LONG-TERM OUTCOME AFTER PCI

2007 | BEDSIDE
Predictors of long-term outcomes following saphenous vein graft intervention: an observational analysis of 1,310 patients from the British Columbia Cardiac Registry

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Background: Saphenous vein grafts (SVG) intervention is associated with worse clinical outcomes compared with intervention of native coronary arteries. The use of a distal protection device (DPD) is a Class I indication, and whilst it enhances procedural safety, its effect on long-term outcomes is unknown. Data on the benefit of drug-eluting (DES) in these patients is conflicting. We evaluated whether DPD or DES use was associated with improved long-term outcomes.

Methods: We analyzed 1,310 patients undergoing isolatedSVG intervention between 2008–2013 in the British Columbia Cardiac Registry, and analyzed mortality and target vessel revascularization (TVR) at 3 years. Multivariable models were used to determine independent predictors for outcomes.

Results: The overall mortality and TVR at 3 years was 19% and 25%. A DPD was used in 7.3%; and DES in 63% (first-generation DES (F-DES) in 25% and second-generation DES (S-DES) in 75%). Multivariable analyses identified increasing age, diabetes, renal disease, cardiogenic shock, IABP use, peripheral vascular disease, ACS presentation, reduced post-procedural TIMI flow and bare metal stent (BMS) use as predictors of increased mortality. Although DPD use was a strong predictor for post-procedural TIMI 3 flow (OR=2.10, 95% CI: 1.31–3.33, p<0.001), we could not confer a mortality benefit (HR=1.13, 95% CI: 0.69–1.85, p=0.620). DES use was not associated with a reduction in TVR (HR=1.16, 95% CI: 0.89–1.51, p=0.281), and Kaplan-Meier analyses demonstrated comparable TVR for BMS, F-DES and S-DES.

Conclusions: This study represents the largest reported study with longest follow-up following SVG intervention. The use of DPD was not a predictor for long-term survival. Whilst DES use was a predictor for long-term survival, its use was not associated with reduced TVR.

2008 | BEDSIDE
Very long-term (10 to 14 years) outcomes after implantation of bare-metal stent

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Background: Long-term outcomes (>10 years) after BMS implantation have not been well documented despite large-scale real-world registries.

Methods: The CREDO-Kyoto (Coronary Revascularization Demonstrating Outcome study in Kyoto) registry is a multicenter registry enrolling consecutive patients undergoing first coronary revascularization between January 2000 and December 2002, excluding those with acute myocardial infarction within a week before the index procedure. A total of 5313 consecutive patients comprised of the current long-term (>10 years) follow-up study.

Results: Mean follow-up duration for the survivors was 10.3±3.1 years (median 11.3 years, interquartile range 10.3–12.2 years, range 0.0–14.1 years). Late clinical follow-up information was obtained in 4901 (92.2%) patients at 5 years, and 4515 (85.0%) patients at 10 years. The all-cause mortality was 28% at 10 years. The incidences of myocardial infarction, definite stent thrombosis (ST) and target lesion revascularization (TLR) were 2.5%, 1.2% and 27% at 1 year; 4.8%, 1.4% and 32% at 5 years; and 8.8%, 2.1% and 36%, respectively. The steady rate of very late ST (>1 year) and TLR beyond 1 year were 0.1%/year and 1.0%/year, respectively, without any evidences of a plateau beyond 10 years (Figure). Multivariable Cox regression analysis showed younger age, male gender, and total stent length >28mm were independent risk factors for late TLR >5 years, while current smoking habits at the time of index procedure was an independent predictor for definite ST beyond 5 years.

Conclusions: TLR beyond 1 year and very late ST (>1 year) after BMS implantation continued to occur without attenuation beyond 5 years.

Acknowledgement/Funding: the Research Institute for Production Development (Kyoto, Japan).

2009 | BEDSIDE
Long-term clinical outcomes of STEMI patients treated with BVS


Background: Biodegradable vascular scaffolds (BVS) are the newest interventional treatment for coronary artery disease. However BVS usage for patients presenting with ST-segment elevation myocardial infarction (STEMI) is still considered investigational.

Purpose: To examine the performance and feasibility of BVS usage in STEMI patients.

Methods: This is a prospective, single-arm, single-center study reporting data after implantation of a BVS in STEMI patients. Quantitative coronary angiography (QCA) data was evaluated and clinical events were reported. STEMI patients with age >18 years and a culprit lesion in vessels between 2.0mm and 3.8mm (by online QCA) were included. Major exclusion criteria were known intolerance to contrast medium, previous CABG, previous PCI with the implantation of a metal stent, and age >75 years.

