-Meier methodology and univariate regression analysis was carried out for risk analysis.

Results: A total of 88 patients were included. Median BW was 1975 g (first-third quartile 1527–2285 g), median gestational age was 34 weeks (first-third quartile 32–37 weeks). Most frequent diagnoses were: aorta coarctation (22%), ventricular septal defect (19%), tetralogy of Fallot (8%), transposition of great arteries (8%). Weight at operation was 2057 g (first-third quartile 1795–2300 g), Median age at operation was 16 days (first-third quartile 8–34 days). Fifty-one patients underwent palliation procedure, and 37 had a surgical correction. Risk stratified for levels of creatinine (p=0.046) between HRDW group and non-HRDW group. After multivariate analysis HRDW was independently associated with odds ratio of 24.6 (p=0.014) for end-diastolic pressure ≤12.6 mmHg, 14.0 (p=0.001) for hemoglobin levels ≤18 mg/dl, 6.1 (p=0.002) for oxygen saturation of aorta ≤85%, and 4.2 (p=0.017) for levels of creatinine ≥0.68 mg/dl. In monovariate analysis HRDW was significantly related to end-diastolic volume of systemic ventricle (≥74 mm3/m2) and n-terminal pro brain natriuretic peptide (≥553 pg/ml). Explanatory coefficient was 0.46.

Abstract P4724 – Etiology of SCD and family history

<table>
<thead>
<tr>
<th>&lt;1 year of age</th>
<th>&gt;1 year of age</th>
<th>Total</th>
<th>Family history (SCD, primary electrical disease, CMP), n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aborted SCD</td>
<td>Aborted SCD</td>
<td>Pos.</td>
<td>Unknown</td>
</tr>
<tr>
<td>SCD</td>
<td>SCD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary electrical disease</td>
<td>–</td>
<td>–</td>
<td>11 (47.8)</td>
</tr>
<tr>
<td>Cardiomyopathy</td>
<td>3 (9.4)</td>
<td>6 (26.1)</td>
<td>6 (20.0)</td>
</tr>
<tr>
<td>Primary non-inheritable cardiac etiology</td>
<td>3 (7.5)</td>
<td>7 (15.0)</td>
<td>93 (100.0)</td>
</tr>
<tr>
<td>Unsuspected</td>
<td>4 (50.0)</td>
<td>27 (84.4)</td>
<td>3 (13.0)</td>
</tr>
<tr>
<td>Total</td>
<td>8 (20.0)</td>
<td>32 (80.0)</td>
<td>23 (43.4)</td>
</tr>
</tbody>
</table>

– = low number of cases; data not presented because of privacy regulations. Therefore numbers don’t count up.

P4726 | BEDSIDE

High values of red cell distribution width suggests that Fontan circulation might be failed

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Background: Recently, values of red cell distribution of width (RDW) have been reported to be useful as predictive indicator for prognosis of cardio-pulmonary disorder, such as chronic heart failure, pulmonary hypertension, and lung fibrosis. Pulmonary circulation, like cardiac function, is essential in Fontan patients. We investigated whether high values of RDW are connected with cardio-pulmonary function in Fontan patients.

Methods: The medical records of 159 Fontan patients were reviewed aged from 1.7 to 42.9 years. They underwent cardiac catheterization and measurement of RDW between 2010 and 2015. We defined high values of RDW (HRDW) as diagnostic levels in the top fifth of 159 Fontan patients (RDW ≥ 15.3, n=32). Cardiac performances and pulmonary circulation factors were determined which affected HRDW.

Results: Following factors were not different between patients with HRDW and without HRDW, such as isomerism, regurgitation of atro-ventricular valves, ist strategy before Glenn, diaphragm paralysis, pulmonary artery index, ages at Fontan procedure, and study ages. There were also no differences in medical intervention: coil embolization for collateral vessels to lung; balloon dilatation for stenotic pulmonary arteries; pacemaker implantation; bypassing lungs with fenestration at Fontan. However, repair of atro-ventricular valve was performed more in HRDW group (37% vs. 18%; p=0.011). No differences were observed in hepatic functions on blood examination. However, there were differences in levels of albumin (4.1 vs. 4.5 g/dl, p=0.005) and levels of uric acid (5.8 vs. 5.2 mg/dl, p=0.046) between HRDW group and non-HRDW group. After multivariate analysis HRDW was independently associated with odds ratio of 2.23 (CI [1.47;3.40]), Weight and age at birth, weight and age at surgery, ductal-dependent CHDs did not influence mortality. The groups of low birth weight (n=69), very low birth weight (n=10) and extremely low birth weight (n=9) infants presented different incidence of respiratory distress syndrome (p=0.004), retinopathy of prematurity (p=0.01) and bronchopulmonary dysplasia (p=0.04). Nine patients developed necrotizing enterocolitis (NEC) and we found a higher incidence in patients with lower gestational age (p=0.03). Heart defect diagnosis was associated with NEC onset (p=0.03) with 45% of NEC cases showing pulmonary atresia with intact ventricular septum.

Conclusion: The short-term mortality rate of LBW infants operated for heart disease was high, similar to other surgical series and largely attributable to early perioperative events. Accordingly, rapid plateauing of survival curve in the long term was observed. RACHS-1 category represents a reliable mortality risk indication for mortality in CHD in LBW infants. Although the limited number of morbidities of prematurity in our population, we observed a relationship between complex ductal-dependent heart defects and NEC onset.
Discussion: Our study showed HDRW in Fontan patients was associated with some limit values which indicated failed Fontan, such as high end-diastolic pressure of ventricle, high pressure of central vein, and low oxygen-saturation levels. High values of RDW might be employed as predictive indicator for prognosis in Fontan patients.

P4727 | BENCHMARK
Drivers of hospital resource utilization in infants with hypoplastic left heart syndrome undergoing surgical stage I palliation
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Background: Infants with hypoplastic left heart syndrome (HLHS) who undergo surgical stage I palliation often require complex postoperative care. While the degree of hospital resource utilization in these patients has been described, there is little data describing the drivers and variation of hospital resource utilization.

Methods: The objective of this study was to identify the most commonly utilized hospital resources after stage I palliation for HLHS, their associated billed charges, and possible variation.

Results: A total of 911 infants underwent surgical stage I palliation for HLHS at 42 hospitals. Billed charges totaled USD$760 million. Laboratory charges totaled $130 million, followed by clinical ($120 million), pharmacy ($90 million), and imaging charges ($40 million). The remainder of hospital charges were attributed to supply, nursing, and room charges. Among the 465,802 billed laboratory units, arterial blood gas (ABG) was most commonly utilized (28,448, 6%; $28.2 million) with wide inter-hospital variation (mean 33 ABGs/patient, range 8–117; figure 1). The most commonly utilized clinical services included respiratory (78,626 units, 71%; $85.4 million), rehabilitation (14,641 units, 13%; $3 million), and cardiovascular (8,724, 8%; $11.6 million) services. Electrolyte replenishment (139,035 units, 25%; $25.7 million), analgesics and sedatives (78,553, 15%; $8.3 million), and diuretics (63,237, 12%; $13.6 million) were the most commonly used pharmacologic agents. Inotropic support accounted for 6% of total billed units and charges of $3.9 million. Out of a total of 66,668 billed imaging units, chest radiography (30,616 units, 46%; $10.4 million) and echocardiography (6,067 units, 9%; $14.9 million) were the most commonly obtained. Across hospitals, a phi statistic of 0.86 showed the most commonly utilized hospital resources after stage I palliation for HLHS, their associated billed charges, and possible variation.

Conclusions: Significant hospital resources are utilized in the postoperative care of infants with HLHS undergoing surgical stage I palliation. Laboratory testing across hospitals varied widely, with ABG being the most commonly utilized. Only a fraction of billed hospital services were categorized into specific hospital services. Further categorization of hospital services and inter-hospital variation across hospital services can be increased. Increased awareness of areas of high hospital utilization and potential practice variation may assist in future efforts to maximize efficient healthcare delivery to these patients.

P4728 | BENCH
Left atrial contractile dysfunction and fibrosis occur in anthracycline-treated long-term survivors of childhood cancers
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Background: An animal model of anthracycline-induced cardiotoxicity has revealed significant left atrial (LA) remodeling.

Objective: We tested the hypothesis that LA mechanics and myocardial calibrated integrated backscatter (cIB), a marker of myocardial fibrosis, are altered in anthracycline-treated long-term survivors of childhood cancers and explored their associations with left ventricular (LV) functional indices and fibrosis.

Method: Forty-nine patients (26 males) aged 22±5.8 years at 14±5.4 years after anthraccline therapy and 25 controls (13 males) were studied. Left atrial volumes were measured using biplane Simpson’s method, while LA positive, negative, and total strain and strain rate at ventricular systole, early diastole, and atrial contraction were interrogated using speckle tracking echocardiography. Calibrated integrated backscatter of the LA posterior wall, ventricular septum and LV posterior wall were determined. Doppler and three-dimensional echocardiography was used to determine LV systolic and diastolic function.

Results: Compared with controls, patients had significantly smaller maximal (p=0.009) and minimal (p=0.017) LA volumes, lower peak negative LA strain (-25±1±6% vs -30±4±5%, p=0.001), and LV posterior wall (-25±3±9% vs. -25±3±9%, p=0.012) were significantly greater in patients than controls. For the entire cohort, peak negative LA strain correlated positively with early diastolic mitral annular velocity (r=0.27, p=0.018), while LA cIB correlated positively with the average of septal and LV posterior wall cIB (r=0.54, p=0.001), but not indices of atrial deformation. There were no significantly relationships between cumulative dose of anthracycline and indices of LA deformation and cIB.

Conclusion: Left atrial remodelling as characterised by LA contractile dysfunction and fibrosis occurs in adult survivors of childhood cancers, and is related to LV diastolic function and fibrosis.

CONDITIONS WITH INCREASED CORONARY ARTERY DISEASE RISK

P4729 | BENCHMARK
Ongoing myocardial ischemia as an alternative to traditional ST-segment classification of acute coronary syndromes
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Background: Acute coronary syndromes (ACS) are classified on the basis of ST-segment elevations presence (STEMI) or absence (non-STEMI). In 2013 the Czech Society of Cardiology proposed the new classification based on presence versus absence of ongoing myocardial ischemia (OMI) signs at the time of first medical contact. ACS with OMI was defined as ongoing ischemic symptoms plus at least one of the following: ST elevations, ST depressions, new bundle branch block (BBB), malignant arrhythmias, acute heart failure or cardiogenic shock. The aim of this study was to compare clinical outcomes of patients with OMI versus the groups: STEMI, nonSTEMI and without OMI.

Methods: Prospective registry of consecutive patients (pts) hospitalized for an ACS in a tertiary center from January to December 2014. The relative frequency and in-hospital mortality were determined for both ACS classifications.

Results: The study group consisted of 692 pts (age 67±12.9y, women 28.8%). Distribution of pts in traditional and new classifications is shown in Table 1. The overall in-hospital mortality was 7.1% (49pts): 47 (96%) of deceased had signs of OMI. In-hospital mortality in OMI pts was 11.4% versus 0.7% in without OMI pts. 12.5% in STEMI pts and 3.8% in nonSTEMI pts. Mortality of OMI pts (11.4%) was comparable to STEMI pts (12.5%), but mortality of pts with nonSTEMI (3.8%) was more then five times higher than in without OMI pts (0.7%). Mortality of pts with ST depression (9.17%) was comparable to mortality of pts with STE (12.7%) or without OMI (11.5%).

Conclusion: The newly proposed classification of ACS based on the presence or absence of OMI signs may be more suitable for early risk stratification and management decision than the old classification originating on patients’ eligibility for thrombolysis. OMI concept deserves further studies.

Table 1

| Distribution of pts in Traditional and new ACS classification, (n=692) |
|-----------------------------|-----------------|
| STEMI | nonSTEMI |
| 263 | 429 |
| ACS with OMI vs without OMI |
| with OMI | 411 |
| STEI elevation | 257 | 57.66 |
| New BBB | 26 | 6.33 |
| ST depression | 109 | 26.52 |
| Cardiogenic shock with non-diagnostic ECG | 3 | 0.73 |
| Malignant arrhythmia | 20 | 4.67 |
| Acute heart failure with non-diagnostic ECG | 18 | 3.69 |

Conclusion: The newly proposed classification of ACS based on the presence of or absence of OMI signs may be more suitable for early risk stratification and management decision than the old classification originating on patients’ eligibility for thrombolysis. OMI concept deserves further studies.

P4730 | BENCHMARK
Short and mid-term prognostic outcomes in patients with elevated systolic blood pressure on admission after acute myocardial infarction
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fracture and bowel motion disturbances were independent predictors of increased non-cardiovascular readmissions.

Conclusions: In an octogenarian patient cohort with ACS, cardiovascular diseases were the main causes of deaths, whereas non-cardiovascular diseases were the main causes for hospital readmissions. The high percentage of cardiovascular deaths indicates the need for further improvement in secondary prevention in this patient group.

P4732 | BEDSIDE
The prognostic value of troponin elevation in the emergency department in patients without type 1 myocardial infarction

Introduction: There is high incidence of troponin elevation in emergency department patients. Besides type 1 myocardial infarction, there are multiple causes of troponin elevation and this is usually associated with high mortality. There is no consensus about the management of these patients.

Objective: The aim of this study was to characterize population of patients with troponin elevation in the emergency department excluding Type 1 myocardial infarction and find clinical and laboratory predictors of death in this type of patients.

Methods: Data concerning all patients with positive troponin (high sensitive troponin, cut-off 0.056ng/ml) on emergency department between 18th of June until 18th of July of 2014 was collected retrospectively. Type 1 myocardial infarctions were excluded based on established criteria. Follow-up was achieved through hospital and "national" records revision, during 16 months or until the occurrence of death on these patients.

Results: One hundred and fifty three emergency patients had positive troponin on admission to type 1 MI, age of 74.4±16 years, 53 female (52.3%) and 59 (38.6%) died during follow-up. Median follow-up was of 477 days. Survivors were significantly younger (71±17 years vs 80±12 years, p=0.004) and featured higher proportion of two consecutive isolated troponin elevation, without CK-MB and myoglobin elevation (48 (85.7%) with isolated troponin elevation survived) vs 8 (14.3%) with isolated troponin elevation died; p<0.001, with lower rates of antiplatelet treatment (22 (23.9%) vs 25 (45.5%), p=0.01) and of hospitalization on the same day (52 (55.3%) vs 51 (86.4%) p<0.001).

Using Cox multivariate analysis with the described variables corrected to gender: two consecutive isolated troponin elevation (HR 0.43; CI 0.17–0.96; p=0.039; Kaplan-Meier Curves, Figure 1), hospitalization (HR 4.7; CI 1.7–13.4; p=0.004), previous treatment with antiplatelet agents (HR 1.82; CI 1.1–3.0; p=0.019) and age (HR 1.03; CI 1.0–1.1; p=0.038) remained independently associated with mortality.

P4733 | BEDSIDE
In-hospital and long-term mortality in Tako-tsubo cardiomyopathy: a community hospital experience
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Purpose: Tako-tsubo cardiomyopathy (TTC) is characterized by reversible left ventricular dysfunction, frequently precipitated by a stressful event. Despite the
favorable course and good long-term prognosis, a variety of complications may occur in the acute phase of the disease. The aim of this study was to evaluate the in-hospital and long-term outcomes of a cohort of TTC patients.

**Methods:** Fifty-five patients (mean age 68.1±12 years) were prospectively followed for a mean of 69.6±32.2 months (6–4635 days). In-hospital (death, heart failure, arrhythmias) and long-term events (death and recurrences) were recorded.

**Results:** Patients were predominantly women (87.3%) who experienced a recent stressful event (emotional or physical) and were admitted to hospital for chest pain. Eleven patients (20%) had a diagnosis of depressive disorder, and arterial hypertension was the most frequent cardiovascular risk factor. The ECG revealed ST-segment elevation in 43.6% of patients. At angiography, 7 cases (12.7%) had at least one significant (≥50%) coronary artery stenosis and 4 patients (7.3%) had myocardial bridging of the left anterior descending artery. During hospitalization, 3 patients died (one from cardiac causes) and cardiovascular complicat-ions occurred in 12 patients. During follow-up, 5 patients died (none from cardiac causes), 6 patients had recurrences within the first year. Two patients had two recurrences. One after 114 days, triggered by an asthma attack as the first event, and the other after 1860 days.

**Conclusions:** In TTC patients, in-hospital and long-term mortality is primarily due to noncardiovascular causes. Recurrences are not infrequent and coronary artery disease is not an uncommon finding.
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LDL4: Predicting coronary artery disease severity and adverse cardiovascular outcomes at 1 year

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Background: Hyperlipidemia (HLD) is a well-established risk factor for coronary artery disease (CAD). As previously noted, LDL4 (an LDL particle subtype) has been observed to be more atherogenic compared to other cholesterol subtypes and has been associated with CAD severity. We aim to provide further clinical data for this marker with results on 1-year patient follow-up outcomes.

Methods: Blood samples were obtained immediately prior to cardiac catheterization in 179 consecutive patients with suspected CAD. Detailed lipid profiling was performed using VAP cholesterol test and OxLDL/s2GPI (Atherox) testing was performed using immunoassay on patients not on lipid lowering therapy. CAD severity categorized angiographically as none/minor CAD (less than 20% luminal diameter stenosis [LDS]), moderate CAD (20% to 74% LDS) and severe CAD (more than 75% LDS of any major coronary vessel). LDL4 was divided into quartiles (quartile 1 – 8 mg/dL; quartile 2 as 8–13mg/dL; quartile 3 and 4 were 13.1–20 mg/dL and >20 mg/dL, respectively). Patients were followed up for 1 year and major adverse cardiovascular events (MACE) were defined as death due to cardiovascular causes, non-cardiovascular causes, recurrent myocardial infarction, target vessel revascularization and re-hospitalization for angina.