Results: From November 2012 until December 2014, 160 STEMI patients underwent PCI with placement of one or more BVS. Mean age was 55.8 years, 73.1% was male, 10% had diabetes mellitus, 71.9% presented with single vessel disease. In ~50% of the patients, the culprit lesion was located in the LAD. Thrombectomy was used in 79.4%. Predilatation was performed in 62.5%; post-dilatation in 42.5%. Clinical device success was 94.5%. Post-procedural TIMI III flow was achieved in 94.6%. Mean post-procedural %DS was 14%. Epifibatide was given in 33.8% of the patients. Survival status was available in 100%. 36 patients were excluded from further follow-up because of protocol-related exclusion criteria. 30/36 patients refused study related follow-up. In 109/124 (87.9%) patients, there was follow-up >30 days available. During a median follow-up time of 369 days (IQR 190–548), there were three cases of all-cause mortality, 9 cases of myocardial infarction (MI), 5 definite scaffold thrombosis (ST) (3 acute, 1 subacute and 1 very late), 5 target lesion revascularization (TLR), 7 target vessel revascularization (TVR) and 8 non-target vessel revascularization (nTVR).

Conclusions: BVS for primary PCI resulted in good procedural outcome, but the unexpected high number of definite stent thrombosis drives the search for optimal implantation strategy during primary PCI.

Acknowledgement/Funding: The institution Erasmus MC received research grants from Abbott. Robert-Jan van Geuns and Nicolas van Mieghem have received speakers fees from Abbott.

2010 | BEDSIDE
Long-term prognosis after exenatide treatment in patients with ST-segment elevation myocardial infarction

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Background: Treatment with the glucagon-like peptide-1 analogue exenatide aden
dermined, at the time of reperfusion, increases myocardial salvagew in a population of ST-elevation myocardial infarction patients treated with primary percutaneous coronary intervention. Whether this effect will translate into improved clinical outcome remains unknown.

Purpose: In a post-hoc analysis we wanted to test if the cardioprotective effect of exenatide would have a beneficial effect on long-term outcome.

Methods: This is a post-hoc analysis of a randomized, double blind, placebo-controlled trial evaluating the cardioprotective effect of exenatide treatment performed at two university hospitals in Denmark. Outcome data were collected from Danish nationwide medical registries. All patients were followed from date of inclusion until death or December 2014. The primary endpoint was major adverse cardiac events (MACE), which was a composite of all-cause mortality and admis-
sion for heart failure. The secondary endpoints were admission for heart failure and all-cause mortality, respectively.

Results: A total of 334 patients with a first acute ST-elevation myocardial infarction were included in the present study and were randomized to receive exenatide (n=175) or placebo (n=159) in adjunct to primary percutaneous coronary intervention. Patient follow-up was a median of 5.2 years. MACE occurred in 95 (25%) patients with no difference between groups (24% versus 27%; p=0.52). However, admission for heart failure was significantly lower in patients treated with exenatide (11%) compared to patients treated with placebo (20%), yielding a hazard ratio of 0.53 (95% confidence interval: 0.30–0.93; p=0.042). There was no difference in all-cause mortality (14% versus 9%; p=0.18).

Conclusions: In ST-elevation myocardial infarction patients treated with primary percutaneous coronary intervention additional treatment with exenatide at the time of reperfusion reduced the rate of admission for heart failure, but did not reduce all-cause mortality or a composite endpoint of the two. Owing to small sample size these findings may only be considered hypothesis generating, but may encourage a larger multicenter study.

2011 | BEDSIDE

The longest available clinical follow-up of a cohort of real-world patients treated exclusively with drug-eluting stents


Background: There is still uncertainty about the durability of the results of drug-eluting stents (DES) in real-world complex patients (pts). We sought to provide the longest clinical follow-up data on outcomes of unselected patients treated solely with DES.

Methods: The DESIRE registry is a prospective, single-center registry encompassing all consecutive patients treated solely with DES since May 2002. The primary goal is the very long-term occurrence of MACE and stent thrombosis (ST). Patients were clinically followed at 1, 6 and 12 months and then annually. A multivariate model was built to determine independent predictors of MACE and ST.

Results: A total of 5,614 pts (8,825 lesions/9,980 DES) were included. The mean age was 64±11 years. DM was detected in 31.5% and 41.8% presented with acute coronary syndrome (STEMI) represented 16.8% of the cohort. Follow-up was obtained in 98.4% of the patients (median 5 years). Currently, 78.9% of the population is free of any MACE. Ischemia-driven TVR was performed in 7.3% of the patients. Q-wave MI rate was only 1.7% while cumulative incidence of definite/probable ST was 4.1%. Independent predictors of MACE were initial presentation as ACS (HR 1.4; 95% CI, 1.1 to 1.7, p=0.001), lesion length > 20mm (HR 1.4; 95% CI, 1.2 to 1.6, p<0.001), residual stenosis (HR 1.02; 95% CI, 1.01 to 1.03, p<0.001), DM (HR 1.6; 95% CI, 1.1 to 2.2, p=0.005) and severe coronary calcification (HR 1.4; 95% CI, 1.1 to 1.8, p<0.004) while use of 2nd generation DES was protective (HR 0.7; 95% CI, 0.5 to 0.9, p=0.027). Independent predictors of ST were PCI for STEMl (HR 2.6; 95% CI, 1.6 to 4.3, p<0.001) and treatment of small vessels (HR 2.0; 95% CI, 1.3 to 3.3, p=0.002).

Conclusion: In our single center experience, the use of DES was associated with very long-term safety and effectiveness with acceptable low rates of adverse clinical events, including ST. Treatment of patients with ACS, in particular STEMI, increase the risk of adverse events while use of 2nd generation DES might be protective.

2012 | BEDSIDE

Differential prognostic impact between 1st and 2nd generation drug-eluting stents in coronary bifurcation lesions: pooled analysis of the COBIS II, Excellent, and Resolute-Korea registries

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Background: The 2-stenting has been regarded to show worse clinical outcomes than 1-stenting after bifurcation PCI with 1st generation DES. However, there has been paucity of data comparing 1- and 2-stenting techniques with the use of 2nd generation DES.

Purpose: To investigate the differential clinical outcomes after percutaneous intervention (PCI) for coronary bifurcation lesions with 1-stenting or 2-stenting techniques with the use of 1st or 2nd generation drug-eluting stent (DES).

Methods: Pooled analysis was performed with patients undergoing PCI using 1st or 2nd generation DES for bifurcation lesions with side branch diameter ≥2 mm from the dedicated bifurcation PCI registry (COBIS II) and the largest 2nd generation DES registry (EXCELLENT, RESOLUTE-Korea registry) in Korea. The 3-year clinical outcomes were compared between 1- and 2-stenting techniques, stratified by the type of DES (1st or 2nd generation). Primary clinical outcome was target lesion failure (TLF), and secondary clinical outcomes were patient-oriented composite outcomes (POCO, a composite of all death, any MI, any repeat revascularization, and cerebrovascular accidents).

Results: Of 3,162 patients with bifurcation lesions, 52.9% of patients showed true bifurcation lesion. 2,475 patients with 1st generation DES were treated with 1-stenting (72.8%) or 2-stenting (27.2%) techniques. Among the 687 patients with 2nd generation DES, 59.5% or 40.5% were treated with 1- or 2-stenting techniques, respectively. The rates of TLF or POCO at 3-year were significantly higher after systemic 2-stenting with 1st generation DES (TLF: 8.6% vs. 17.5%, p<0.001; POCO 18.1% vs. 28.5%, p<0.001), however, there was no difference between 1- and 2-stenting techniques with 2nd generation DES (TLF: 5.4% vs. 5.8%, p=0.760; POCO: 11.2% vs. 12.9%, p=0.995). The differential impacts of 2-stenting techniques according to the type of DES were also corroborated by similar results with inverse probability weighted model. 2-stenting technique was significant independent predictor for TLF in 1st generation DES (HR 2.046, 95% CI 1.144–3.759, p<0.001), but not in 2nd generation DES (HR 0.667, 95% CI 0.247–1.802, p=0.425).

Conclusion: The 2-stenting showed significantly worse clinical outcomes with the use of 1st generation DES. However, with the use of 2nd generation DES, 2-stenting technique showed comparable outcomes with 1-stenting technique. Considering enhanced safety and efficacy of 2nd generation DES, individualized treatment strategy for bifurcation lesion is warranted rather than universal application of the 1-stenting strategy.

2013 | BEDSIDE

Predictors of late coronary thrombotic events after percutaneous coronary intervention: insights from the PARIS registry

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Background: Ischemic risk after percutaneous coronary intervention (PCI) with drug-eluting stent (DES) implantation is dynamic, being highest early after the procedure with attenuation over time. Accurate knowledge of the ischemic risk factors is essential in guiding the optimal duration of dual antiplatelet therapy (DAPT). The predictors of late thrombotic events are unclear.

Objectives: We sought to identify baseline clinical variables independently associated with thrombotic events after 30 days among patients undergoing PCI with DES.