Results: A total of 179 patients with severe CAD had significantly higher levels of LDL4 compared to the patients with mild or moderate CAD (19.0±11.8 vs [vs] 16.1±10.9 vs 14.3±8.6 mg/dL respectively; p=0.03). Patients in 4th quartile of LDL4 had an odds ratio (OR) of 2.59 (95% CI 0.90-6.74; p=0.05) to develop severe CAD. Atherox levels were significantly higher between the 4th and 1st quartiles of LDL4 (0.56±0.7 vs 0.25±0.16 U/mL respectively; p=0.03). At 1 year follow-up (n=179), 25.5% of patients in 4th quartile had a MACE event compared to 6.5% of patients in 1st quartile (p=0.01) which was not associated with severity of CAD at presentation.

Conclusion: Elevated LDL4 levels are associated with severity of CAD and appear to be adversely related to 1-year MACE events. Further investigations are needed to evaluate the utility of LDL4 in predicting future cardiovascular events.

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Systemic lupus erythematosus is associated with poor outcome after acute myocardial infarction

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Background: Systemic lupus erythematosus (SLE) is associated with poor outcome after acute myocardial infarction (AMI) and that SLE is associated with poor outcome after acute myocardial infarction (AMI) is not clear. We conducted a population-based study with the inpatient data from the Taiwan National Health Insurance Research Database. Patients admitted to hospital under the major diagnosis of acute myocardial infarction (ICD-9-CM code 410) were enrolled. We identified SLE group as AMI patients with concurrent discharge diagnosis of SLE (ICD-9-CM code 710.0), and non SLE group as AMI patients without the diagnostic code of SLE. The diagnosis of AMI was based on the diagnostic codes of the ICD-9-CM treatment codes were used to investigate the usage of invasive procedure, and the admission ICD code was used to identify the comorbidities. We selected an age-, sex-, hospital level-, and admission calendar year-matched non-SLE group from the total non-SLE group. The study end-points were in-hospital mortality and prolonged hospitalization. A multivariate logistic regression analysis was used to evaluate the risk of outcomes.

Result: Between 1 January 2001 and December 31, 2011, 151 patients with SLE, 113791 patients without SLE, and 451 matched patients without SLE were identified. Patients with SLE were younger, female predominant and more likely to have chronic kidney disease than those without SLE. The territory of AMI and the usage of invasive procedures such as PTCA, and CABG were similar between the three groups. The in-hospital mortality rates were 12.6%, 9.0%, and 4.2% in the SLE total non-SLE and matched non-SLE group. The risk of mortality and prolonged hospitalization is significantly higher in the SLE group (compared with total non-SLE group: mortality OR: 1.98; 95% CI: 1.23–2.26; prolonged hospitalization OR: 1.49; 95% CI: 1.06–2.01; compared with matched non-SLE group: mortality OR: 2.20; 95% CI: 1.06–4.58; prolonged hospitalization OR: 1.38; 95% CI: 0.89–2.14).

Conclusion: SLE is associated with higher risk of in-hospital mortality and prolonged hospitalization after acute myocardial infarction.

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Influence of renal function on the treatment effect of revascularization versus medical therapy in patients with chronic total occlusions


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Objectives: The purpose of this study was to investigate whether the outcome of revascularization therapy that is different in chronic kidney disease (CKD) and non-CKD patients with chronic total occlusions (CTO) disease.

Background: There is a paucity of data on long-term outcomes after revascularization versus medical therapy for chronic total occlusions (CTO) in patients with different chronic kidney disease status.

Methods: Between March 2003 and February 2012, 2074 patients with CTO were enrolled in a retrospective, observational registry. Of these, a total of 2,010 patients with CTO who underwent revascularization (n=1385, including percutaneous coronary intervention (n=878) and coronary artery bypass grafting (n=477)) or received medical therapy alone (n=655) were examined. The clinical outcomes were evaluated according to renal function divided by estimated glomerular filtration rates (eGFR; normal: eGFR ≥ 90 mL/min/1.73m2; CKD: eGFR <60 mL/min/1.73m2). We compared the differential effects on these 2 treatments on long-term clinical outcomes according to CKD status. The primary outcome was all-cause death during follow-up.

Results: The median follow-up duration was 49.3 (interquartile range: 23.7 to 74.2) months. The non-CKD population, the revascularization group had a lower incidences of all-cause death (hazard ratio [HR] 0.59, 95% confidence interval [CI] 0.43–0.81, p=0.001) than the medical therapy group. Whereas, in the CKD population, the incidence of all-cause death (HR 0.79, 95% CI 0.51–1.12, p=0.28) was similar in the revascularization and MT groups. There was a significant interaction between kidney function and treatment strategies (revascularization vs. medical therapy) on all-cause mortality (p interaction = 0.044 by multivariate analysis)

Conclusions: In CTO patients with preexisting chronic kidney disease, revascularization via percutaneous coronary intervention or bypass surgery might not be effective as patients who have normal renal function.

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Premature occurrence of atherosclerotic lesions evaluated by coronary computed tomography angiography in young patients with ankylosing spondylitis


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Background: Ankylosing spondylitis (AS) is a chronic, progressive inflammatory disease comprising sacroiliac, spinal and peripheral joints. According to possible proatherogenic mechanisms, the aim of the study was evaluation of possible early cardiovascular involvement in young patients with AS.

Methods: A cross-sectional study included 40 consecutive patients with AS, diagnosis based on the modified New York criteria for AS. The study included men and women aged 23–60 years with a disease duration <10 years: ankylosing spondylitis group (ASG). There were 90 patients in a control group (CG) with performed CT coronary angiogram, who corresponded to ASG by age, gender, hyperlipidemia, smoking and BMI. Cardiovascular assessment was performed using clinical and laboratory exams, echocardiographic examinations, carotid arteries ultrasound and CT coronary angiogram.

Results: The mean age of ASG was 42.6 years, 23–60 years (30% women) and...
CG: 42.4–23–59 years (46.7% women). The mean duration of disease was 18 months. Inflammatory disease activity was considered as high by an independent rheumatologist. HLA-B27 Antigen was present in 31 (83.8%) of AS patients. In AS group hiperlipidemia occurrence was significantly higher than in the general Polish population (NATPOL 2011 Study): 36.5% vs 61.0%, p=0.0043. LDL cholesterol concentrations in ASG were lower: 103.2±29.8 vs. 126.3±37.7 mg/dL, p=0.0015. There was no significant correlations between atherosclerotic lesions in carotid arteries and risk factors of coronary artery disease. But in CT coronary angiogram atherosclerotic lesions were more frequent than in ASG in comparison with control (p=0.024). In addition - patients with AS had more degenerative changes within the aortic and mitral valves, more frequent mitral re-gurgitation and the pericardium involvement.

Conclusions: In patients with ankylosing spondylitis structural changes in the cardiovascular system including atherosclerosis of coronary arteries and valves involvement, are significantly increased in comparison with the control group. Lower levels of LDL cholesterol in the study group may be the result of an ongoing inflammatory process. It confirms possible inflammatory etiology in the development of atherosclerotic and degenerative coronary lesions in these patients.

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Serum uric acid as independent predictor of the clinical presentation of acute coronary syndromes

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Background: Patients with serum uric acid (SUA) levels above 7 mg/dL are at increased risk of developing both chronic kidney disease (CKD) and coronary artery disease (CAD). Renal dysfunction has shown a predictive role in determining if a patient has a subtypes of acute coronary syndromes (STEMI) vs. non-ST elevation acute coronary syndromes (NSTE-ACS) or ST-segment elevation myocardial infarction (STEMI). However, the adjunctive role of SUA in predicting acute coronary syndrome clinical presentation has never been defined so far.

Purpose: In view of clarifying a possible pathophysiological role of SUA in the wide spectrum of coronary artery diseases, we studied the ability of SUA to predict the type of ACS clinical presentation (STEMI vs. NSTE-ACS), independently of CKD class.

Methods: We analyzed a cohort of 1193 European patients with acute coronary syndromes (both STEMI and NSTE-ACS). We measured serum creatinine and SUA levels on admission and before coronary angiography. Estimated glomerular filtration rate (eGFR) was calculated according to 4+MDRD formula and, depending on CKD stages, patients were divided into three classes defined by: class I (stage I, eGFR >90 mL/min/1.73 m²), class II (stage II, eGFR 60–90 mL/min/1.73 m²) and class III (stages III-V, eGFR –60 mL/min/1.73 m²).

Results: Among the study patients, 568 (47.7%) had STEMI and 625 (52.3%) had NSTE-ACS. Age and gender distribution were similar between groups (61.3±11.7 vs. 62.0±11.4 yrs; males 68.1% vs. 65.6%; both p=ns). Global cardiovascular risk profile assessed by the Framingham Risk Score (FRS) was similar between groups (p=ns). Overall, 273 patients (22.9%) were in CKD class I, 441 (36.7%) in class II and 267 (22.4%) class III. Patients with SUA >7 mg/dL were 109 (9.1%). Independently of the FRS, CKD class resulted predictive of NSTE-ACS vs. STEMI proportionality to the grade of renal dysfunction: class II vs. I OR 3.3 (CI 95%: 2.4–4.5; p<0.0001). In class III vs. I OR 3.3 (CI 95%: 2.4–4.5; p=0.0017). In class III vs. II OR 2.3 (CI 95%: 1.6–3.3; p<0.0017).

Conclusion: In patients with an acute coronary syndrome, our results confirm the ability of CKD class to predict the presentation (NSTE-ACS vs. STEMI), proportionally to renal function impairment. Moreover, hyperuricemia plays an additional role, with SUA levels >7 mg/dL, predicting NSTE-ACS vs. STEMI independently of renal function impairment. This results are consistent with the greater systemic inflammation and cardiovascular risk profile in patients with renal dysfunction.

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LDL-cholesterol levels are related to the clinical severity of non-obstructive coronary artery disease

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Background/Introduction: Non-obstructive coronary artery disease (nobCAD) represents independent predictor of adverse clinical outcome. However, the current data on factors that may influence the clinical course of nobCAD are scarce. Proctor PIOWe therefore the relationship between LDL-cholesterol levels and clinical presentation in patients with nobCAD.

Methods: We recruited 1378 patients admitted for suspected coronary artery disease and no relevant coronary stenosis (i.e. ≥50%) in the subsequent coro-

angiography (764 men, median age 62.0 years [interquartile range [IQR]: 54.0–70.0]). Among these patients, nobCAD was defined by the history of angina pectoris symptoms detected by standardized Rosé questionnaire. In all patients, lipid status including direct measurement of LDL-cholesterol in peripheral venous blood was performed.

Results: We identified overall 813 patients with nobCAD (407 men [50.1%]; mean age 61 years [IQR: 53 -70]) according to the presence of traditional chest pain classification categories: 1. definite angina (n=265; 33%), 2. probable angina (n=335; 41%), and non-anginal chest pain (n=213; 26%). The presence of nob-

CAD was detected more frequently in females in comparison to males (66% vs. 54% in males; p=7.31x10–06). Patients with nobCAD symptoms showed higher mean LDL-cholesterol Levels (3.32±0.97mmol/l) in comparison to controls (3.12±0.95 mmol/l; p=1.31x10–04). In subgroup of patients with chest pain provoked by exertion (n=899) the mean LDL-levels increased within higher CCS classes (CCS I: 3.25±0.91; CCS II: 3.31±0.98; CCS III:3.39±0.99 mmol/l) p=4.0x10–04). Upon adjustment for traditional cardiovascular risk factors, previous statin treatment, angiographic presence of epicardial coronary atherosclerosis, and NNYA class, elevated LDL-level (i.e. >mean value 3.32 mmol/l) was an independent predictor of nobCAD (OR 95% CI: 1.46 [1.13–1.86]; p=0.004).

Conclusion: In patients with nobCAD, LDL-cholesterol levels are related to the severity of clinical presentation independent of epicardial coronary atherosclerosis detection and of statin treatment. These results suggest that nobCAD patients could benefit from LDL-lowering management.

Acknowledgement/Funding: European Regional Development Fund (ERDF) and Free State of Saxony within the framework of the excellence initiative excellency initiative

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Usefulness of baseline and early changes in high sensitivity tropon T to predict 1 year mortality in type 2 acute coronary syndromes

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Background: High-sensitivity cardiac tropon T (hs-cTnT) is useful for predicting mortality in type-1 acute coronary syndromes (ACS), however the prognosis role of early changes in hs-cTnT in type-2 ACS has not been studied.

Purpose: The aims of this study was to assess the prognosis value of hs-cTnT at presentation in patients with type-2 ACS; and to evaluate whether early changes in hs-cTnT add information to GRACE risk score.

Methods: We performed a retrospective analysis of a prospective registry including 243 consecutive patients (pts) with type-2 ACS admitted to the cardiology department of a tertiary hospital between January 2012 to January 2015. Blood samples were collected to measure hs-cTnT at presentation and within 6 hours of admission in an unblinded fashion. Pts with <2 hs-cTnT measurements were excluded (12%). GRACE risk score was calculated in 92% of cases. Pts were clinically followed and 1-year vital status was recorded by 3 trained cardiologists in all.

Results: A total of 215 type-2 ACS pts (72±12 years, 54% male) were included. Most common causes of type-2 ACS were tachycardia (33%), heart failure (14%) and hypertensive emergency (13%). During the follow-up, 37 (17%) patients died. Baseline hs-cTnT levels (OR=100 pg/ml, 1.11 95% CI 1.02–1.20; p=0.015) and GRACE risk score (OR=point, 1.03 95% CI 1.02–1.05; p<0.001) were associated with an increased mortality, whereas absolute and relative hs-cTnT changes did not (p>0.05). As shown in Table 1, early changes in hs-cTnT did not add prognostic information to hs-cTnT at presentation (both p>0.05). ROC analyses also showed that neither hs-cTnT at presentation nor changes in hs-cTnT levels improve the predictive ability of GRACE risk score (all p>0.05).

In reclassification analyses the results remains the same (all p>0.05).

Conclusions: High baseline hs-cTnT levels, but not hs-cTnT changes, are associated with higher 1-year mortality in type-2 ACS pts. Neither baseline levels nor changes in hs-cTnT add information to GRACE risk score.
compared to Arab patients. Aggressive risk factors modifications to reduce the burden of CAD in the Middle East are urgently needed.

Methods: All patients hospitalized with first AMI during the study period were included. Group 1 (1993–2002) and group 2 (2003–2012) were compared in term of prevalence and burden of CVRFs in Indian Subcontinent and Arab patients presenting with AMI in the Middle Eastern countries.

Results: Between 1993 to the end of 2012, a total of 12,253 consecutive patients were prospectively hospitalized with first AMI. The overall mean age was 53±12 years. 86% were males and the rate of hospitalization increased from 3,553 (29%) to 8,700 (71%) (p-trends <0.001 for all) during the 20-year period. Most of the patients (79%) had at least 1 modifiable major CVRFs, and 42% were Arabs. Smoking (40%), followed by diabetes (39% for each) were the most prevalent CVRFs. Compared to Arabs, SA patients were younger and more likely to be smoker (p <0.001). Hypertension, diabetes, obesity and dyslipidemia were less common in SA patients.

Conclusion: Our findings highlight increased burden of CAD in the Middle East. Furthermore, SA patients living in the Middle East have lower CVRF profile when compared to Arab patients. Aggressive risk factors modifications to reduce the burden of CAD in the Middle East are urgently needed.

P4745 | BENDSIDE
No association between CKD and TVR in patients with STEMI treated by PCI

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Aim: To determine, potential associations between CKD severity and post-PCI events in patients with STEMI and chronic kidney disease (CKD), as these patients are often excluded from clinical trials.

Methods and results: Among 2101 (79% male) consecutive patients with STEMI who underwent PCI (52% primary PCI) during their initial hospitalization between October 2003 and March 2014, 2030 had qualifying creatinine levels. Between October 2003 and March 2014, 2030 had qualifying creatinine levels. We examined ethnic difference in the prevalence of five modifiable CVRFs (hypertension, diabetes mellitus, current smoking, dyslipidemia, and obesity), and trials specifically examining these patients are warranted.

Results: We included 2030 patients with acute coronary syndrome. Aggressive risk factors and comorbidities. Besides being taken more frequently evidence-based medication than those who had single bed disease, they were far from the ideal situation. These facts can both influence in-hospital as six-month mortality. It is crucial to consider more strictness strategies for secondary prevention in patients with multiple vascular beds disease.

P4745 | BENDSIDE
Type 2 diabetes compromises the value of non-invasively measured augmentation index in predicting the severity of coronary artery disease

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Introduction: Central hemodynamics has been shown to predict cardiovascular events in coronary artery disease (CAD) patients. Emerging advancement of non-invasive technique to measure central blood pressure has allowed for safer and wider application in more patients. Recently, non-invasively measured central hemodynamic parameters have been reported to be related with CAD. There is lack of conclusion on the reliable cut-off value for such parameters.

Purpose: To determine whether the coexistence of type 2 diabetes exert any influence on the relationship between central hemodynamic parameters and CAD is unclear.

Methods: A total of 187 patients who underwent coronary angiography at our center from September 2015 to January 2016 were analyzed. We non-invasively measured central hemodynamic parameters by BPro device. The severity of CAD was defined according to SYNTAX scores. Type 2 diabetes was defined as fasting glucose >7mmol/L or HbA1c >6.5% or use of oral antidiabetic agents/insulin.

Results: The mean age and BMI of the population were 59 years old and 25.2 kg/m², respectively. 79 (42.2%) of studied subjects were diabetic patients. Given that AIx is inversely related to heart rate, we used AIx normalized to heart rate of 75 bpm (AIx@75) as an alternative. Our principal findings were that (1) AIx@75 was significantly correlated with the severity of coronary artery disease. (ROC curve analyzed AUC= 0.635, 95% CI 0.548–0.721, p<0.05) (2) In non-diabetic patients, univariate regression analysis showed that AIx@75, augmentation pressure, central pulse pressure and peak relative time were significantly correlated with CAD severity. After adjustment, AIx@75 remained as the only independent predictor of moderate to severe CAD (odds ratio 1.12, 95% CI 0.91–1.42; p<0.05). In diabetic patients, the correlation between central hemodynamic parameters and the severity of CAD didn’t exist.

The correlation of AIx@75 and SYNTAX score.
Conclusion: Aortic augmentation index was significantly related to the severity of CAD and was an independent predictor of more severe CAD. However, its value in DM populations was compromised and clinical practitioners should be aware of it. Future studies investigating the underlying mechanism should be performed.

P4748 | BEDSIDE
High central aortic pulse pressure is linked to heightened thrombogenicity and predicts poorer outcomes in patients with coronary artery disease
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Background: Central aortic pulse pressure (CPP) and high thrombin-induced platelet-fibrin clot strength (TIP-FCS) have been independently associated with isch-emic outcomes. The interrelation between CPP, thrombogenicity, and ischemic outcomes is unknown.

Methods: Consecutive patients (n=334) had thrombogenicity assessed by thrombelastography at catheterization and were followed for up to 3 years.

Results: Patients who had the occurrence of MI and the composite endpoint (CV death, MI or ischemic stroke) had greater CPP (86±18 mmHg vs. 63±19 mmHg, p<0.001; and 84±17 mmHg vs. 63±19mmHg, p<0.001, respectively) and TIP-FCS (60±6 mmHg vs. 65±5.3 mmHg, p=0.005, respectively). Patients with CPP>60mmHg had higher TIP-FCS (67±05.3 mm vs. 64.7±5.0 mm, p<0.001), combined endpoint occurrence; CV death; MI; total ischemic events; and all-cause death (10.6% vs. 0%, p=0.001; 4.4% vs. 0%, p=0.02; 7.2% vs. 0%, p=0.002; 30.5% vs. 11%, p=0.001; and 6.1% vs. 0%, p=0.005, respectively). CPP >60mmHg was an independent predictor of composite endpoint occurrence (HR 4.7, 95% CI: 1.2–18.3 (p<0.025). CPP >60mmHg + TIP-FCS>60mm was associated with a markedly increased risk of composite endpoint occurrence (HR 6.4, 95% CI: 2.0–20.4 (p<0.002).

Conclusion: High CPP may mediate ischemic event occurrence by enhancing thrombogenicity. Further investigation of the mechanisms underlying direct effects of CPP on platelet physiology are warranted.

P4749 | BEDSIDE
Reduction in coronary artery disease progression in patients with severe psoriasis treated with biologic agents
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Background: Inflammation may entail progression of atherosclerotic plaques, but the effects of anti-inflammatory drugs on the development of coronary atherosclerosis remains essentially unknown.

Purpose: Using psoriasis as a model of an inflammatory disease with an acknowledged association with increased cardiovascular risk, we investigate whether treatment with biologic drugs affects coronary artery disease progression.

Methods: In an open-label, controlled study, we compared the progression of coronary atherosclerosis in patients with severe psoriasis (n=28, mean (±SD) age 49.2±10.2 years, 71% men, mean Psoriasis Area Severity Index (PASI) 15±4.3) initiating biological therapy. The intervention group was compared with a matched control group not receiving systemic therapy (n=28, age 52.8±10.6 years, 71% men, PASI 12.4±3.9). Patients underwent non-contrast coronary artery calcium (CAC) computed tomography (CT) and contrast-enhanced coronary CT angiography (CTCA) at baseline and after 13 months of follow-up. CAC scores were quantified using the Agatston method. CTCA results were analyzed using the 18-segment model of the coronary tree and by automated analysis of the vessel wall volume.

Results: Disease control in the intervention group was good during the study period with a mean PASI reduction of 88±15% and 78% of patients achieved a ≥ 75% reduction. CAC scores remained stable in the intervention group (baseline: 98±282, follow-up: 82±235, P=0.15) and increased in the control group (baseline: 777±178, follow-up: 91±206, P=0.025) (intervention vs. controls: P=0.049). The number of segments with luminal abnormalities remained unchanged in both groups. The severity of luminal narrowing in the diseased segments was unchanged in the intervention group, but increased at follow-up in the control group (P=0.019). Automated vessel wall volume index remained unchanged from baseline to follow-up in the intervention group (baseline 7.3±1.6, follow-up 7.3±1.8, P=0.78), while controls demonstrated a borderline statistically significant progression (baseline 8.4±1.6, follow-up 9.0±2.2; P=0.06).

Conclusions: Clinically effective treatment with biologic agents was associated with reduced coronary artery disease progression in patients with severe psoriasis. The results may serve as proof of concept regarding the ability of anti-inflammatory biologic therapies to prevent progression of atherosclerosis.

Acknowledgement/Funding: Aage Bang Research Foundation; Central Den-mark Region Research Foundation; AbbVie

P4750 | BEDSIDE
Impact of hemodialysis in patients with acute myocardial infarction
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Introduction: End-stage renal disease (ESRD) requiring renal replacement ther-apy (RRT), namely hemodialysis, is an important comorbidity in acute myo-cardial infarction (AMI) that can impact therapy and prognosis in these pa-tients. However, chronic kidney disease (CKD) patients beyond stage 4 are fre-quently excluded from most international studies, so its real impact is under-eval-uated.

Purpose: To characterize the population with AMI and CKD requiring hemodialysis (HD), and to assess the impact of HD on in-hospital therapy and mortality and mortality rate at 1-year follow-up.

Methods: We studied 11949 patients (P) with AMI included in a multicentre na-tional registry. We compared two groups: patients on dialysis and patients not on dialysis (n=7038) (censored on date of renal failure). We registered data concerning demo-graphic features, patient history including cardiovascular and non-cardiovascular co-morbidities, and clinical and electrocardiographic presentation), medical and inva-sive therapy. We considered the following in-hospital complications: heart failure (HF), cardiogenic shock, new-onset atrial fibrillation and major bleeding. We performed multivariate data analysis to assess if HD is an independent predictor of in-hospital complications and mortality.

Results: Eighty-one (0.7%) of P were on HD. These P were older (65±11 vs. 60±14, P<0.001), had a higher prevalence of hypertension (58.9 vs 88.8%, p<0.01), diabetes (48.1 vs 29.7%; p<0.001), previous history of AMI (40.0 vs. 18.8%; p<0.001), previous percutaneous coronary intervention (31.6 vs 13%; p<0.001), HF (16.0 vs 5.7%; p<0.001) and peripheral vascular disease (29.6 vs 5.1%; p=0.001). At hospital admission dialysis P exhibited lower prevalence of STEMI (14.8 vs 45%; p<0.001) and a higher class of Killip-Kimball. (KK≥2: 26.3 vs 15.9%; p=0.002. During hospital stay these P were less frequently treated with ACE inhibitors or angiotensin- receptor blockers (60.5 vs 87.2%; p=0.001), beta-blockers (69.1 vs 80.7%; p<0.005) and more frequently treated with calcium channel blockers and ibabradine (8.9 vs 4.3%; p=0.023). Dialysis P were also less frequently submitted to coronary angiography (80.2 vs 87.9%; p=0.036) and presented more frequently 3-vessel disease (34.5 vs 21.5%; p=0.016). There was no difference concerning left ventricular function. HD was associated with a higher frequency of HF during hospital stay (27.2 vs 17.2%; p=0.016) but no differences were found regarding the other complications considered, in-hospital mortality or 1-year follow-up mortality.

Conclusions: The prevalence of CKD on HD was 0.7% in AMI. Dialysis P re-ceived less frequently coronary angiography and medical therapy with prognostic significance. HD is an independent predictor of HF but does not predict in-hospital mortality.

P4751 | BEDSIDE
Monocyte to high-density lipoprotein cholesterol ratio has independent prognostic value in coronary artery ectasia
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Background/Introduction: Monocyte to high-density lipoprotein cholesterol ratio (MHR) is significantly higher and associated with coronary artery ectasia (CAE). MHR is a new cardiovascular prognostic marker but its prognostic value has not been evaluated in CAE.

Purpose: The aim of this study was to investigate the association between MHR and CAE outcomes.

Methods: The study population was consecutively collected from the patients who were diagnosed with CAE via coronary angiography in our hospital from January 2009 to December 2013. Follow-up results were collected from telephone interview and medical records in our hospital. The observational end-point was the combination of all-cause death and non-fatal myocardial infarction.

The median level of MHR of these CAE patients was regarded as cut-off point for composite end-point. The association between MHR and CAE outcomes was evaluated and curved in Cox regression model and Kaplan-Meier curve.

Results: Two-year follow-up results of 501 CAE patients could be obtained. Twenty two-end-point events were observed, including 15 all-cause deaths and 7 non-fatal cardiac infarctions. There were no significant differences between the baseline characteristics of two groups divided by median level of MHR (0.455*1012/mmol), except for the age and Gensini score. The univariate hazard ratio of MHR for end-point events was 2.732 (95% CI: 1.069–6.981, P=0.036). Several models were conducted and the hazard ratio was 3.400 (95% CI: 1.299–8.901, P=0.013), adjusting for age, gender, diabetes mellitus, hyperlipidemia and
Gensini score. In the Kaplan-Meier analysis, the event-free survival rate of CAE patients with MHR \( \leq 1012/mmol \) significantly distinguished from those with MHR \( > 1012/mmol \) (P=0.028).

**Table 1**

<table>
<thead>
<tr>
<th>Pain</th>
<th>N PTP Patients with coronary artery lesions</th>
<th>N PTP Patients with coronary artery lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical angina</td>
<td>401</td>
<td>80.34%</td>
</tr>
<tr>
<td>Atypical angina</td>
<td>75</td>
<td>53.09%</td>
</tr>
<tr>
<td>Non-anginal pain</td>
<td>102</td>
<td>37.42%</td>
</tr>
<tr>
<td>Total</td>
<td>578</td>
<td>69.23%</td>
</tr>
</tbody>
</table>

**Conclusions:** MHR, an easily available and relatively cheap test, provides prognostic value for CAE patients. MHR is associated with the two-year outcomes (all-cause death and non-fatal myocardial infarction) of CAE patients.

**Acknowledgement/Funding:** This work was supported by the Beijing Municipal Science and Technology Commission (Grant number: Z151100004015045, Beijing, China).

**P4753 | BEDSIDE**

**Validation of pre-test probability of coronary artery disease in a Portuguese centre**

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**Introduction:** Electrocardiogram stress test (EST) is indicated to investigate patients with signs and symptoms of stable coronary artery disease (CAD) with pre-test probability (PTP) of CAD between 15% and 85%. The PTP present in 2013 ESC guidelines of stable CAD results from a worldwide multi-centre study. However, the prevalence of CAD differed considerably in that study between centres (39.4% in USA to 75.5% in Russia). So, the PTP currently in use can be far from the reality of a specific country, with consequences in the diagnostic management of patients.

**Purpose:** The authors propose to validate the PTP of CAD in a sample of patients from a centre in Portugal, who performed coronaryography to evaluate the presence of CAD due to a positive EST, as well as to calculate the positive predictive value of the EST in the studied sample.

**Methods:** Retrospective single-centre study with a sample of 923 consecutive patients who performed coronaryography to evaluate the presence of CAD due to a positive EST. PTP of each patient was calculated using the updated and extended Diamond-Forrester model present in 2013 ESC guidelines of CAD. Patients were grouped by symptoms (typical angina, atypical angina or non-anginal pain), sex and age. In each group the mean PTP was compared with the prevalence of CAD and the p-value calculated using Student’s t-test. The positive predictive value of the EST was calculated from the proportion of patients with positive EST who had coronary artery lesions in the coronaryography.

**Results:** 578 (62.6%) male patients, with mean age of 63.8 (± 9.93) years. 660 (71.5%) patients had typical angina, 117 (12.7%) atypical angina and 146 (15.8%) non-anginal pain. 466 (50.49%) patients had coronary artery lesions in the coronaryography. Further results in table 1.

**Conclusions:** The PTP overestimated the prevalence of CAD in the studied sample, in male and female patients with typical and atypical angina. The PTP underestimated the prevalence of CAD in male patients with non-anginal pain, with non-significant statistically difference in female patients with non-anginal pain. The positive predictive value of the EST was 50.49%.
sility was positively associated with survival. There are likely several explanations for the higher survival in higher populated areas, including lower time-interval from call to rhythm analysis and higher frequency of shockable rhythms.

P4754 | BEDSIDE

Successful cardiopulmonary resuscitation after cardiac arrest as a sepsis-like-syndrome

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Background: The mechanisms after successful cardiopulmonary resuscitation probably involve whole-body ischemia and a reperfusion syndrome that triggers a systemic inflammatory response. In the present study we investigated the predictive value of inflammatory plasma cytokine levels and kinetics on neurologic outcome in patients with resuscitated cardiac arrest.

Methods: We enrolled 82 patients. Mild therapeutic hypothermia (33°C) was initiated on admission. Serum values of TNF-alpha, IL-6 and IL-10 were measured 0h and 6h after admission and daily for six consecutive days. Clinical and neurologic outcome was assessed by the Cerebral Categories Scale (CPC 4–5: poor outcome; CPC 1–3: good outcome).

Results: A favourable neurologic outcome was achieved in 37 patients (45%). Immediately following hospital admission, IL-6 (1724±808 pg/ml vs. 80±93 pg/ml, p<0.001) and TNF-alpha (230±330 pg/ml vs. 65±113 pg/ml, p<0.001) demonstrated significantly higher values in patients with poor outcome. These differences were maintained up to 6 days. In ROC analysis, the AUC to predict poor neurologic outcome was 0.76 for IL-6 and 0.83 for TNF-alpha measured on admission, respectively. IL-10 had lower predictive ability, with significant differences only 6 hours after admission (535±1783 pg/ml vs 54±70 pg/ml, p<0.013, AUC 0.54) and 72 hours after admission, but not at other time points.

Conclusion: In the present study we demonstrated a pronounced systemic inflammatory response in patients who were successfully resuscitated after cardiac arrest. There was a substantial increase of respective cytokines especially in patients with poor outcome. Especially TNF-alpha and IL-6 seem to be promising biomarkers for early prognostication in patients with successfully resuscitated cardiac arrest.

P4756 | BEDSIDE

Techniques of target temperature management with surface cooling versus intravascular cooling after out-of-hospital cardiac arrest

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Background: The Target temperature management (TTM) between 32°C and 36°C for the higher survival in higher populated areas, including lower time-interval from call to rhythm analysis and higher frequency of shockable rhythms.

Methods: This multicenter retrospective study was conducted in 14 hospitals between January 2005 and March 2011. A total of 477 OHCAs underwent TTM, targeting temperature was 34±1°C and maintenance time was 24–48 hours. Among 328 OHCAs excluded 114 patients with introduction of extracorporeal cardiopulmonary resuscitation and 35 patients underwent combination of surface cooling and intravascular cooling, we compared 192 patients who underwent surface cooling (Group-S) with 136 patients who underwent intravascular cooling by using continuous renal replacement therapy (Group-I). The endpoint was a favorable neurological outcome defined as Cerebral Performance Category 1–2 at 3 months after collapse.

Results: There were no significant differences of age, sex, witnessed, bystander cardiopulmonary resuscitation and the rate of shockable rhythm between the 2 groups. In Group-I, the mean time from collapse to return of spontaneous circulation was significantly shorter compared Group-S (23±14 minutes vs. 19±14 minutes, p=0.013). Regarding the technique of TTM, in Group-I, time from cooling initiation to achieving target temperature was shorter (301±261 minutes vs. 248±195 minutes, p=0.047) and the accuracy of management is significantly higher compared Group-S (53% vs. 93%, p<0.001). There was no significant difference in the rate of withdrawal from TTM between the 2groups (Group-I 5% vs. Group-S 6%, p=0.0001). At first 30 days and 3 months after collapse, there was no significant difference in survival rate (Group-I 71% vs. Group-S 81%, p=0.321) and favorable outcome achieving rate (Group-I 57% vs. Group-S 65%, p=0.245) between 2 groups.

Conclusion: This multicenter registry found that the intravascular cooling could shorten the time from cooling initiation to achieving target temperature and permit more accurate TTM. However, the cooling techniques for TTM might not impact for survival rate and neurological outcomes in OHCAs.

P4757 | BEDSIDE

Long-term outcomes of patients treated with unplanned venoarterial extracorporeal membrane oxygenation

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Background: Venoarterial extracorporeal membrane oxygenation (ECMO) could rapidly provide haemodynamic support in emergencies. However, the long-term prognosis of patients treated with ECMO is still unclear.

Purpose: To assess the long-term outcomes of patients treated with venoarterial ECMO.

Methods: Patients who were treated with unplanned venoarterial ECMO between 2004 and 2016 were enrolled in this study. Data of the study patients, including baseline characteristics, in-hospital findings, and survival status were collected. Five-year survival curves were constructed by using the Kaplan-Meier method in order to assess survival durations.

Results: The follow-up durations of the study patients (n=238) ranged from 0 to 4359 days (median, 5 days [interquartile range, 1–202 days]). The median age of patients was 61±14 years (median, 5 days [interquartile range, 1–202 days]). The median age of patients was 61±14 years (median, 5 days [interquartile range, 1–202 days]). The median age of patients was 61±14 years (median, 5 days [interquartile range, 1–202 days]).
the study patients was 64 years (interquartile range, 55–72). Of the patients, 71% were men, 82% were percutaneously cannulated. 77% received ECMO during cardiopulmonary resuscitation, 47% had acute coronary syndrome, and 11% had acute pulmonary embolism. Targeted temperature management was performed in 45% of the study patients; coronary angiography, in 69%; and subsequent coronary revascularization, in 38%. Of the study patients, 74 (31%) had survived at 90 days after initiation of ECMO and 9 died after the 90-day period. Among the 9 patients, 6 died from cardiac failure, and 1 died from multi-organ failure, severe neurologic deficit, and colon cancer, respectively. The 5-year Kaplan-Meier curves and the 5-year Kaplan-Meier curves after the 90-day period of initiation of ECMO are shown in the figure.

Conclusion: The prognosis of the patients who were treated with venoarterial ECMO and had survived the 90-day period after ECMO initiation was acceptable. Cardiac failure was the most frequent cause of death after 90 days of ECMO initiation.