Methods: Participants in the PARIS registry were categorized according to the development of a late intra coronary thrombotic event (ICTE) after 30 days from the procedure to 2 years. ICTE was defined as the composite of de/prob stent thrombosis or myocardial infarction. Patients in whom baseline laboratory variables were missing were excluded from the analysis. Multivariate analysis was performed using a Cox regression model, with candidate variables for analysis chosen via backward stepwise selection.

Results: Of 3449 patients enrolled in the PARIS study, 134 (3.9%) had an ICTE. Patients with ICTE were more commonly hypertensive, anemic, diabetics, with chronic kidney disease (CKD) and presented with an acute coronary syndrome. Independent predictors of ICTE are reported in Table 1. The strongest predictors of late ICTE were CKD and insulin-treated diabetes.

Predictors of late ICTE

<table>
<thead>
<tr>
<th>HR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age*</td>
<td>0.97 (0.96–0.99)</td>
</tr>
<tr>
<td>Anemia</td>
<td>1.94 (1.32–2.83)</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>2.21 (1.49–3.29)</td>
</tr>
<tr>
<td>Acute coronary syndrome</td>
<td>1.55 (1.10–2.19)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>1.71 (1.11–2.62)</td>
</tr>
<tr>
<td>Insulin-treated diabetes</td>
<td>2.02 (1.42–2.87)</td>
</tr>
<tr>
<td>Previous revascularization</td>
<td>1.91 (1.24–2.74)</td>
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</tbody>
</table>

*HR for age expressed as 1 year increase.

Conclusions: We identified 7 variables independently associated with late ICTE following PCI with DES in a real-world population. CKD and insulin-treated diabetes were the strongest predictors. Accurate knowledge of commonly identifiable clinical risk factors for ICTE events may be useful in individualizing potency and duration of DAPT after PCI.

Acknowledgement/Funding: Bristol-Myers Squibb and Sanofi - Aventis.
2014 | BEDSIDE
Relative survival and excess mortality following unprotected left main stem percutaneous coronary intervention: a national cohort study of 11079 emergent and elective cases
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Background: There are no whole country studies of survival following percutaneous coronary intervention (PCI) to the unprotected left main stem (UPLMS) which account for background mortality.

Methods: We identified 11079 cases with ST-elevation myocardial infarction (STEMI), non ST-elevation acute coronary syndrome (NSTEACS) and elective chronic stable angina (CSA) who received UPLMS PCI, 2005 to 2014. We used age, sex, and calendar year-specific population mortality rates for England and Wales to calculate expected survival, and 5-year cumulative relative survival rate ratios (RSR) using the Ederer II approach and Poisson regression to estimate excess mortality rate ratios (EMRR) for key covariates of interest.

Results: One and 5-year RSRs were better in CSA group (97.5% versus 93.8%) compared to STEMI (64.1% versus 57.0%) and NSTEACS (84.6% versus 73.1%). Excess mortality increased significantly with age. For STEMI EMRR was 2.18% (95% CI; 1.67 to 2.58) and 2.01% (95% CI; 1.47 to 2.75) for STEACS. For CSA, EMRR was associated with diabetes 2.21% (95% CI; 1.44 to 3.38), previous AMI 2.27% (95% CI; 1.39 to 3.71) and poor left ventricular ejection fraction (LVEF) 2.50% (95% CI; 1.44 to 3.35). For NSTEACS EMRR was associated with renal failure 2.75% (95% CI; 2.23 to 3.22), moderate 2.20% (95% CI; 1.74 to 2.78) and poor LVEF 3.25% (95% CI; 2.58 to 4.10) while for STEMI EMRR was associated with renal failure 2.16% (95% CI; 1.47 to 3.29) and cardiogenic shock 6.95% (95% CI, 5.75 to 8.42).

Conclusion: Survival after UPLMS PCI for CSA is excellent and contrasts with STEMI and NSTEACS where patient characteristics are significantly associated with excess mortality. These phenotype-specific differences have implications for clinical risk assessment, patient prognosis, and future treatment strategies.

2015 | BEDSIDE
The optimal duration of dual antiplatelet therapy in patients receiving percutaneous coronary intervention with drug-eluting stents
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Background: To determine the optimal duration of DAPT following DES implantation.

Methods: MEDLINE, EMBASE, Scopus, CENTRAL and ClinicalTrials.gov were searched for eligible randomized controlled trials (RCTs) that compared outcome in patients receiving short-term (<6 months) DAPT with long-term (>12 months) DAPT following DES implantation. The primary end point was a composite of all cardiovascular death, myocardial infarction, target vessel revascularization, stroke or major bleeding. The secondary outcome were the individual components of the primary outcome, cardiovascular death, stent thrombosis and any bleeding episode. Pooling was performed according to the fixed effect model with summary effect estimates (95% confidence intervals). Heterogeneity was determined using the I2 statistic.