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Background: Recent trends in nationwide survival after in-hospital cardiopulmonary resuscitation (ICPR) in younger patients aged 18–64 years, in the United States is not well elucidated. Patient and hospital level characteristics predicting survival after ICPR in younger patients is not well known. Purpose: We sought to study the recent trends and predictors of survival after ICPR in younger patients in the United States. Methods: We identified hospitalizations with principal procedure ICD-9CM codes 99.60 and 99.63 in the Healthcare Cost and Utilization Project’s Nationwide Inpatient Sample (NIS) database for years, 2007 to 2012, in the United States. Weights provided by NIS were used to generate national estimates. We used logistic regression analyses to identify predictors associated with survival. Results: From 2007 to 2012, we identified a total of 235,960 younger adults (18–64 years) undergoing ICPR. Overall incidence of CPR in 2007 was 1.81 per 1,000 hospitalizations and it increased to 2.37 per 1,000 hospitalizations in 2012 (p-trend <0.001). Overall survival-to-discharge rate was 30.4% (improved from 27.4% in 2007 to 32.9% in 2012; p-trend <0.01). We noted nonshockable rhythms (pulsless electrical activity/asystole) in 76.7% and shockable rhythms (ventricular tachycardia/ventricular fibrillation/ventricular flutter) in 23.3%. Patients aged 50–64 years had significantly lower survival as compared to young adults (adjusted odds ratio [adjusted-OR] 0.85; CI:0.82–0.88; p<0.001). Female gender was associated with better survival in comparison to males (adjusted-OR 1.12; CI: 1.09–1.14; p<0.001). Black patients were significantly associated with poor survival compared to whites (adjusted-OR 0.75; CI: 0.73–0.77; p<0.001). Weekend admission also predicted poor survival (adjusted-OR 0.99; CI: 0.87–0.92; p<0.001). However, shockable ventricular rhythm was associated significantly improved survival after ICPR (adjusted-OR 1.68; CI: 1.64–1.72; p<0.001), compared to nonshockable rhythms. Teaching status of the hospital did not predict survival (p=0.22).

Conclusions: There was significant improvement in survival-to-discharge rates after ICPR in young and middle aged adults from 2007 through 2012, in the United States. However, there was increase in overall incidence of ICPR during the study period. Female gender and shockable rhythm were associated with better survival after ICPR. But, Black race was associated with significantly lower survival rates in young and middle aged adults from 2007 through 2012, in the United States. However, there was increase in overall incidence of ICPR during the study period.

P4759 | BEDSIDE Effect of gender on cardiac repolarization during mild therapeutic hypothermia after out-of-hospital cardiac arrest

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Background: Mild therapeutic hypothermia (MTH) has become a routine procedure in survivors after cardiac arrest. Hypothermia is known to cause potentially arrhythmogenic effects, including prolonging action potential duration and prolongation of the QT interval. Methods: We studied 202 patients (46 females) after out-of-hospital cardiac arrest (OHCA). Of these, 124 (61%) underwent MTH for 24h. QTc was measured at baseline, 3h, 6h, 12h, 24h (end of hypothermia), 48h and 72h. To analyze the QTc changes over time, we used a repeated-measures mixed effect model. The model included fixed factors for MTH, time, MTH-by-time interaction, gender, gender-by-MTH interaction, and a random effect for the patient. The model adjusted for age, concomitant amiodarone therapy, serum levels of potassium and magnesium, acute myocardial infarction, initial rhythm and neurological status. Results: During MTH, the QTc interval increased progressively peaking at 12h. The QTc interval remained stable between 12h and 24h (end of hypothermia), and subsequently declined toward baseline levels at 72h. In the mixed model, there was a strong gender effect (P<0.0001) and a significant gender-by-MTH interaction (P<0.002). At baseline, there was a trend toward higher QTc among woman compared to men (488±62 vs. 473±46 ms, P=0.09). At 12h, the QTc interval was markedly longer in woman as compared with men (570±81 vs 510±58 ms, P<0.002). The Figure depicts the gender effect in patients with and without hypothermia. During MTH, the rate of QTc increase from baseline to 12h was 2.63 ms/h (95% CI 1.44 to 3.83 ms/h) in men and 6.96 ms/h (95% CI 4.63 to 9.23 ms/h) in women. In the same model, hypokalemia (P=0.002) and anoxic brain injury (P=0.02) were also positively associated with higher QTc interval. The mean increase in QTc was 19.77 ms (95% CI 7.12 to 32.41 ms) with hypokalemia (K<3.0 mmole/l) and 16.30 ms (95% CI 6.18 to 26.43 ms) with anoxic brain injury. Two women developed typical torsade de pointes during hypothermia.

Effect of Gender on QTc During MTH

Conclusion: MTH may serve as a provocative maneuver capable of unmasking latent QT abnormality. During a potent stimulus for QT prolongation such as hypothermia, the magnitude and rate of QT interval prolongation greatly increases in women owing to their latent reduced repolarization reserve. Women may be more susceptible to torsade de pointes during hypothermia.
every day in the event of angioplasty (prasugrel: n=10, clopidogrel: n=3). Clinical, biological and angiographic characteristics were similar in both aspirin groups. Using LTA-AA, mean maximum aggregation intensity was significantly lower in the intravenous group compared to the oral group (15% vs. 29%, respectively; \( p<0.04 \)). Overall, 10 patients (45%) had HPR-ASA (38% intravenously vs. 56% orally; \( p<0.07 \)). Similarly, closure time was significantly increased in the IV group (277s vs. 155s, respectively; \( p=0.04 \)). Clopidogrel was associated with HPR-ADP in all the patients (n=3) irrespective of the method of assessment. Under prasugrel (n=10), HPR-ADP was found in 10% of the samples with VASP-PR1 and 20% with LTA-ADP.

**Conclusion:** This study suggests that in comatose patients resuscitated from OHCA, HPR is common. Daily intravenous aspirin is more effective than gastric plate. Platelet inhibition under prasugrel appears to be superior to clopidogrel in such setting.

### P4762 | BEDSIDE

**What characteristics of coronary artery disease would be the potential risks factors for ventricular fibrillation with acute coronary syndrome**

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**Background:** We often had experienced the patients with acute coronary syndrome (ACS) had ventricular fibrillation (VF), it was serious and fatal complication. However, even though it was well known that ischemia was the risk for occurrence of VF, what is the influential factors of the ACS patients related to VF and CC was still unclear. We treated with extracorporeal cardiopulmonary resuscitation (ECPR) for VF patients with the ACS and performed coronary angiography to make definite diagnosis. Accordingly, We sought to the risk factors for VF with ACS.

**Methods:** Consecutive 328 ACS patients hospitalized and underwent emergent coronary revascularization from September 2010 to December 2015 were enrolled. In these, patients with VF were categorized into VF group, and patients without VF were into non-VF group. We reviewed patients’ characteristics, including medications, past histories and laboratory findings, and CC findings (number of disease vessels, existence of chronic total occlusion (CTO) and left-main coronary artery (LMCA) lesion diseases), retrospectively.

**Results:** Seventy-six patients developed ACS with VF (VF group), and 250 patients were without VF (non-VF group). Comparing between the groups, the morbidity of previous angina pectoris or coronary artery bypass grafting were significantly higher in VF groups (34.2%-17.2%, \( p<0.005 \), 11.8%-1.2%, \( p<0.001 \), respectively). The prevalence of Complex lesion characteristics, such as multi vessel disease, CTO and LMCA lesion, was also higher in VF group (76.3%-44.0%, 11.8%-0.0%, \( p<0.001 \), respectively). Moreover, multiple logistic regression analysis revealed multi vessel disease, CTO and LMCA lesion, was also higher in VF group (76.3%-44.0%, 11.8%-0.0%, \( p<0.001 \), 11.8%-1.2%, \( p<0.001 \), respectively). Moreover, multiple logistic regression analysis revealed multi vessel disease, CTO and LMCA lesion, was also higher in VF groups (76.3%-44.0%, 11.8%-0.0%, \( p<0.001 \), 11.8%-1.2%, \( p<0.001 \), respectively). Moreover, multiple logistic regression analysis revealed multi vessel disease, CTO and LMCA lesion, was also higher in VF groups (76.3%-44.0%, 11.8%-0.0%, \( p<0.001 \), 11.8%-1.2%, \( p<0.001 \), respectively).

**Conclusion:** VF group had more complex characteristics of coronary artery disease. Complex lesion characteristics, such as multi vessel disease, CTO and LMCA lesion, would be potential risk factors of VF with ACS patients.

### P4763 | BENCH

**Performance of new mechanical chest compressions LifeLine ARM device during transport with ongoing resuscitation: a randomized, crossover, manikin study**

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**Background:** Out of hospital cardiac arrest is a major cause of death and morbidity. ERC 2015 guidelines for cardiopulmonary resuscitation (CPR) state the importance of chest compression (CC) quality, including reducing the time without CC during CPR.

**Purpose:** The aim of our study was to evaluate the new mechanical CC device LifeLine ARM (Defibtech, USA) in nurses in a simulated model of cardiac arrest during transport with ongoing CPR.

**Methods:** Study was designed as randomized, crossover, manikin trial. 38 nurses working in Emergency Medical Service were enrolled, they had been trained on manual and mechanical CPR scenario according to the ERC 2015 guidelines. Manual CC were compared with LifeLine ARM device using the Resusci-Anne manikin (Laerdal, Norway). Participants performed 2mn of aspirin CC described in the ERC guidelines for aspirin CC. Participants were randomly split into 2 groups and to determine the order of CPR technique. The 1.group started manual CPR and 2. CPR using LifeLine ARM. After completing the 1. CPR procedure participants had a 20min break before performing CPR attempt using a different method. Data were recorded by the Laerdal Skill Reporting System. The primary endpoint was the percentage of correct CC relative to the total number of CC. Secondary endpoints were depth, pressure point, complete pressure release, rate of CC and hands-off time. The measurements were performed in a standard ambulance vehicle during transport on a preferred track of 5.0 km.

**Results:** Manual CC was performed correctly less often than mechanical CC (29% vs. 93%, \( p<0.001 \)). The median CC depth was deeper with LifeLine ARM (55 mm vs. 40 mm \( p<0.001 \)). The results with ARM were significantly better than with manual CC (\( p<0.001 \)) for all the analyzed variables (Table1).

### Table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Manual CC</th>
<th>LifeLine ARM CC</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Correct CC (%)</td>
<td>29 (25–31)</td>
<td>93 (90–96)</td>
<td>-0.001</td>
</tr>
<tr>
<td>Correct CC depth (%)</td>
<td>30 (21–42)</td>
<td>93 (90–97)</td>
<td>-0.001</td>
</tr>
<tr>
<td>CC too deep (%)</td>
<td>25 (4–44)</td>
<td>3 (2–4)</td>
<td>0.001</td>
</tr>
<tr>
<td>CC too shallow (%)</td>
<td>36 (10–65)</td>
<td>4 (2–5)</td>
<td>0.001</td>
</tr>
<tr>
<td>Mean CC rate (mm⁻¹)</td>
<td>128 (121–157)</td>
<td>100 (99–101)</td>
<td>-0.001</td>
</tr>
<tr>
<td>Mean CC depth (mm)</td>
<td>40 (36–45)</td>
<td>55 (54–56)</td>
<td>-0.001</td>
</tr>
</tbody>
</table>

**Conclusion:** In manikin simulated controlled conditions, during transport with ongoing resuscitation LifeLine ARM compared to manual CC increased CPR quality. Further clinical trials are warranted to confirm our results.
P4764 | BEDSIDE
Bispectral index: an early predictor of neurological outcomes in cardiac arrest survivors

Background and objectives: Sudden cardiac arrest (SCA) is a major cause of mortality and neurological impairment in Europe. Predicting neurological outcomes during the early post-arrest period remains to be a challenge, especially since the implementation of therapeutic hypothermia itself, and the need of concurrent use of sedation and neuromuscular blockade. Unlike other methods such as electroencephalogram or neuron-specific enolase, Bispectral index (BIS) allows early assessment of neurological status. We aimed to evaluate its accuracy for the prediction of neurological outcomes.

Methods: Prospective study of 185 successfully resuscitated patients (P) admitted to an intensive cardiac care unit from January 2012 to January 2016. All patients were unconscious at arrival (with a Glasgow coma score (GCS)<8) and underwent therapeutic hypothermia during 24 hours. During this period they received an intravenous infusion of midazolam and cisatracurium and BIS monitoring was performed for at least 48 hours continuously. Neurological assessment was performed before discharge using the Cerebral Performance Evaluation (CPC) score.

Results: 75.2% (140 patients) were male with a mean age of 73.8 years. Coronary angiography was performed before discharge using the Cerebral Performance Evaluation (CPC) score. Ninety-one patients (49.2%) had a good neurological outcome (defined by CPC 1–2 at discharge) whereas ninety-four (50.8%) presented CPC 3–5 (important neurological impairment or death). The mean BIS value was significantly higher in the first subgroup and this difference was maintained from the beginning and throughout the monitoring (figure). None of the patients with good neurological outcome had a BIS value below 10 nine hours after the initiation of therapeutic hypothermia, therefore being this cut-off value appropriate for the identification of cardiac arrest survivors without significant neurological impairment (sensitivity of 64.9% and specificity of 97.3%). Other variables significantly associated with better neurological prognostication were: higher pH (7.19 vs 7.10, p=0.0006) and lower lactate levels at hospital arrival (21.3 vs 10.3 mg/dl, p<0.0001), ventricular fibrillation as initial rhythm (p<0.011), male sex (p<0.0111), non-diabetes status (p<0.0015) and younger age (59.5 vs 66.9 years, p<0.0006).

Conclusion: Bispectral index is an early predictor of neurological outcome. Although further investigation is needed, we propose a value >10 in the ninth hour may help identify cardiac arrest survivors with further CPC 1–2.

P4765 | BEDSIDE
Out-of-hospital cardiac arrest: is LUCAS a basic or advanced CPR tool?
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Background: Out of hospital cardiac arrest (OHCA) is a major cause of death in the Western world. The most of patients (pts) with OHCA died before arriving to the hospital. The quality of external chest compression (ECC) can improve the survival. A prompt action, reducing the pauses and improving the quality of cardiopulmonary resuscitation (CPR) with mechanical device could be the key, even if 3 recent randomized controlled trials (RCT) missed this goal. Based on these results, the last ILCOR 2015 Guidelines recommend the use of mechanical device only in special circumstances.

Purpose: We evaluated the safety of Lund University Cardiac Arrest System (LU-CAS) device and its impact on survival of people with OHCA.

Methods and analysis: We report in a retrospective and observational study our experience using LU-CAS in among 591 cases of OHCA of presumed cardiac origin in our Province, from January 2011 to December 2014. Results: Of 142 (24%) pts were treated with LUCAS by Emergency Medical System (EMS) because of refractory cardiac arrest. These pts were mainly male (72 vs 55%, p=0.0000), younger (67 vs 75 yr, p=0.007), with OHCA in public place (39.3% vs 26%, p=0.019) and ventricular fibrillation (VF) as initial rhythm (32% 23.4%, p=0.049). They had a more frequent return of spontaneous circulation (ROSC) (36.6% vs 22.9%, p=0.001) but no difference in hospital (10 vs 11%, p=0.723) and 1-year survival (5.8 vs 6.6%, p=0.717), despite a more aggressive post-resuscitation care (emergency coronary angiography 22 vs 10.7%, p=0.001) (target temperature management 19 vs 7%, p=0.0011). But if we pay specific attention to the 45 pts (31.7%) with shockable initial rhythm, they had a better pre-hospital (44.4% vs 27.1%, p=0.040), hospital (24.4 vs 3.1%, p=0.000) and 1-year (11.9 vs 3.1%, p=0.042) outcome. The incidence of complication was 3.9%, all non-fatal.

Conclusion: Contrary the most recent RCT we used LUCAS not as basic but as advanced life support device in refractory OHCA, with good results on safety and survival, especially in case of shockable rhythms. Now we are waiting for new evidences about selection of patients that have to be treated.

P4766 | BEDSIDE
Risk prediction in elderly patients suffering out-of-hospital cardiac arrest
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Background: Following the epidemiological development among the elderly population in the western society, robust data on mortality and quality of survival after Out-Of Hospital Cardiac Arrest (OHCA) are of major importance. Moreover the assessment of predictors for survival and good outcome seems to crucial assist physicians and healthcare providers, which are faced with an ethic dilemma to decide for or against the initiation of full resuscitation efforts in especially elderly victims of OHCA.

Methods: Out of 7039 patients suffering OHCA in Vienna during our observation period (09/2013–09/2015), a total of 2223 individuals, receiving resuscitation attempts by the Municipal Ambulance Service of Vienna, were included in the final analysis. Patients were stratified according to age in “middle-aged individuals” (<65 years), “young old individuals” (65–74 years), “old individuals” (75–84 years) and “very old individuals” (>85 years).

Results: Despite equal cardiac arrest related characteristics and similar performance in advanced life support comparing age-groups, we found an increasing rate of 30-day mortality (+21.8; p=0.001) and unfavorable neurological outcome (+18.8%; p=0.001) with increasing age, comparing the youngest to the oldest age-group. Moreover, established predictors for mortality – according to “Witnessed Cardiac Arrest”, “Bystander Basic Life Support” or “Cardiovacular Cause of Cardiac Arrest” – lost their predictive potential on survival with increasing age even after adjustment for potential confounders. Independently an initially shockable ECG proved to be predictive on survival among all age groups with an adjusted hazard ratio of 2.32 (95% CI 1.54–4.16, p=0.001) for “<65 years”, 2.43 (95% CI 1.54–4.16, p=0.001) for “65–74 years”, 1.64 (95% CI 1.04–2.63, p=0.035) for “75–84 years” and 2.04 (95% CI 1.89–2.38, p=0.003) for “>85 years”. Moreover “trajily” was directly associated with mortality (HR of 1.22 (95% CI 1.01–1.50, p=0.049), showing a 30-day survival of 3% with the exceptionally poor favorable neurological outcome of 1.1% among elderly individuals.

Conclusion: An initially shockable ECG proved to be a suitable tool for risk-assessment and decision-making to predict outcome in elderly victims of OHCA. However, the outcome of elderly cardiac arrest patients seemed to be exceptionally poor in frail individuals and needs to be taken into considerations in order to reduce the burden of unnecessary treatment decisions.

P4767 | BEDSIDE
Transthoracic impedance data used to compare the quality of resuscitation of in-hospital cardiac arrests in critical care departments and general wards
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Background: Staff in critical care departments such as the emergency department, the cardiology care unit and intensive care unit deal with critically ill patients on a daily basis. Staff in these departments presumably have more experience in providing life support. Whether this translates into a higher quality of basic life support decisions and needs to be taken into consideration in order to reduce the burden of unnecessary treatment decisions.

Methods: All in-hospital cardiac arrests (IHCA) occurring at a regional hospital in Denmark over a 3-year period from 2011 until 2014 were prospectively included in the study. The quality of resuscitation was evaluated primarily through transthoracic impedance data which provide information on response times, chest compression rate, and no flow fraction (fraction of time without chest compressions). Data were collected from the hospital switch board (time of arrest), from transthoracic impedance data from automated- and manual defibrillation devices.

Results: Combination of transthoracic impedance data and automatic defibrillation was seen in 7.1% of all IHCA during the study period. For the remaining 92.9% of IHCA, automatic defibrillation was not used. Transthoracic impedance data showed that the quality of basic life support decisions was significantly better in critical care departments compared to general wards (p<0.001). Furthermore, when performing CPR, critical care staff provided significantly more chest compressions, had a significantly faster response time and significantly more effective no-flow fractions (p<0.001). The quality of chest compressions were also significantly better in critical care departments compared to general wards (p<0.001). When comparing to the quality of basic life support decisions and the quality of chest compressions, critical care staff did not show any significant difference.

Conclusion: Transthoracic impedance data is a useful tool to evaluate the quality of basic life support decisions. Staff in critical care departments should be encouraged to use transthoracic impedance data to improve the quality of basic life support decisions.
fibrillators. Transthoracic impedance data were analysed using CODE-STAT re-
viewer software. Out-of hospital cardiac arrests were excluded.

**Results:** A total of 335 cardiac arrest calls were recorded in the study period; 189 were identified to be IHCA of which 85 cardiac arrests occurred in a critical care department and 104 in the general wards. Mean episode duration was 514 seconds in the critical care departments vs 544 seconds in the general wards (P=0.75). Significantly more shockable rhythms were detected at first rhythm analysis in the critical care departments 35% versus 11% in the general wards (P=0.004). Time to first rhythm analysis was on average 77 seconds in critical care departments vs 96 seconds in general wards (P=0.81) and time to first shock was 60 seconds vs 188 seconds respectively (P=0.41). The chest compression rate per minute in the critical care departments was significantly closer to the in-
ternational guidelines (100–120 min-1) with 122 compressions per minute versus 127 in the general wards (P=0.04). The no flow fraction (21% vs 25%, P=0.11) and 30-day survival was not statistically different among critical care departments and general wards respectively (29% vs 21%. P=0.24).

**Conclusions:** The quality of BLS showed trends towards a better quality in the critical care departments when compared to general wards. There were signifi-
cantly higher rates of initial shockable rhythms in the critical care departments, however, survival rates were not statistically different to general wards. Transth-
racic impedance data can be used to evaluate quality of resuscitation from IHCA.

**Acknowledgement/Funding:** The Research Pool of the Region of Southern Denmark, The Developmental Council and Chief Physicians' Council Vejle Hos-
pital, The Hede-Nielsen Foundation.

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**P4769 | BEDSIDE**

**Deoxyribonucleic acid damage measured by comet assay in succefully resuscitated humans**

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**Background:** Out-of-hospital cardiac arrest (OHCA) results in a whole body is-
chemia. The prognostication of outcome based on deoxyribonucleic acid (DNA) damage remains unknown.

**Purpose:** To test, whether OHCA may induce DNA damage measured by comet assay in successfully resuscitated victims.

**Methods:** The prospective, controlled and blinded study (1/2013–1/2014). In pa-
ients successfully resuscitated from non-traumatic OHCA (n=17; 63±14 years; men 71%, arrest of cardiac aetiology 32%, witnessed arrest 83%). DNA damages (double strand breaks /DSBs/) were measured using comet assay in peripheral lymphocytes sampled at admission. Data records: according to the Utstein proto-
tocol. The good prognostic outcome: alive at 30-days. Healthy controls (n=10). Data expression (mean±standard deviation).

**Results:** From patients: 81% (33/41) were alive at 30-days, 19% (8/41) died in a hospital. DSBs were: 11.2±7.9 in survivors; 10.4±6.8 in patients who died; 1.96±1.63 in controls with significant differences between patients and controls (Fig). DSBs measured by comet assay seem to be not able to predict good prog-
nosis (AUC = 0.527; 95% CI 0.284-0.706).

**Conclusion:** Five variables easy-to-obtain in the early moments after cardiac resuscitation are useful to predict 6 months prognosis after induced hypothermia in patients with out-of-hospital cardiac arrest.

**Acknowledgement/Funding:** Supported in part by the Spanish Ministry of Sci-
ence and Innovation (Red RIC, PLE2009-0152).

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**P4770 | BEDSIDE**

**SYNTAX score as a prognostic tool in non-STEMI patients resuscitated from sudden cardiac arrest**


**Purpose:** Sudden cardiac arrest (SCA) is one of the leading causes of death in developed countries. The prognostic impact of coronary artery disease (CAD) is uncertain in non-STEMI patients. Therefore, our purpose was to evaluate the association between SYNTAX score (CAD extension/complexity index) and mor-
tality.

**Methods:** We retrospectively collected single-center data from 184 non-STEMI patients resuscitated from SCA admitted between March 2004 and January 2015 who underwent coronary angiography (CA). We selected for the analysis only those patients with shockable rhythm at admission. We calculated the SYNTAX score for each patient, and residual-SYNTAX for those with previous revascular-
ization. Survival was recorded up to 5-year follow up (mean 30.4±23.8 months).

**Results:** A total of 136 patients with a mean age of 61±15.3 years were included, 88.2% with ventricular fibrillation and 11.8% with ventricular tachycardia as initial rhythm, 68.3% were out-of-hospital SCA, and 82.2% were comatose at admis-
sion. Excluding patients with SYNTAX 0 (38.2%), median SYNTAX score was 14.3 (IQR 8 to 24.4). Survival to discharge was 81.6%. SYNTAX score was predictive of long-term mortality ( Cox proportional hazards univariate regression OR 1.03, p=0.018). Using a ROC-curve, a SYNTAX score of 10 had the best sensitivity (55%) and specificity (63.5%) for predicting survival. Kaplan-Meier curves showed higher survival in the group with SYNTAX score
Cardiac arrest

≤10 (Log Rank, p=0.043). In landmark analysis, mortality differences were found in the first year after SCA (Figure).

Conclusions: In this selected SCA population, SYNSTAT score was a valuable tool to assess the prognosis of patients resuscitated from shockable rhythm SCA without STEMI. Further studies are warranted to confirm this hypothesis.

P4771 | BEDSIDE

Comparison of neurological outcome between the primary percutaneous intervention-first and target temperature management-first strategies in out-of-hospital cardiac arrest patients

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Background: Target Temperature Management (TTM) improves neurological outcome in out-of-hospital cardiac arrest (OHCA) patients. It is noted that TTM should be performed for OHCA patients as soon as possible. On the other hand, we also have to perform emergency coronary angiography and primary percutaneous coronary intervention (PCI) against ongoing myocardial ischemia for the patient after cardiac arrest of cardiac etiology. However, there have been few studies showing which therapy should be done first.

Methods: J-PULSE-Hypo Registry consisted of 14 institutes and retrospectively collected the patient post cardiac arrest of cardiac etiology between January 2005 and March 2011 to study the effect of TTM. These patients were divided into the PCI first group and the TTM first group to compare neurological outcomes after cardiac arrest. The PCI first group was defined as that we performed PCI before induction of TTM, whereas the TTM first group was defined as that we introduced TTM before PCI. A favorable outcome was defined as a Cerebral Performance Category (CPC) of 1–2.

Results: A total of 401 patients after cardiac arrest of cardiac etiology were enrolled in the present study. All patients underwent both PCI and TTM. There were no significant differences between the PCI first group (n=95) and the TTM first group (n=106) in age, the rate of witnessed arrest, by standar coronary resuscitation (CPR) and initial cardiac rhythm. The frequency of multi-vessel disease and mechanical support usage also had no significant differences. The PCI first group had a longer median interval from collapse to induction of TTM (PCI-first, 178 [87–246] min vs TTM-first, 48 [32–65] min; P=0.01), from the ROSC to induction of TTM (PCI-first, 150 [52–219] min vs TTM-first, 21 [8–48] min; P=0.05) and the time to achieve target core temperature (PCI-first, 330 [203–467] min vs TTM-first, 179 [80–295] min; P=0.01) than the TTM first group. There were no significant differences in the rate of favorable outcome at 30 days (PCI-first, 54% vs TTM-first, 50%; P=0.67) and 90 days (PCI-first, 52% vs TTM-first, 51%; P=0.98). There were no significant differences between the PCI-first and TTM-first groups in terms of neurological outcome and survival in OHCA patients although PCI-first strategy delayed the induction of TTM. The application of both treatment seems to be superior to their sequences for the particular OHCA patients.

Conclusions: The present multicenter registry studies indicate that the timing of PCI did not significantly affect neurological outcome and survival in OHCA patients although PCI-first strategy delayed the induction of TTM. The application of both treatments seems to be superior to their sequences for the particular OHCA patients.

P4772 | BEDSIDE

Neuron specific enolase (NSE) as marker of outcomes in out of hospital cardiac arrest acute myocardial infarction survivors treated with endovascular mild therapeutic hypothermia


Background: The prediction of outcome in comatose patients after out of hospital cardiac arrest (OHCA) was major ethical and socioeconomic implications. At present, there is a lack of data comparing the predictive value of serial measurement of neuron specific enolase (NSE) in OHCA survivors treated with endovascular therapeutic hypothermia.

Methods: 86 OHCA patients (4414 years, 69 men) were evaluated after OHCA due to ventricular fibrillation (VF) during an acute myocardial infarction (MI). All patients (NSTEMI 28%, STEMI 72%) were indicated for urgent coronary angiography (percutaneous coronary intervention was performed in 79% patients, NSTEMI 58%, STEMI 89%), echocardiography for left ventricular ejection fraction (LVEF) estimation using Simpson biplane formula and treated with mild therapeutic hypothermia (MTH) using intravascular temperature management to maintain target temperature (33 °C) for 24 hours. Serial measurements of serum NSE were performed on day 1, 2, and 3 after admission. The Cerebral Performance Categories scale (CPC) was used as the outcome measure and was assessed 3 months post admission; a CPC of 3–5 was regarded as a poor outcome (n=45), and a CPC of 1–2 (n=41) as a good outcome.

Results: Baseline NSE levels were not significantly higher on day 1 (p=0.26) giving than in patients with non-diagnostic electrocardiogram after SCA (33.2; 19.2–57.4 μg/L vs NSTEMI ≤ 30 μg/L). On day 2, NSE levels were significantly higher (p=0.001) in CPC 3–5 group (baseline 42.8; 28.6–67.5 μg/L vs CPC 1–2 patients 20.6; 11.8–50.6 μg/L). On day 3, NSE levels were significantly higher (p=0.001) in CPC 3–5 group (mean 46.1; 95th percentile 16.6–208.3 μg/L) compared with CPC 1–2 patients (17.2; 7.8–43.7 μg/L). No significant differences in NSE (40; 22–50 vs 40; 21–62; p=0.028) and peak cardiac troponin T (1.5; 0.08–10.00 vs. 0.64; 0.04–5.26 μg/L; p=0.078) were found in CPC 3–5 and CPC 1–2 groups comparison. Using an optimal cut-off value ≥ 31.8 μg/L calculated from the receiver operating characteristic curve (area under curve = 0.85; p=0.01), the sensitivity of predicting survival with poor neurological outcome was 77% and the specificity was 84%. Multivariate analysis model analysis revealed that 72 hours post admission NSE > 6.4 μg/L was an independent pre- dicator of CPC 3–5 outcome, with an adjusted odds ratio of 6.4 (95% confidence interval 1.98–20.48; p=0.001).

Conclusions: In patients after out of hospital cardiac arrest for ventricular fibrillation with acute myocardial infarction, serial neuron specific enolase (especially within 72 hours after hospital admission) measurements give reliable and on myocardial infarction extent independent information concerning outcome and prognosis after cardiopulmonary resuscitation.

P4773 | BEDSIDE

Burden of coronary artery disease and acute coronary lesions in patients resuscitated from cardiac arrest and non-diagnostic electrocardiogram


Background: Although coronary artery disease (CAD) represents the most common cause of sudden cardiac arrest (SCA), there is uncertainty regarding the indication and timing of coronary angiography (CA) in this setting. Treatment of acute coronary lesions (ACL) has demonstrated prognostic impact and they might remain undetected without CA in patients with non-STEMI post-resuscitation electrocardiogram.

Methods: From March 2004 to January 2015, 183 consecutive patients resuscitated from SCA and non-STEMI electrocardiogram who underwent CA during hospitalization were prospectively and consecutively recruited. For purposes of analysis patients were classified in two groups: shockable rhythm (n=136; 73.9%) and non-shockable rhythms (n=47; 26.1%). Analysis patients were classified in two groups: shockable rhythm (n=136; 73.9%) and non-shockable rhythms (n=47; 26.1%).

Result: SCA was witnessed in 95.9% of cases, 66.5% were out-of-hospital SCA and 70.7% were male patients. There were no significant differences in baseline characteristics between groups except for higher mean time to return of spontaneous circulation (median 19.1 vs. 13 min; p=0.031) and higher mean age (67.7 vs. 61.1 years; p=0.003) in the non-shockable rhythm group. Main CA findings are shown in Table. Overall 1-year mortality was 31.5%, higher in patients with non-shockable rhythms (47.9% vs. 25.7%; p=0.004). One-year survival of the overall cohort was lower in patients with untreated ACL (mean survival 6.8±1.24 months vs treated ACL or no ACL (8.9±0.38 months), p=0.260.

Table 1

<table>
<thead>
<tr>
<th></th>
<th>Shockable rhythm (n=136)</th>
<th>Non-shockable rhythm (n=47)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Syntax Score</td>
<td>10.52±11.88</td>
<td>9.42±12.6</td>
<td>0.53</td>
</tr>
<tr>
<td>Normal coronaries</td>
<td>41 (30.1%)</td>
<td>17 (35.4%)</td>
<td>0.50</td>
</tr>
<tr>
<td>Any coronary lesion (≥50%)</td>
<td>86 (63.2%)</td>
<td>26 (54.2%)</td>
<td>0.27</td>
</tr>
<tr>
<td>Any severe lesion (≥70%)</td>
<td>77 (57%)</td>
<td>24 (50%)</td>
<td>0.40</td>
</tr>
<tr>
<td>ACL</td>
<td>40 (29.6%)</td>
<td>7 (14.6%)</td>
<td>0.04</td>
</tr>
<tr>
<td>AChP-PCI</td>
<td>29 (21.6%)</td>
<td>4 (8.3%)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

AChP-PCI was defined as critical (non-CTO ≤ 90%) or thrombus containing lesions. PCI: punctaneous coronary intervention.

Conclusion: In this selected SCA cohort with non-diagnostic electrocardiogram, initial shockable rhythm patients had the same global burden of CAD (defined as similar Syntax score). However, this group had higher incidence of ACL and higher need for ad-hoc PCI. Giving that one in four patients with non-diagnostic electrocardiogram after SCA will have an ACL, early CA should probably be mandatory at least in shockable rhythm patients.
P4774 | BEDSIDE
Usefulness of the change in neuron specific enolase levels in out-of-hospital cardiac arrest survivors prognosis

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**Background:** Determination of the neurological prognosis after an out-of-hospital cardiac arrest (OHCA) in patients undergoing mild therapeutic hypothermia (TH) is challenging. Among different clinical and laboratory findings, neuron specific enolase (NSE) levels, and specifically its changes during the first days after OHCA, have emerged as markers of neurologic outcome.

**Purpose:** To determine the relationship between changes in NSE blood levels during the first days of admission and neurological and hospital mortality. 

**Methods:** Prospective registry of all patients admitted in two public hospitals after an OHCA due to a shockable rhythm and treated with TH for persistent unconsciousness, from October 2006 to October 2015. Our protocol includes rapid endovascular cooling to target temperature T=33°C to be maintained during a 24-hour period, and progressive re-warming. First NSE (NSE1) level was obtained during the first 72 hours of hospitalization and second NSE (NSE2) after the first 72 hours. Neurological prognosis at discharge was measured with cerebral performance category (CPC) scale.

**Results:** During this 7-year period, 141 patients were included, but only since May 2011, NSE has been determined. Thus, in 62 patients, 53 men and 9 women, mean age 57.9 years (SD 12.5 years), two measurements (NSE1 and NSE2) were obtained. NSE level was obtained in 99 hours (mean) after OHCA, and 82.9 hours (mean) after OHCA. The frequency of cardiovascular risk factors was: tobacco use 48.4%, arterial hypertension 56.5%, diabetes mellitus 16.1%, dyslipidemia 46.8% and chronic renal failure 21%. Only 22.6% of the patients suffered from previous known heart disease. The final diagnosis was: acute coronary syndrome (ACS) 62.9%, ischemic heart disease (non-ACS) 9.7%, cardiomyopathies 14.5%, congenital heart disease 3.2% and channelopathies 3.2%. Global hospital mortality was 25.8%. The change in neuron specific enolase levels (ΔNSE) (ΔNSE = NSE2−NSE1; NSE1 > 100) was not associated with time form OHCA to cardiopulmonary resuscitation or time from OHCA to return of spontaneous circulation (ROSC). However, we could establish an association between ΔNSE and CPC at discharge (ΔNSE−33.2±25.5 μg/ml in patients with CPC 1–2 at discharge; ΔNSE=28.3±14.1 μg/ml in patients with CPC 3–5 at discharge; p=0.003). Moreover, ΔNSE was also associated with hospital mortality: ΔNSE−30.4±26.7 μg/ml in patients discharged alive; ΔNSE+43.3±92.0 μg/ml in patients who died during admission (p=0.006).