Results: 15,378 patients from seven RCTs were studied. 7672 patients were randomized to receive short-term DAPT, while 7706 patients were randomly assigned to receive long-term DAPT. There was a statistically significant evidence between the short-term and long-term DAPT groups with respect to the occurrence of the primary outcome (Risk ratio (RR) 1.017 (0.872–1.186), I2 = 0%), all cause death (RR 0.896 (0.708–1.134), cardiovascular death (RR 0.924 (0.688–1.279)), myocardial infarction (RR 1.139 (0.887–1.461)), target vessel revascularization (RR 1.174 (0.916–1.505)), stent thrombosis (RR 1.264 (0.786–2.032)) and stroke (RR 0.876 (0.685–1.111)). However there was a statistically significant increased risk of any bleeding episode in the long-term DAPT group (RR 0.640 (0.485–0.845), p = 0.002) with number needed to harm of 149. There was a trend towards a higher risk of major bleeding in patients receiving long-term DAPT, however this finding did not reach statistical significance (RR 0.607 (0.363–1.016), p = 0.057). There was no statistically significant difference in the sub-group analysis of patients with diabetes and patients presenting with acute coronary syndrome, (RR 1.026 (0.745–1.421) and RR 1.062 (0.785–1.436), respectively.

Conclusions: There was no difference in efficacy outcomes between short-term and long-term DAPT following DES. Short-term DAPT was equally effective as long-term DAPT in preventing the primary outcome even in high-risk patients. However, longer duration of DAPT is associated with increased risk of bleeding and is probably not necessary. Larger, adequately powered RCTs for low event rates are needed to confirm these findings.

2016 | BEDSIDE
1-year angiographic and 5-year mortality of cobalt-chromium everolimus-eluting versus zotarolimus-eluting coronary stents in patients with multivessel CAD
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Objective: To determine the optimal duration of DAPT in patients with multivessel PCI for CSA who received UPLMS PCI, 2005 to 2014. We used age, sex, and calendar year-specific population mortality rates for England and Wales to calculate expected survival, and 5-year cumulative relative survival rate ratios (RSR) using the Ederer II approach and Poisson regression to estimate excess mortality rate ratios (EMRR) for key covariates of interest.

Results: One and 5-year RSRs were better in CSA group (97.5% versus 93.8%) compared to STEMI (64.1% versus 57.0%) and NSTEACS (84.6% versus 73.1%). Excess mortality increased significantly with age. For STEMI EMRR was 2.18% (95% CI; 1.67 to 2.58) and 2.01% (95% CI; 1.47 to 2.75) for STEACS. For CSA, EMRR was associated with diabetes 2.21% (95% CI; 1.44 to 3.38), previous AMI 2.27% (95% CI; 1.39 to 3.71) and poor left ventricular ejection fraction (LVEF) 2.50% (95% CI; 1.44 to 3.35). For NSTEACS EMRR was associated with renal failure 2.75% (95% CI; 2.23 to 3.22), moderate 2.20% (95% CI; 1.74 to 2.78) and poor LVEF 3.25% (95% CI; 2.58 to 4.10) while for STEMI EMRR was associated with renal failure 2.16% (95% CI; 1.47 to 3.29) and cardiogenic shock 6.95% (95% CI, 5.75 to 8.42).

Conclusion: Survival after UPLMS PCI for CSA is excellent and contrasts with STEMI and NSTEACS where patient characteristics are significantly associated with excess mortality. These phenotype-specific differences have implications for clinical risk assessment, patient prognosis, and future treatment strategies.
tions as in the second Marelly group i.e sepal defects, coarctation of aorta, patent ductus arteriosus and Ebstein’s anomaly, the mortality was still nearly 10 times greater than in controls.

**Conclusions:** Despite the increased rate of survival in patients with congenital heart disease, the mortality risk in children and young adults is still high compared to general population. Our results stress the importance for further research about underlying mechanisms of death in this group of young patients.

**Acknowledgement/Funding:** Sahlgrenska Academy and Swedish Medical Research Council

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**2926 | SPOTLIGHT**

Down syndrome and congenital heart disease: surgical therapy, development of Eisenmenger syndrome and survival in 1,549 patients from the German national register for congenital heart defects

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**Background and introduction:** Patients with Trisomy 21 (Down syndrome, DS) are frequently affected by congenital heart disease (CHD) and are at a higher risk for developing pulmonary hypertension and Eisenmenger syndrome (ES).