Conclusions: A decrease in NSE levels, obtained in the first days of admission, was a powerful mortality and poor neurological prognosis predictor at discharge, while a decrease was associated with better outcomes. The change in NSE could be very helpful in decision making.

P4775 | BEDSIDE
Protein S100-beta as a marker of outcomes in out of hospital cardiac arrest acute myocardial infarction survivors treated with endovascular mild therapeutic hypothermia

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**Background:** The prediction of outcome in comatose patients after out of hospital cardiac arrest (OHCA) has major ethical and socioeconomic implications. Predictive value of protein S-100B was examined in OHCA survivors treated with endovascular therapeutic hypothermia.

**Methods:** 86 patients (64±14 years, 89 men) were evaluated after OHCA due to ventricular fibrillation (VF) due to acute coronary syndrome. 30 patients suffered from previous known heart disease (STEMI n=23; NSTE MI n=13). Patients (NSTEMI 28%, STEMI 72%) were included for urgent coronary angiography, echocardiography for left ventricular ejection fraction (LVEF) estimation using Simpson biplane formula and treated with mild therapeutic hypothermia (MTH) using intravascular temperature management to maintain target temperature (33 °C) for 24 hours. Measurements of serum NT-proBNP, S-100B and NT-proANP were performed within 2 hours after admission. The Cerebral Performance Categories scale (CPC) was used as the outcome measure and was assessed 3 months post admission; a CPC of 3–5 was regarded as a poor outcome (n=45), and a CPC of 1–2 as a good outcome.

**Results:** On day 3 protein S100 levels were significantly higher (p<0.01) in patients with poor outcomes (CPC 3–5) after OHCA (median 0.12; 5–95th percentile 0.05–1.18 g/L) compared with CPC 1–2 patients (0.09; 0.03–0.25 g/L). No significant differences in NT-proANP were observed on day 1, but in patients with STEMI, NT-proANP was significantly higher (p=0.008). Mean levels of NT-proANP were 348±370 pg/ml in patients discharged alive and 72 h after return of spontaneous circulation (ROSC). However, we could establish an association between NT-proANP and CPC at discharge (NT-proANP > 300 pg/ml in patients with CPC 1–2 at discharge; NT-proANP=739±312 pg/ml in patients with CPC 3–5 at discharge; p=0.0001) and in ROC curves (AUC 0.74, 95% CI 0.63–0.86). Kappa revealed the duration of survival was dependent on levels of NT-proANP (above or below 1.5 pg/ml; p<0.0002 in Cox test).

Conclusions: Higher concentration of NT-proANP, reflecting superior function of endothelium and better counteracting postresuscitation inflammatory response, enhances survival after CA.

P4776 | BEDSIDE
High sensitivity Troponin T as a prognostic marker after out of hospital cardiac arrest. A Targeted Temperature Management (TTM) trial substudy

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**Background:** Prognostication of unconscious patients after successful resuscitation is challenging and better prognostic markers are highly needed. Ischemic heart disease is a common cause of out of hospital cardiac arrest (OHCA). Whether or not high-sensitivity troponin T (hs-TnT) is a prognostic marker among survivors of OHCA with both ischemic and non-ischemic aetiologies remains to be settled.

**Purpose:** We sought to evaluate the ability of hs-TnT to prognosticate all-cause mortality, death due to cardiovascular causes or multi organ failure and death due to cerebral causes after OHCA. The influence of the level of target temperature management on hs-TnT as a marker of infarct size was also assessed.

**Methods:** A total of 699 patients treated with TTM (46% in the TTM-1 substudy) were included and hs-TnT was analysed in blood samples from 24, 48 and 72 h after return of spontaneous circulation (ROSC). A logistic regression model was used to assess the association between hs-TnT and 180-day all-cause mortality, death due to cardiovascular causes or multi organ failure and death due to cerebral causes. Subgroups based on the initial ECG after ROSC (ST-elevation myocardial infarction (STEMI) vs other ECG presentations) were analysed.

**Results:** hs-TnT was independently associated with all-cause mortality (at 48h: OR 1.10, CI 1.01–1.20, p<0.05). hs-TnT was also an independent predictor of death due to cardiovascular causes or multi organ failure (at 48h: OR 1.13, CI 1.01–1.26, p<0.05). In patients with STEMI, hs-TnT was independently associ-
ated with death due to cardiovascular causes or multi organ failure (at 48h: OR 1.47, CI 1.10–1.95, p<0.01). No association between hs-TnT and death due to cerebral causes could be detected. Therapeutic hypothermia treatment at 33 °C did not reduce hs-TnT compared to 36 °C.

Conclusions: After OHCA due to both ischemic and non-ischemic causes, hs-TnT is an independent marker of both all-cause mortality and death due to cardiovascular causes or multi organ failure. Therapeutic hypothermia treatment at 33 °C did not reduce hs-TnT compared to 36 °C.

Acknowledgement/Funding: This work was funded by the Swedish Heart-Lung Foundation and the Swedish Research Council.

**BIOMARKERS AND PROGNOSTICATION IN ACUTE CARDIOVASCULAR CARE**

**P4778 | BEDSIDE**

The value of NT-proBNP during and after primary PCI in predicting major adverse cardiovascular events and short term mortality

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Background: NT-proBNP predicts mortality over and beyond risk scores in STEMI patients, treated with primary percutaneous coronary intervention (PPCI). However, optimal time of NT-proBNP measurement and its predictive value for non-fatal major adverse cardiovascular events (MACE) is still under investigation.

Purpose: To determine the optimal time of NT-proBNP measurement for MACE prediction in STEMI patients treated with PPCI.

Methods: PPCI patients in the On-Time 2 study, a randomized trial assessing the effect of additional Tirofiban, were candidates (N=861). NT-proBNP levels on admission, at 18–24 hours, at 72–96 hours, and the change in NT-proBNP from baseline to 18–24 hours (delta NT-proBNP) were measured. Also, in each patient the Zwolle Risk Score (ZRS) was assessed. We compared the predictive value (receiver operator curves) of the NT-proBNP levels and ZRS for mortality, non-fatal MACE and major bleeding at 30 days follow-up.

Results: 845 patients were included. On multivariate analyses, NT-proBNP at the different periods of time and ZRS all independently predicted death at 30 days (AUC 0.87–0.94, all P<0.01). However, optimal discriminatory accuracy was reached with NT-proBNP at 18–24 hours (AUC of 0.94, 95% CI 0.90–0.99). For non-fatal MACE and major bleeding NT-proBNP at 18–24 hours showed a moderate predictive value, particularly in combination with the ZRS revealing AUC's of 0.70 (0.62–0.79) and 0.78 (0.68–0.87) respectively.

Conclusions: NT-proBNP measured at 18–24 hours after PPCI has excellent predictive value, particularly in combination with the ZRS revealing AUC's of 0.70 (0.62–0.79) and 0.78 (0.68–0.87) respectively.

**P4779 | BEDSIDE**

Diagnostic and prognostic value of the V-index in patients with symptoms suggestive of acute myocardial infarction


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Introduction: The V-index is an ECG marker quantifying the spatial heterogeneity of ventricular repolarization. We prospectively investigated the diagnostic and prognostic value of the V-index in patients with symptoms suggestive of acute myocardial infarction (AMI).

Methods: We enrolled 582 patients presenting with suspected AMI to the emergency department (ED) in a prospective observational study. Twelve lead ECGs of five minutes were recorded at presentation to the ED. The V-index was calculated in a blinded fashion. Final diagnosis was adjudicated by two independent cardiologists. Patients were followed for the endpoint of all-cause mortality.

Results: AMI was the final diagnosis in 16% of patients. Values for the V-index at presentation were higher in patients with AMI compared to other causes of chest pain (23ms (IQR 18–28) vs. 18ms (IQR 15–24), p<0.001). The diagnostic accuracy of the V-index at presentation for the diagnosis of AMI as quantified by the area under the receiver operating characteristic curve (AUC) was 0.64 (95% CI 0.57–0.71). The use of the V-index in addition to conventional ECG criteria improved the sensitivity of the ECG for MAI from 41% to 85% (p<0.001). Median V-index levels in deceased patients were significantly higher as compared to survivors (28ms (IQR 22–37) vs. 19ms (IQR 15–24), p<0.001). Cumulative 24-month mortality rates were 99.5%, 97.2% and 90.4% according to tertiles of the V-index (p<0.001). In multivariable Cox proportional hazard analysis, the V-index significantly predicted mortality independently of age and high-sensitive cardiac Troponin T (hs-cTnT).

**P4780 | BEDSIDE**

Clinical value of serum procalcitonin for diagnosis of infection in patients with acute myocardial infarction

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Background: A significant proportion of patients with acute myocardial infarction (AMI) also present with signs or symptoms of Systemic Inflammatory Response Syndrome (SIRS) but the exact incidence of infection in this population is unknown. Thus, when AMI patients become febrile, it may be difficult for the clinician to decide whether empirical antibiotic treatment is warranted. Serum Procalcitonin (PCT) is known to be elevated in bacterial infections but may also be elevated to a small extent in AMI patients. It is unknown whether PCT levels can be utilized to differentiate between AMI patients with and without bacterial infection, in order to avoid unnecessary antibiotic use.

Methods: Serum PCT was collected within 24 hours from patients presenting with AMI. Baseline characteristics, clinical and bacteriological data were collected prospectively. Determination of infection was determined by two experienced physicians and one infectious diseases specialist. Patients with procalcitonin values above the 95th percentile were excluded. Four cut-points for procalcitonin were examined (based in part on prior literature): 2.0, 0.5, 0.2, and 0.1 ng/mL. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and area under the ROC curve (AUC) were calculated for each cut-point. The value with the highest Youden’s index was chosen as the best cut-point.

Results: After censoring 9 patients that had PCT value above the 95th percentile, this analysis included 171 patients (age 62.8±14), from which 25 (14.8%) were determined to be infected. Mean PCT values was 0.35 [IQR 0.049–0.13]. The predictive performance of the 4 possible cut-points for procalcitonin is presented in the figure. **Conclusion:** The V-index, an ECG marker quantifying the spatial heterogeneity of ventricular repolarization, significantly improves the sensitivity of the ECG for the diagnosis of AMI and predicts mortality in patients with suspected AMI independently of age and hs-cTnT.
in the Table 1. The cut-point of 0.1 had the highest Youden’s index (76%). This cut-point was 92% sensitive and 84% specific; the AUC for this cut point was 0.88.

Table 1. Performance of PCT cut points

<table>
<thead>
<tr>
<th>Cut-point</th>
<th>Patients classified as at-risk</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive predictive value</th>
<th>Negative predictive value</th>
<th>Youden’s index</th>
<th>AUC 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥0.2</td>
<td>5%</td>
<td>16%</td>
<td>97%</td>
<td>50%</td>
<td>87%</td>
<td>13%</td>
<td>0.57</td>
</tr>
<tr>
<td>≥0.5</td>
<td>15%</td>
<td>52%</td>
<td>92%</td>
<td>52%</td>
<td>92%</td>
<td>44%</td>
<td>0.72</td>
</tr>
<tr>
<td>≥0.5</td>
<td>19%</td>
<td>68%</td>
<td>92%</td>
<td>52%</td>
<td>92%</td>
<td>44%</td>
<td>0.72</td>
</tr>
<tr>
<td>≥0.1</td>
<td>27%</td>
<td>92%</td>
<td>84%</td>
<td>54%</td>
<td>97%</td>
<td>76%</td>
<td>0.76</td>
</tr>
</tbody>
</table>

Conclusions: By utilizing serum PCT≥0.1ng/mL as a benchmark value for infection, serum PCT may be utilized to exclude infection in other AMI patients. The utilization of this readily available test should be explored in a large prospective interventional trial.

Acknowledgment/Funding: The study was funded in part by bioMérieux, Marcy l’Etoile, France

P4781 | BEDSIDE

Hypocalcemia at admission as a prognostic marker in STEMI patients


Purpose: Hypocalcemia is prevalent among critically ill patients, and has been linked with disease severity and mortality. Nowadays, the impact of hypocalcemia in patients with acute coronary syndrome remains unknown. Our aim was to analyze the value of total calcium as a prognostic marker in patients with ST-segment elevation myocardial infarction (STEMI).

Methods: From January of 2013 to December of 2015, 550 consecutive STEMI patients admitted to an Acute Cardiac Care Unit of a tertiary hospital were prospectively recruited. All clinical, analytical, echocardiographic and angiographic features were recorded. Patients were followed up to 6 months after hospital discharge.

Results: Mean age of our population was 64 (13.5) years and 415 patients (75.5%) were men. Main cardiovascular risk factors were also identified: hypertension (53.1%) diabetes (21.5%), hypercholesterolemia (38.5%), smoking habit (51.3%), peripheral vascular disease (5.3%); 11.8% had a previous myocardial infarction (MI) and 5.1% a previous stroke. At admission, mean systolic blood pressure and heart rate were 123 (24.9) mmHg and 77 (17.7) bpm, respectively while mean calcium level was 8.7 mg/dl (0.66). During hospitalization 28 (5.1%) patients died. We performed a multivariate analysis to identify independent risk factors associated with a high mortality. We included in the analysis those variables that resulted statistically significant in the univariable analysis and those considered clinically relevant: age, gender, previous MI, previous coronary artery bypass grafting, number of arteries with severe disease, calcium level at admission, CRUSADE score, ejection fraction and the worst Killip-Kimball (KK) class during hospitalization. We identified hypocalcemia [OR 4.76: 95% CI [1.12–20); p=0.034], age [OR 1.13: 95% CI [1.02–2.15]; p=0.01] and the worst KK class [OR 3.59: 95% CI [1.39–9.28]; p=0.008] as independent predictors of in-hospital mortality in STEMI patients.

Conclusion: In our population of STEMI patients, hypocalcemia is independently associated with a higher mortality. Total calcium level is a cheap and easy laboratory parameter to obtain and allows early identification of STEMI patients at a higher mortality risk.

P4782 | BEDSIDE

Additive prognostic value of copeptin and NT-proBNP in patients with acute heart failure

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Background: Patients suffering from acute heart failure (AHF) requiring admission to an intensive care unit (ICU) have a poor prognosis. The C-terminal portion of prooppressin (Copeptin) represents a surrogate parameter for vasopressin and has been described as a marker for endogenous stress. Besides its use as a rule-out marker in patients with NSTE-ACS it acts as a prognostic marker in critically ill patients with various diseases.

Purpose: The aim of this study was to analyze whether admission levels of copeptin are associated with 30-day survival in patients with AHF admitted to a cardiac ICU.

Methods: We included 90 consecutive patients with AHF admitted to our cardiovascular ICU (33% with cardiogenic shock, 21% with acutely decompensated HF and 46% of patients suffered from AHF after cardiac arrest). Blood was taken at admission and levels were measured by real-time PCR while copeptin was measured by an automated sandwich immunofluorescent assay.

Results: Mean age was 62.1±16.0 years, 76.7% of patients were male and mean NT-proBNP levels were 4986 (1525–23842) pg/mL. 30-day survival was 64.4%. Non-survivors had significantly higher values of both copeptin (139.8 (44.7–311.2) pmol/L vs. 31.4 (17–77.1) pmol/L; p<0.001) and NT-proBNP (23778 (2981–35000) pg/mL vs. 3828 (1000.3–8212.3) pg/mL; p<0.001). Interestingly, copeptin and NT-proBNP showed additive prognostic value. When patients were stratified according to the median of NT-proBNP and copeptin, those with both high NT-proBNP and NT-proBNP levels above the median had the highest risk of dying (HR 4.6, p<0.003).

Conclusion: In a cohort of patients with AHF requiring ICU admission, copeptin levels measured at admission added prognostic value to NT-proBNP levels.

P4783 | BEDSIDE

Early diagnosis of acute myocardial infarction in patients with just minimally elevated levels of high-sensitive troponin T: Incremental value of copeptin and of high-sensitive troponin deltas


Background: The early diagnosis of AMI in patients with only mild elevations of high-sensitivity cardiac troponin (hs-cTn) is a particular diagnostic problem. It is unclear whether copeptin, a marker of endogenous stress, or 1h-hs-cTn changes are better suited to address this important unmet clinical need.

Purpose: To investigate the diagnostic and prognostic accuracy of copeptin and 1h-hs-cTn deltas when used in combination with hs-cTnT.

Methods: We prospectively enrolled 1439 unselected patients presenting with symptoms suggestive of AMI. The final diagnosis was adjudicated by two independent cardiologists. Mild hs-cTnT elevations were defined as blood concentrations between 14ng/L (99th percentile) and 50ng/L. We compared the diagnostic accuracy of copeptin, 1h-hs-cTn deltas and its combinations.

Results: Of all patients, 316 (22%) had hs-cTnT concentrations between 14–50ng/L. Within this group, AMI was the final diagnosis in 90 patients (29%). The diagnostic accuracy for the diagnosis of AMI as quantified by the receiver-operator characteristics curve (AUC) was only moderate for hs-cTnT (AUC 0.65, 95% CI 0.59–0.72). The additional use of copeptin failed to improve diagnostic accuracy (AUC 0.66, 95% CI 0.59–0.72, p=0.63 for comparison). However, the addition of absolute 1h-hs-cTn deltas did improve diagnostic accuracy (AUC 0.85, 95% CI 0.79–0.90, p<0.001 for comparison).

P4784 | BEDSIDE

Hyperglycemia on admission and coronary reperfusion therapy during the acute phase of a STEMI in non-diabetic patients

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Introduction: The relation between hyperglycemia on admission and the mortality in short term after an acute coronary syndrome is a well-known notion that has been reported before and after the era of coronary revascularisation in particular among non-diabetic patients.

Objective: To analyse the effect of coronary reperfusion in the acute phase on the relation between the glycemia on admission and the in-hospital mortality of STEMI in non-diabetic patients.

Methods: We included patients admitted for STEMI based on their initial treatment and were followed during their hospital stay. Mild hs-cTnT elevations were defined as blood concentrations between 14–50ng/L. Within this group, AMI was the final diagnosis in 90 patients (29%). The diagnostic accuracy for the diagnosis of AMI as quantified by the receiver-operator characteristics curve (AUC) was only moderate for hs-cTnT (AUC 0.65, 95% CI 0.59–0.72). The additional use of copeptin failed to improve diagnostic accuracy (AUC 0.66, 95% CI 0.59–0.72, p=0.63 for comparison). However, the addition of absolute 1h-hs-cTn deltas did improve diagnostic accuracy (AUC 0.85, 95% CI 0.79–0.90, p<0.001 for comparison).

ROC-Curves for diagnostic accuracy

Conclusions: One fifth of all patients presenting with symptoms suggestive of AMI had minimal hs-cTnT elevations between 14–50ng/L at admission. The use of copeptin in addition to hs-cTnT could not improve the early diagnosis of AMI in these patients, but the use of 1h-hs-cTn deltas did.

Acknowledgment/Funding: Various diagnostic and therapeutic companies

Population and method: A prospective, multicentric study about 1222 non-
Hyperglycemia on admission is an independent predictive factor of short-term mortality in non diabetic patients during the acute phase of STEMI, its impact is more important in patients who benefit from a revascularisation therapy at an early stage.

### P4785 | BEDSIDE

**Predictors of in-hospital mortality in cardiogenic shock, prognostic and therapeutic implications**

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**Background:** Cardiogenic shock has a poor prognosis. The heterogeneity in the mortality through different subgroups suggests that some factors can be useful to perform risk stratification and guide management. We aimed to find predictors of in-hospital mortality in these patients.

**Methods:** We analyzed all the cases of cardiogenic shock due to medical conditions admitted in our intensive care coronary unit from 2010 till 2015. Clinical, biochemical, and hemodynamic variables were registered, as was INTERMACS profile.

**Results:** From a total of 281 patients, 28 died within the first 24 hours and were not included in the analysis. The 253 patients that survived the first 24 hours had a mean age of 69±14.3 years, and 68.8% were men. The most frequent aetiologies were: acute coronary syndrome (57.3%), acute heart failure (22.5%), and arrhythmias (13.8%). In-hospital mortality was 36.0%. The independent predictors of mortality were: age (OR 1.03 [1.003–1.062]), blood glucose (OR 1.004 [1.001–1.007]), heart rate (OR 1.014 [1.001–1.028]), and INTERMACS profile (OR 0.168 [0.107–0.266]).

**Baseline characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n=68.7 (14.4)</th>
<th>n=76 (30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men, n (%)</td>
<td>174 (88.8)</td>
<td>61 (24.1)</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>175 (69.2)</td>
<td>55 (21.7)</td>
</tr>
<tr>
<td>Diabetics, n (%)</td>
<td>92 (36.4)</td>
<td>35 (13.8)</td>
</tr>
<tr>
<td>Dyslipidemia, n (%)</td>
<td>203 (80.2)</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** INTERMACS profile at 24 hours is associated with higher in-hospital mortality in patients with cardiogenic shock. This and other prognostic variables (age, blood glucose, and heart rate) may be useful for risk stratification and selecting patients for advanced therapies.

### P4786 | BEDSIDE

**The additional prognostic value of anemia on admission over grace risk score in patients with acute coronary syndrome - a retrospective cohort study**

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**Introduction:** The GRACE risk score is the preferred tool for risk assessment in the current clinical practice guidelines in acute coronary syndromes (ACS). However, the GRACE score has several significant limitations, including an insufficient or almost absent data on the additional prognostic value of admission hemoglobin levels.

**Methods:** A total of 11,505 consecutive patients admitted to cardiac units in Israel with ACS (including ST elevation myocardial infarction (MI), non ST elevation MI and unstable angina) were included in our retrospective observational cohort study. The study population consisted of patients from the ACSIS registry (Acute Coronary Syndrome Israel Survey) between 2008 and 2013. Demographic data, risk factors for coronary disease and laboratory results were collected in all patients. The study population was classified into two main groups according to the GRACE score: (1) high GRACE score (≥140) and (2) low GRACE score (<140). The patients were then classified by hemoglobin levels on admission into three groups: HaB level ≥ 8/10 (severe anemia), Hb levels 8–12 gr/dl (mild anemia) and Hb level < 12 gr/dl (no anemia). We used in-hospital, 30-day and one-year mortality data in all patients.

**Results:** Patients with GRACE score ≥140 were more likely to die in-hospital and to have higher one-year mortality rate than patients with GRACE score below 140 (10.8% vs. 2.1% respectively, p<0.001). Patients with anemia had also higher one-year mortality rate than patients without anemia on admission (4.7% vs. 2.7%, respectively, p<0.001). In the low GRACE group, patients with severe anemia had higher mortality rate than patients with mild or without anemia (4% vs. 2%, respectively, p<0.001). In the high GRACE group, the presence of any anemia (mild or severe) was associated with an increased one-year mortality risk (12% vs. 7%, p<0.007).

**Conclusions:** Severe anemia is a high-risk predictor in ACS regardless of the GRACE risk score category. Our data suggest that anemia on admission in patients with ACS is associated with an increased one-year mortality rate regardless of the GRACE risk score category. Further prospective studies are necessary to further elucidate the additional prognostic value of hemoglobin levels on admission for risk assessment.

### P4787 | BEDSIDE

**The impact of admission blood glucose level on prognosis in cardiogenic shock**

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**Introduction:** Critically ill patients often present with hyperglycaemia, regardless of previous history of diabetes mellitus (DM). Stress hyperglycaemia has been associated with adverse outcome in acute myocardial infarction and acute heart failure, but data regarding cardiogenic shock (CS) are sparse.

**Purpose:** To investigate the impact of admission plasma glucose level on clinical picture and short-term mortality in CS.

**Methods:** We enrolled 219 adult CS patients, that were divided into five categories according to admission plasma glucose level (hyperglycaemia (glucose ≥140 mg/dl), normoglycaemia (glucose <120 mg/dl) and hypoglycaemia (blood glucose <40 mg/dl)). The patients were then classified by hemoglobin levels on admission into three groups: Hb levels <8 gr/dl (severe anemia), 8–12 gr/dl (mild anemia) and ≥12 gr/dl (no anemia). We used in-hospital, 30-day and one-year mortality data in all patients.

**Results:** Glucose levels were distributed equally between normoglycaemia (26% of patients) and mild (27%), moderate (20%) and severe (25%) hyperglycaemia, while hypoglycaemia (2%) was rare. Severe hyperglycaemia was associated with higher blood leukocyte count (17.3 E9/L), higher plasma lactate level (4.4 mmol/L) and lower arterial pH (7.23) compared with normoglycaemia or mild to moderate hyperglycaemia (p<0.001 for all). The hyperglycaemic patients presented with hyperlactatemia (8.3 mmol/L), acidosis (arterial pH 7.19) and high levels of NT-proBNP (26300 ng/L) and alamine aminotransferase (466 U/L), suggesting pro-
found hyperperfusion and hepatic congestion. In contrast, the normoglycaemic patients had normal levels of arterial pH (7.35) and plasma lactate (1.8mmol/L) despite the clinical manifestation of shock. 90-day mortality was highest among hyperglycaemic and severely hyperglycaemic patients (50% for both) compared with 26% in normoglycaemic patients (Figure 1.). Severe hyperglycaemia was an independent predictor of in-hospital mortality (OR 3.72, 95% CI 1.18–11.7, p=0.025), when adjusted for age, gender, LVEF, lactate and DM. Mean glucose level of survivors and non-survivors differed significantly among non-diabetic patients (10.1 vs. 12.9 mmol/L, p<0.009), but not among patients with prior DM (16.3 vs. 17.4 mmol/L, p=0.59).

Conclusions: Glucose level significantly affects the outcome in CS, and prior DM status modifes the prognostic value of plasma glucose. Mortality is highest among hyperglycaemic and severely hyperglycaemic patients. Moreover, severe hyperglycaemia is present at the moment of diagnosis in most patients and is associated with biochemical findings of hyperperfusion.

P4778 | BEDSIDE
Are there differences in the clinical presentation of men and women with acute myocardial infarction?

Background: Women are less likely to be diagnosed with myocardial infarction than men and have poorer outcomes. This has been partly attributed to diagnostic under-recognition. We report here more than any other typical symptoms and less reliable findings on electrocardiography. Whether these observations remain relevant with the use of sex-specific criteria for the diagnosis of myocardial infarction in men and women is uncertain.

Purpose: To identify whether gender differences exist in the presenting characteristics of men and women with myocardial infarction.

Methods: We prospectively characterised patients presenting with suspected acute coronary syndrome to an Emergency Department of a tertiary care centre in Scotland, UK (NCT 01852123). Detailed assessment of the presenting symptoms, cardiac risk factors and the electrocardiogram was performed by independent research nurses. Time from symptom onset to presentation was noted. The diagnosis of type 1 myocardial infarction was adjudicated by two independent cardiologists using all available clinical information and sex-specific thresholds for cardiac troponin I.

Results: In 1,298 patients (39% women) with suspected acute coronary syndrome, 190 patients had an adjudicated diagnosis of myocardial infarction with similar proportions of men and women (15.8% v 12.9%; p=0.18). There were no differences in the time from onset of symptoms to hospital presentation between men and women. Women were older (66.1 v 72.4 years, p=0.003), but just as likely to present with chest pain (88.8% v 89.2%, p=0.53) and less likely than men to display atypical pain features such as sharp, burning or stabbing pain (40% v 23%, p=0.03). No differences in ST-segment or T-wave changes on the electrocardiogram were observed. There was no difference observed in the major cardiovascular risk factors other than cigarette smoking which was more common in men (68% v 49%, p=0.02).

Conclusions: We observe no differences in cardiovascular risk symptoms, electrocardiographic findings or the frequency of diagnosis between men or women with myocardial infarction. Clinical suspicion for the diagnosis of myocardial infarction should not be influenced by gender if we hope to address disparities in treatment and outcomes.

Acknowledgement/Funding: Edinburgh Lothian Health Foundation

P4779 | BEDSIDE
Correlation of the measured and derived 22-Lead electrocardiogram from 3 measured leads
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Background: The cardiac electrical field is known to be dipolar and as such may be described by a 3-lead-vector space. There are 22 electrocardiogram (ECG) leads used in clinical practice including the standard 12-lead ECG, 4 right heart leads V3R-V6R, 3 posterior leads V7-V9, and 3 Frank lead vectorcardiography (VCG) leads X, Y, Z. It would be advantageous to derive this 22-lead ECG set from just 3 measured leads of the standard 12-lead ECG using a universal parameter space. (VCG) leads X, Y, Z. It would be advantageous to derive this 22-lead ECG set from just 3 measured leads and quantify the correlation with the measured 22-lead ECG.

Methods: ECGs were synthesized (mECG) including 123 standard 12-lead ECGs, 122 right heart ECG leads (V3R, V4R, V5R, V6R), and 42 posterior heart ECG leads (V7, V8, V9), and 112 VCGs (X, Y, Z Frank leads). Each ECG was interpreted by 2 physician reference standards including 11.7% interpreted as acute myocardial ischemic injury (AMI). Measured leads I, aVf, and V2 were chosen as the 3 lead-vector basis orthogonal set from which the derived ECGs (dECG) were synthesized from a UPTM using a NLO technique. The derived vs. measured test case ECGs were compared quantitatively using Pearson correlation (r), mean absolute deviation (MAD), root-mean-square error (RMSE), and a similarity coefficient.

Results: The dECGs showed very high quantitative correlations with mECGs with Pearson (r) average correlation 0.88±0.071 and similarity coefficient 0.99±0.019. The average MAD and normalized MAD were 5.8±4.54 and 0.185±0.048 respectively. No clinically significant differences were noted in any dECGs compared to the corresponding mECG. ECG rate, rhythm, segment, and axis interpretations showed 100% correlation. ECG morphologies interpreted as AMI showed 100% concordance.

Conclusions: The 22-lead ECG can be derived from the 3 measured ECG lead set (I, aVf, V2). The comparison of the mECGs and dECGs shows high quantitative and qualitative correlations. Using this technology a 22-lead ECG can be derived and displayed instantaneously and continuously in a real-time cardiac rhythm monitor to enhance patient observation capabilities to detect AMI and will allow for convenient and cost effective acquisition and analysis of the ECG in emergency departments, telemetry, and critical care areas of health care.

P4779 | BEDSIDE
Biomarkers and prognostication in acute cardiovascular care
979

Biomarkers and prognostication in acute cardiovascular care

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Background: At the time of symptom onset to presentation was noted. The diagnosis of type 1 myocardial infarction was adjudicated by two independent cardiologists using all available clinical information and sex-specific thresholds for cardiac troponin I.

Methods: We prospectively characterised patients presenting with suspected acute coronary syndrome to an Emergency Department of a tertiary care centre in Scotland, UK (NCT 01852123). Detailed assessment of the presenting symptoms, cardiac risk factors and the electrocardiogram was performed by independent research nurses. Time from symptom onset to presentation was noted. The diagnosis of type 1 myocardial infarction was adjudicated by two independent cardiologists using all available clinical information and sex-specific thresholds for cardiac troponin I.

Results: In 1,298 patients (39% women) with suspected acute coronary syndrome, 190 patients had an adjudicated diagnosis of myocardial infarction with similar proportions of men and women (15.8% v 12.9%; p=0.18). There were no differences in the time from onset of symptoms to hospital presentation between men and women. Women were older (66.1 v 72.4 years, p=0.003), but just as likely to present with chest pain (88.8% v 89.2%, p=0.53) and less likely than men to display atypical pain features such as sharp, burning or stabbing pain (40% v 23%, p=0.03). No differences in ST-segment or T-wave changes on the electrocardiogram were observed. There was no difference observed in the major cardiovascular risk factors other than cigarette smoking which was more common in men (68% v 49%, p=0.02).

Conclusions: We observe no differences in cardiovascular risk symptoms, electrocardiographic findings or the frequency of diagnosis between men or women with myocardial infarction. Clinical suspicion for the diagnosis of myocardial infarction should not be influenced by gender if we hope to address disparities in treatment and outcomes.

Acknowledgement/Funding: Edinburgh Lothian Health Foundation

P4779 | BEDSIDE
High-sensitivity cardiac troponin and sex-specific thresholds for the diagnosis of myocardial infarction

Background: High-sensitivity assays have identified important differences in cardiac troponin I concentrations between men and women. The use of contemporary troponin assays and a single threshold for the diagnosis of myocardial infarction may lead to under-diagnosis, particularly in women.

Methods: All consecutive patients with suspected acute coronary syndrome (n=738, 56.5% male) presenting to an Emergency Department were included. Troponin I concentrations were identified during the validation phase of a prospective clinical trial (NCT01852123). Cardiac troponin I concentrations were measured in parallel using a contemporary (single threshold 50 ng/L) and high-sensitivity (single threshold 3.5 ng/L for women and 16 ng/L for men) assay. Clinical decisions were based on the contemporary assay. The diagnosis of myocardial infarction was adjudicated by two independent cardiologists. Patients were stratified by peak high-sensitivity cardiac troponin concentration during the index presentation: women

Conclusion: A single hs-TnI measurement combined with a normal ECG ruled out AMI safely without need for serial troponin testing. Additionally, long-term prognosis in the general population was low when hs-TnI was below 3 ng/L, as compared to higher concentrations.

Table 1. Rule-out results using a hs-TnI 3 ng/L cut-off concentration with and without the information of a normal ECG

<table>
<thead>
<tr>
<th>hs-TnI</th>
<th>&lt;3 ng/L</th>
<th>&lt;3 ng/L</th>
<th>ECG normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>NPV</td>
<td>99.3 (97.4, 99.9)</td>
<td>100.0 (97.5, 100.0)</td>
<td></td>
</tr>
<tr>
<td>F-N+Tn</td>
<td>2+276=278</td>
<td>0+218=218</td>
<td></td>
</tr>
<tr>
<td>% of all Non-AMI</td>
<td>35.4 (32.1, 38.9)</td>
<td>28.0 (24.5, 31.3)</td>
<td></td>
</tr>
<tr>
<td>6 months mortality (%)</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

Conclusions: A single hs-TnI measurement combined with a normal ECG ruled out AMI safely without need for serial troponin testing. In addition, long-term prognosis in the general population was low when hs-TnI was below 3 ng/L.
<16 ng/L, >16 ng/L to <50 ng/L and >50 ng/L; men <34 ng/L, >34 ng/L to <50 ng/L and >50 ng/L. The primary outcome was a composite of recurrent myocardial infarction or cardiac death at one year. Logistic regression models were constructed with adjustment for age and co-variates. In secondary analysis we compared outcomes between single and sex-specific thresholds.

**Results:** The index diagnosis was type 1 myocardial infarction in 13.7% (651/4,738). Use of a high-sensitivity assay and sex-specific thresholds increased the diagnosis from 8.7% (180/2,061) to 13.0% (267/2,061) in women and from 6.5% (171/2,677) to 14.3% (384/2,677) in men (P < 0.001 for both). During 4,315 patient years follow up, patients with troponin concentrations below sex-specific diagnostic thresholds were at lowest risk of recurrent myocardial infarction or cardiac death (Figure 1). Women with troponin concentrations >16 ng/L and <50 ng/L and men >34 ng/L and <50 ng/L were at increased risk of adverse events (odds ratio [OR] 6.8, 95% confidence interval [CI] 2.2 to 21.4, and OR 5.8, 95% CI 1.9 to 16.2 respectively). In secondary analysis, event rates in women with troponin concentrations >16 ng/L and ≤26 ng/L were 10-fold higher than in those with troponin concentrations ≤16 ng/L (11% versus 0.9%, OR 6.1, 95% CI 1.2 to 24.6).