**Purpose:** To characterize DS patients based on the data of the German National Register for Congenital Heart Defects (NRCHD), to identify temporal changes in therapeutic strategies over the last decades and to analyze the impact of medical progress on developing ES as well as DS patients’ overall survival.

**Methods:** Inclusion of all patients in the NRCHD diagnosed with DS. Results: Overall, 1,549 DS patients were identified (53.2% female, mean age 14.4±10.4 years; leading diagnoses: AVSD [53.2%], VSD [25.8%], ASD [10.1%]). N=797 patients (50.3%) have been operated or treated interventionally before the age of seven years. The likelihood of being treated with curative intention increased significantly over time (OR 1.013, [95% CI 1.004 - 1.024], p=0.006).

In parallel the likelihood of developing an ES, decreased over time (OR 0.872 [95% CI 0.849–0.893], p<0.0001). Comparing the rate of ES we found that 46.7% of patients in the birth cohort 1960–1969 had ES compared to only 0.25% for the birth cohort 2000–2009 (p<0.0001). Overall survival after 1, 10, 20 and 40 years was 98%, 96%, 94% and 79%, respectively. Patients with an ES had a significantly worse survival compared to those without an ES (HR 25.9 [95% CI 11.0–60.8], p<0.0001).

Kaplan Meier time dependent

**Conclusion(s):** The notion of generally poor survival prospects of DS patients with CHD is obsolete due to the available treatment options. Patients with DS who develop an ES still have a poor prognosis, but long-term outcome in those undergoing timely curative operation is excellent.

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**2927 | BEDSIDE**

NOACs, Are they safe in congenital heart disease? First results of an international multicenter registry

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**Purpose:** Adults with congenital heart disease (ACHD) and non-valvular atrial

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**Hot topics in congenital heart disease**

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**2928 | BEDSIDE**

Prognostic value of NT-proBNP after atrial redirection surgery

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**Background:** In systemic morphological right ventricles after atrial redirection surgery, NT-proBNP is correlated with NYHA-class, ventricular function and subaortic AV-valve regurgitation (TR).

**Purpose:** To assess the impact of NT-proBNP on adverse clinical outcomes using multivariate Cox regression analysis. The primary endpoints were all causes of hospitalisation, heart failure, transplantation and death.

**Methods:** This prospectively designed, longitudinal, observational study evaluated NT-proBNP in 116 patients (24.9±4.2 years old, NYHA class I/II/III=97/18/1, 71 men) relative to all cardiac causes of hospitalisation, heart failure, transplantation and death.

**Results:** The mean observation time was 7.3±2.4 years. In univariate Cox proportion analysis, the predictors for all causes of hospitalisation were NT-proBNP (HR: 5.99, [95% CI: 3.21–11.18], NYHA class (HR: 2.98, [95% CI: 1.62–5.5]), ventricular function (HR: 1.96, [95% CI: 1.27–3.02), TR (HR: 2.39, [95% CI: 1.48–3.59), ventricular septal defect repair (HR: 1.29, [95% CI: 1.08–1.53) and a history of supraventricular tachycardia (SVT) (HR: 7.13, [95% CI: 3.74–13.59). In multivariate Cox proportion analysis, NT-proBNP (HR: 3.71, [95% CI: 1.82–7.57), SVT (HR: 4.27, [95% CI: 2.03–8.94) and ventricular septal defect repair (HR: 1.41, [95% CI: 1.15–1.72) remained independently associated with all causes of hospitalisation.

For heart failure, transplantation and death, the single predictors were NT-proBNP (HR: 20.67, [95% CI: 4.69–91.78), NYHA class (HR: 6.45, [95% CI: 2.75–15.14), ventricular function (HR: 2.70, [95% CI: 1.48–4.92), TR (HR: 4.11, [95% CI: 1.99–8.87) and SVT (HR: 1.06–12) and SVT (HR: 8.00, [95% CI: 2.82–22.69). Multivariate Cox proportion analysis identified NT-proBNP (HR: 6.82, [95% CI: 1.32–35.04) and NYHA class (HR: 6.79, [95% CI: 1.75–26.28).

Using ROC curves, the ability of NT-proBNP to detect patients at risk was greater than for all causes of hospitalisation (AUC: 0.94, [95% CI: 0.90–0.988) than for all causes of hospitalisation (AUC: 0.8, [95% CI: 0.713–0.887).

**Conclusion:** In systemic right ventricles, NT-proBNP is a useful risk predictor for all causes of hospitalisation and, in particular, for heart failure, transplantation and death. It therefore might be a useful tool for risk assessment in this patient population.
**2029 | BEDSIDE**

Cardiopulmonary adaptation to short-term high altitude exposure in adult Fontan patients


**Introduction:** In Fontan patients, even a mild increase in pulmonary artery pressure can decrease cardiac preload and circulatory output. Nowadays, Fontan patients can easily travel to high altitude (3500 m) during holidays or for leisure activities. High altitude induced hypoxia mediates pulmonary vasoconstriction. Whether Fontan patients tolerate hemodynamically short-term high altitude exposure is unknown.

**Methods:** 17 adult Fontan patients and 15 healthy controls underwent cardiopulmonary exercise testing with measurement of pulmonary blood flow (PBF) with an inert gas rebreathing system in Bern (at 540 m above sea level; low altitude) and at the Jungfraujoch (at 3454 m; high altitude). All tests were performed within 12 weeks. Endpoints were the change of PBF at rest and during submaximal exercise between low and high altitude, and the respective change in exercise capacity measured as peak VO2.

**Results:** Fontan patients and controls were matched for age (28±7 years) and gender (56% female). Fontan patients had at any time lower oxygen saturations than controls (low altitude: rest 92% vs. 96%, high altitude: rest 83% vs. 88%). Effective PBF at rest and at exercise was higher in controls than in Fontans, both at low and high altitude (figure 1). PBF increased 2-fold in Fontan patients and 2.8-fold in the control group during exercise, with no difference from low to high altitude (p=0.209). The relative reduction in peak VO2 at high altitude compared to baseline was more pronounced in the healthy control group than the Fontan patients (17±5% vs. 9±12%, p=0.005).

**Conclusion:** Short term high altitude exposure did not affect PBF in Fontan patients at rest and during exercise. High altitude related reduction of exercise capacity is more pronounced in healthy controls than Fontan patients.

**2030 | BEDSIDE**

Does fontan circulation engender progressive liver dysfunction?

G. Ferraro1, D. Marin1, R. Bordes1, S. Gaia1, P.L. Calvo2, C. Pace Napoleon1, G. Ageni1.

**Introduction:** Total cavopulmonary connection (TCPC) forces systemic venous blood into the lungs, equalizing caval and pulmonary pressure. Chronic hepatic stasis generates a progressive liver dysfunction, eventually leading to cirrhosis.

**Purpose:** To investigate prospectively the hemodynamic changes and the liver status after TCPC.

**Methods:** From March 2013 to December 2014, 64 TCPC patients (pts) underwent cardiac catheterization and liver examination (blood tests, ultrasound and gastroscopy at our center.

**Results:** Median age was 10 (5–32) yrs, median distance from TCPC 10 (1–19) yrs. Catheterization showed the following data: pulmonary arterial pressure (PAP) 11±6±2 mmHg (15 mmHg in 10 pts), ventricular end-diastolic pressure (VEDP) 6.67±2.58 mmHg, pulmonary vascular resistances (PVR) 2±1 WU m², aortic blood flow (QSI) 3.15±1.27 ml/min/m², systemic O2 saturation >95% in 18 pts), QP/QS 0.9±0.2. 37 interventions were performed in 27 pts. Stiffness was 16.63 + 5.96 KPa and significantly related to time from TCPC (r: 0.33, p<0.01). A subgroup of patients showed a negative trend very early after TCPC.

**Conclusions:** This is the largest prospective series showing that TCPC engenders a progressive decrease of QSI and increase in VEDP, with a tendency to PAP and PVR to raise. This is balanced by the progressive development of venous collateral vessels, from both caval and hepatic systems. The hepatic stiffness increases with time, but cirrhosis and esophageal varices are found in few patients. Only a multidisciplinary approach will be able to identify patients at risk.

**2031 | BEDSIDE**

Left ventricular function as a predictor for long-term outcomes in marfan syndrome


**Introduction:** In Marfan syndrome (MFS), left ventricular (LV) function and family history are adverse factors. Left ventricular (LV) function may also be impaired in MFS, but the impact on prognosis is not yet defined.

**Aims:** This study examined the contribution of left ventricular function with other risk factors for adverse prognosis.

**Methods:** From 1988 to 2014, all adult MFS patients were enrolled in a prospective cohort study with annual echocardiographic imaging. Linear and Cox regression models were used to examine risk factors associated with progressive aortic dilatation, aortic dissection and mortality.