Conclusions: Use of a high-sensitivity cardiac troponin I assay and sex-specific diagnostic thresholds identified patients with suspected acute coronary syndrome at increased risk of recurrent myocardial infarction or cardiac death. Implementation of sex-specific diagnostic thresholds for myocardial infarction may improve patient outcomes through better targeting of therapies for coronary heart disease to those at highest risk.

Acknowledgement/Funding: British Heart Foundation

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**P4792** | BEDSIDE

**Safety and efficacy of the novel esc 0h/1h-protocol for rapid rule-out of myocardial infarction among women and men**


**Background:** We aimed to prospectively evaluate the safety and efficacy of the new ESC rapid 0h/1h-rule-out protocol for acute myocardial infarction (AMI), among women and men in order to assess potential gender-inequalities.

**Methods:** We enrolled consecutive patients presenting to the ED with suspected AMI in a prospective international multicenter study. Excluded were patients with ST-segment elevation or no available high sensitivity cardiac troponin (hs-cTnT) levels. The final diagnosis was adjudicated by two independent cardiologists. The safety and efficacy of the ESC 0h/1h-rule-out protocol, based on LOD (Undetectable levels of hs-cTnT at presentation) in combination with hs-cTnT 1h-algorithm was evaluated. Safety was quantified as the negative predictive value (NPV) for AMI in the rule-out zone. Efficacy was quantified as the percentage of the overall cohort assigned to the rule-out zone.

**Results:** Among all 2,213 patients, 32% were women and 68% men. AMI was the final diagnosis in 17% of patients (14% of women and 19% of men, p = 0.019). Using the ESC 0h/1h-rule-out protocol achieved a very high safety, with a NPV of 99.6% (95% CI, 98.4–100%) among women and 100% (95% CI, 99.6–100%) among men, p = ns. Regarding efficacy, the ESC rule-out protocol classified about 64% of women and 57% of men with suspected AMI (p = 0.002).

**Conclusions:** The current ESC 0h/1h-rule-out protocol using the combination of LOD and 1h-algorithm hs-cTnT is safe and effective and provides comparable results.
Coronary CT angiography for suspected acute coronary syndrome in the era of hs-troponins. This observational single-centre study included patients with the chief complaint chest pain and two troponin samples obtained at the ED between 1st of December 2014 and 14th of September 2015. Exclusion criteria were ST-elevation myocardial infarction or ventricular tachycardia on the electrocardiogram at admission. Patients with a baseline value of ≤14 ng/L were categorized to a dynamic (Δ≥3 ng/L) and a non-dynamic (Δ<3 ng/L) group. Primary outcomes were admission rate, MI among admitted and MACE among discharged within 30 days.

Purpose: To evaluate a one-hour algorithm of high-sensitivity cardiac troponin T (hsTnT) for chest pain setting and to assess dynamic changes at low levels (<14 ng/L) were associated with admission rate and MI among admitted as well as re-admissions and major adverse cardiac events (MACE) among discharged within 30 days.

Results: Out of 3581 patients with the chief complaint chest pain, 2863 had one troponin drawn. Out of 1397 patients that had a second troponin obtained within >30–90 minutes, regardless of baseline value, no absolute change (Δ0) occurred in 60.2% and non-dynamic changes occurred in 91.7% of the group. Out of 1091 patients with a baseline value of <14 ng/L, 23 (2.1%) had a dynamic change. Admission rate (62.5% vs. 13.9%, p<0.001) and MI among admitted (26.7% vs. 1.4%, p<0.001) was more common in the dynamic compared to the non-dynamic group. Among those discharged directly from the ED, no MACE occurred in either group during the 30-day follow-up.

Conclusion: One-hour dynamic changes were uncommon in a broad chest-pain population with baseline levels of hs-cTnT ≤14 ng/L, but were associated with admission rate and MI. No MACE within 30 days were observed in discharged patients after discharging with the obtained value. Dynamic changes were uncommon our findings support the use of the algorithm in the clinical assessment of chest-pain patients at the ED but further studies are needed.

Purpose: To assess whether sex affects clinical effectiveness of early CCTA in the work-up of suspected acute coronary syndrome (ACS) patients in the era of hs-troponins. This is the first study to identify a difference in the performance of copeptin to rule out MI between Blacks and Caucasians, with increased NPV and sensitivity in the Black population at a cut-off of 14 pmol/l. Although numbers were small, similar trends exist in the normal troponin I population. This may have significant implications for early rule out strategies using copeptin.

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P4797 | BEDSIDE
Serum pregnancy-associated plasma protein A (PAPP-A) vs GRACE scale for risk estimation in patients with suspected acute coronary syndrome

M. Ojrzanowski, L. Figiel, J.D. Kasprzak. Medical University of Lodz, Cardiology, Lodz, Poland

Introduction: GRACE study produced an accepted scale for assessment and risk stratification in acute coronary syndromes (ACS). Pregnancy-associated plasma protein A (PAPP-A) serum concentration has been implicated as a marker of unstable atherosclerotic plaques. We hypothesized that admission serum concentration of PAPP-A may improve stratification of cardiovascular mortality risk (early and delayed) in suspected ACS patients (pts).

Methods: We studied 70 pts with chest pain suggesting preliminary ACS diagnosis on admission. Serum cardiac biomarkers and PAPP-A were measured on top of standard biochemical panel and GRACE risk score was calculated. Twelve months follow up was completed to record cardiovascular events (MACE): death, myocardial infarction (MI), need for PCI/CABG, unplanned cardiovascular hospitalization.

Results: During 12-months follow-up 38 (54.3%) pts were hospitalized for MACE, 14 (20%) had MI and 5 (7.1%) died. GRACE intermediate risk was found in 23pts (33%) and high – in 12 (17%). Mean PAPP-A was 39.6 mlU/L (25.6 in low, 45.9 in intermediate and 71.7 in high GRACE risk pts). We compared GRACE scores and PAPP-A in pts with different types of events [Table 1].

Intermediate or high in hospital/6-months GRACE had 34.3%/33.3% positive predictive value (PPV) and 94.3%/91.9% negative predictive value (NPV) for MI, 43%/15.2% PPV and 100%/100% NPV for death 74.3%/72.7% PPV and 65.7%/82.2% NPV for any event. 32 pts (45.7%) had elevated PAPP-A (≥ 40 mlU/L) including 9.4%/15.6% with low, 53.1%/46.9% intermediate and 37.5%/37.5% high in hospital/6-months GRACE score. Elevated PAPP-A provided the following PPV and NPV: 15.6%, 100% for death, 31.3%, 89.5% for MI, 65.6%, 55.3% for any event. Combined PAPP-A > 40 mlU/L and/or high or high GRACE in hospital/6-months score was found in 29/27 pts, improv- ing prediction: PPV/NPV: 17.2%/18.5%, 100%/100% for death, 34.5%/33.3%, 93.8%/93.8% for MI, 72.4%/70.4%, 82.6%/82.5% for any MACE.

Conclusions: Serum concentration of PAPP-A on admission correlates with prognosis in patients with suspected ACS. This novel biomarker may enhance GRACE score risk stratification.

Acknowledgement/Funding: Polish Cardiac Society - Club 30

P4799 | BEDSIDE
Upward trend of myocardial infarction in young women: an age-period cohort analysis

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Background: The incidence of myocardial infarction (MI) has declined in Western countries. However, the evolving trends in different age and gender groups have not been well studied.

Purpose: To examine the changes in rates of MI in women using an age-period cohort model.

Methods: We used the New Jersey Myocardial Infarction Acquisition System (Mi- DAS) to identify 89155 women with first hospital admission for MI between the years 1996–2013. Rates per 100,000 population in 5-year groups from 35 to 84 years old were calculated using census estimates for the periods 1996–2001, 2002–07, and 2008–13. Age-period cohort models were used to study changes in the incidence of first MI.

Results: From 1996 to 2013, the rate of ST-elevation MI (STEMI) declined from 163 (95% CI 149–186) to 39 (95% CI 34–44) per 100,000 population (p < 0.0001) and the non-STEMI rate remained constant 116 (95% CI 101–133) to 116 (95% CI 103–130) (p = 0.9). There was a significant decline in the rate of STEMI in each age-period cohort during the course of the study (figure). In contrast, we observed a significant increase in the rate of non-STEMI among women under the age of 54 (+15, 95% CI 14–16, p = 0.0001). In women older than 55 there was a decreasing trend (−41, 95% CI 44–38, p = 0.04).

STEMI - Women

Abstract P4797 – Table 1

<table>
<thead>
<tr>
<th>Death (N=5)</th>
<th>Alive (N=65)</th>
<th>MI (N=14)</th>
<th>No MI (N=56)</th>
<th>MACE (N=38)</th>
<th>No MACE (N=32)</th>
</tr>
</thead>
<tbody>
<tr>
<td>In hospital death probability (GRACE)</td>
<td>4.7% ±1.52</td>
<td>1.0% ±1.6</td>
<td>1.7% ±1.52</td>
<td>1.0% ±3.4</td>
<td>1.6% ±2.13</td>
</tr>
<tr>
<td>p value (ANOVA K-W)</td>
<td>0.001</td>
<td>0.052</td>
<td>0.005</td>
<td>0.003</td>
<td>0.003</td>
</tr>
<tr>
<td>6-months death probability (GRACE)</td>
<td>12.0% ±4.58</td>
<td>2.6% ±5.6</td>
<td>5.3% ±4.86</td>
<td>4.4% ±4.85</td>
<td>4.4% ±4.85</td>
</tr>
<tr>
<td>p value (ANOVA K-W)</td>
<td>&lt;0.001</td>
<td>0.046</td>
<td>0.004</td>
<td>0.004</td>
<td>0.004</td>
</tr>
<tr>
<td>PAPP-A (mlU/L)</td>
<td>69.47±24.48</td>
<td>37.34±22.78</td>
<td>49.3±22.26</td>
<td>37.61±24.29</td>
<td>43.58±26.52</td>
</tr>
<tr>
<td>p value (ANOVA K-W)</td>
<td>0.018</td>
<td>0.073</td>
<td>0.073</td>
<td>0.089</td>
<td>0.089</td>
</tr>
</tbody>
</table>

Downloaded from https://academic.oup.com/eurheartj/article-abstract/37/suppl_1/599/2197552 by guest on 18 April 2019
Background: Activation of the innate immune system contributes to the pathogenesis of acute heart failure (AHF). As key regulators of innate immunity, monocytes may play a crucial role in the development of this disease. Monocytes are a heterogeneous cell population that can be divided into at least three cell populations: Classical monocytes (CM; CD14++CD16-), intermediate monocytes (IM; CD14++CD16+CCR2+) and non-classical monocytes (NCM; CD14+CD16+CCR2-).

Purpose: The aim of this study was to analyze whether monocyte subset distribution was associated with 30-day mortality in patients with AHF requiring ICU admission. Activation status of the innate immune system as reflected by monocyte subset distribution may play a major role in pathophysiology and outcome in this patient cohort.

Methods: We included 90 consecutive patients with AHF requiring ICU admission. Circulating monocyte subsets were analyzed.

Results: Mean age was 62.1±16.0 years. 76.7% of patients were male and median NT-proBNP levels were 4986 (1525–23842) pg/mL. 30-day survival was 64.4%. At admission, no association between monocyte subset and outcome was seen. However on day 4, increased levels of IM (9.4 (4.0–13.8) % vs. 4.3 (2.1–7.9) %; p=0.02) for non-survivors vs. survivors, respectively) and lower levels of CM were predictive of 30-day mortality (86.8 (77.5–88.9)% vs. 90.5 (84.3–92.9). p=0.02 for non-survivors vs survivors, respectively), while the NCM proportion was not associated with mortality. Risk of dying was increased 10.6-fold in the lowest tertile of CM and 9.5-fold in patients in the highest IM tertile (p<0.001). In the same group, the ROC curve analysis showed that a BNP threshold of 200 pg/ml had a sensitivity of 1.0 for predicting 30-day mortality.

Conclusion: Circulating monocyte subsets are associated with 30-day mortality in patients with AHF requiring ICU admission. Activation status of the innate immune system contributes to the pathogenesis of AHF. Mitochondrial DNA that shows similarities to bacterial DNA may be released after tissue damage and activates the innate immune system.

Purpose: The aim of this study was to analyze whether circulating levels of mtDNA predict 30-day survival in patients with AHF.

Methods: We included 90 AHF admitted to our cardiovascular ICU (33% with cardiacogenic shock, 21% with acutely decompensated HF and 46% of patients suffered from AHF after cardiac arrest). Blood was taken at admission and mtDNA levels were measured by real-time PCR.

Results: Mean age was 62.1±16.0, 76.7% of patients were male and median NT-proBNP levels were 4986 (1525–23842) pg/mL. 30-day survival was 64.4%. Median mitochondrial DNA levels at admission were significantly higher in non-survivors when compared with survivors (29.6 (12.1–70.7) ng/mL vs. 20.6 (7.3–31.9) ng/mL; p=0.05). Patients with plasma levels of mtDNA in the highest quartile had a 2.6-fold higher risk of dying after adjustment for age, gender, NT-proBNP levels and APACHE II score (p<0.05).

Conclusion: Circulating levels of mtDNA predict mortality in AHF patients requiring ICU admission.

P4801 | BEDSIDE
Circulating mitochondrial DNA predicts survival in patients with acute heart failure
K.A. Krychtkul1, M. Lenz1, G. Maurer1, K. Huber2, J. Wojta1, G. Heinz1, W.S. Speidl1, E. Ganovska1, M. Arrigo2, J. Parenica1, A. Mebazaa2, W.S. Speidl1, E. Ganovska1, M. Arrigo2, J. Parenica1, A. Mebazaa2, W.S. Speidl1, E. Ganovska1, M. Arrigo2, J. Parenica1, A. Mebazaa2, W.S. Speidl1.
1 Medical University of Vienna, Department of Internal Medicine II, Division of Cardiology, Vienna, Austria; 2 Wilhelminen Hospital, 3rd Department of Internal Medicine, Cardiology and Emergency Medicine, Vienna, Austria

Background: Patients suffering from acute heart failure (AHF) requiring admission to an intensive care unit (ICU) have a poor prognosis. Activation of the innate immune system contributes to the pathogenesis of AHF. Mitochondrial DNA that shows similarities to bacterial DNA may be released after tissue damage and activates the innate immune system.

Purpose: The aim of this study was to analyze whether circulating levels of mtDNA predict 30-day survival in patients with AHF.

Methods: We included 90 AHF admitted to our cardiovascular ICU (33% with cardiacogenic shock, 21% with acutely decompensated HF and 46% of patients suffered from AHF after cardiac arrest). Blood was taken at admission and mtDNA levels were measured by real-time PCR.

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Conclusion: Circulating levels of mtDNA predict mortality in AHF patients requiring ICU admission.

P4802 | BEDSIDE
B-type natriuretic peptide in addition to Zwolle score to enhance early discharge after acute myocardial infarction: a prospective observational cohort study
E. Ganovska1, M. Arrigo2, J. Parenica1, A. Mebazaa2, W.S. Speidl1, 1 Medical University of Vienna, Department of Internal Medicine II, Division of Cardiology, Vienna, Austria; 2 Wilhelminen Hospital, 3rd Department of Internal Medicine, Cardiology and Emergency Medicine, Vienna, Austria

Introduction: Invasive and improved pharmacological treatments of patients with acute myocardial infarction (AMI) lead to decreased hospital length of stay and improvement of their prognosis. Current ESC guidelines for the management of AMI in patients presenting with ST-segment elevation (STEMI) recommended early discharge of low risk patients in 72 hours after primary PCI. To identify low risk patients ZWOLLE risk score can be helpful.

Results: We have hypothesized that low value of BNP, determined exactly in 24 hours of onset of chest pain, can better identify low risk patients with STEMI. Using Zwolle score and BNP in clinical practice can even extend group of patients suitable for early discharge, without increasing of mortality.

Methodology: The study population consisted of 1032 consecutive patients with STEMI. The diagnosis of STEMI and treatment was based according to the current ESC guidelines. For the specific purpose of this study, patients who died during the first 72 hours of hospitalization were excluded. Samples for BNP were drawn in 24 hours after onset of chest pain. The performances of Zwolle score and BNP for predicting 30-day mortality were assessed with calculating the area under the curve (AUC) of receiver operating characteristic (ROC) curves. Differences between ROC curves are tested with c-statistics. The optimal cut off of BNP was defined as highest plasma level with sensitivity of 1.0 for predicting 30-day mortality.

Results: According to the current recommendations, the study population was divided in two groups. The first group (n=387, 38%) consisted of low risk patients (Zwolle score ≤3 points). The second group (n=645, 62%) included patients at higher risk of death (Zwolle score >3 points). There were 2 deaths (0.5%) in the low-risk group. In the group of patients with Zwolle score >3 there were 29 deaths (4.5%). The AUC for Zwolle score (>3 points) to predict 30-day mortality was 0.78 (95% confidence interval 0.67–0.90), p<0.001. In the same group, the AUC of BNP was 0.83 (95% confidence interval 0.77–0.90), p<0.001. ROC curve analysis showed that a BNP threshold of 200 pg/ml had a sensitivity of 100% for predicting 30-day mortality. Among the group of patients with Zwolle score >3 (n=645) there were 183 patients (28%) with BNP >200 pg/ml. These patients could be additionally discharged after 72 hours, without increasing of mortality.

Conclusion: Early discharge after STEMI is possible in low risk patients identified by Zwolle ≤3. Due to results of our study no patients with Zwolle score (>3 points) and low BNP (<200 pg/ml) died during 30-day follow-up. These patients may be considered for early discharge too. This might have increased the number of early discharge patients from 387 (38%) up to 570 (55%) in our study population. Short length of hospital stay reduces the risk for nosocomial complications, facilitates faster return to the patient’s regular life and saves health-care resources.

Acknowledgement/Funding: Supported by Ministry of Health of the Czech Republic, MUNI/A/1362/2015 of the Masaryk University and by a grant of the Czech soc. of cardiology.