**Results:** The cohort of 224 MFS patients (age 28±13.3 years, 55% male) was followed for a median of 9.5 years (interquartile range 4–17 years, total 2488 patient-years). Baseline maximum aortic root diameter was 41.6±8.5 mm (Z-score = 2.6±2.1). Baseline systolic LV fractional shortening (FS) was 36.7±5.6% with a LV end-diastolic-diameter of 53±7.8 mm and a LV end-systolic-diameter of 34.5±6.7 mm. During follow-up, 44 patients died and 41 patients experienced an aortic dissection. Both LV FS and aortic Z-score were independent predictors for mortality when controlled for age (respectively hazard ratio (HR) 0.9, 95% CI 0.9–1.1, p=0.003 and HR 1.35, 95% CI 1.0–1.8, p=0.06). The only independent predictor for aortic dissection was baseline aortic dilatation (HR 0.71, 95% CI 1.3–3.4; p=0.14), whereas annual aortic progression was trending (HR 1.4, 95% CI 0.9–2.1; p=0.072). Neither mortality nor dissection was associated to gender, family history or any of the systemic features in the revised Ghent nosology.

**Conclusion:** The most important predictors of long-term mortality in MFS patients are baseline LV function and aortic diameter. Patients with a baseline aortic diameter >40 mm were 7 times more likely to suffer aortic dissection. The LV systolic function should be included in future risk stratification models. Phenotypic severity, according the revised Ghent nosology systemic score, is unrelated to the risk of death or dissection.

**2032 | BEDSIDE**

Super flexible replicas of complicated congenital heart disease employing with stereotopography and vacuum casting - a reliable simulator for surgical operation


**Introduction:** Total cavopulmonary connection (TCPC) forces systemic venous blood into the lungs, equalizing caval and pulmonary pressure. Chronic hepatic stasis generates a progressive liver dysfunction, eventually leading to cirrhosis.

**Purpose:** To investigate prospectively the hemodynamic changes and the liver status after TCPC.

**Methods:** From March 2013 to December 2014, 64 TCPC patients (pts) underwent cardiac catheterization and liver examination (blood tests, ultrasound and gastroscopy at our center.

**Results:** Median age was 10 (5–32) yrs, median distance from TCPC 10 (1–19) yrs. Catheterization showed the following data: pulmonary arterial pressure (PAP) 11±6±2 mmHg (15 mmHg in 10 pts), ventricular end-diastolic pressure (VEDP) 6.67±2.58 mmHg, pulmonary vascular resistances (PVR) 2±1 WU m², aortic blood flow (QSI) 3.15±1.27 ml/min/m², systemic O2 saturation >95% in 18 pts), QP/QS 0.9±0.2. 37 interventions were performed in 27 pts. Stiffness was 16.63 + 5.96 KPa and significantly related to time from TCPC (r: 0.33, p<0.01). A subgroup of patients showed a negative trend very early after TCPC.

**Conclusions:** This is the largest prospective series showing that TCPC engenders a progressive decrease of QSI and increase in VEDP, with a tendency to PAP and PVR to raise. This is balanced by the progressive development of venous collateral vessels, from both caval and hepatic systems. The hepatic stiffness increases with time, but cirrhosis and esophageal varices are found in few patients. Only a multidisciplinary approach will be able to identify patients at risk.

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and reproducibility of the replicas was evaluated by pediatric cardiologists and cardiac surgeons using questionnaires.

**Results and conclusions:** Wide variety of biomodels of complicated CHDs from neonates to adults was reproduced. Pediatric cardiologists and cardiac surgeons highly evaluated these biomodels as reliable simulators for cardiac surgery. This technology allowed surgeons to precisely understand the internal chambers of the heart and allowed them to perform simulation surgery by way of cutting and suturing like a real heart tissue. These polyurethane biomodels were instructive for medical students, young surgeons, patients and parents to understand the complex structures and hemodynamics of the disease.

**Acknowledgement/Funding:** Japanese Ministry of Health Welfare and Labor

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**2933 | BEDSIDE**

Right atrial flow patterns in the normal heart - a new clue in the patent foramen ovale and cryptogenic stroke story


**Background:** 40% of ischaemic strokes in those under 55 are termed cryptogenic (no identifiable cause). Frequency of patent foramen ovale (PFO) is twice that of the general population in this group (50%±2%). 4D flow MRI may reveal haemodynamic clues to the nature of this relationship.

**Aim:** To determine the nature of right atrial flow in PFO and cryptogenic stroke versus controls.

**Methods:** 12 controls (40±7 years, 7male) with cryptogenic stroke and PFO on TOE and 12 controls (40±7 years, 6male) underwent 4D flow MRI at 3T (retrospective ECG-gated, respiratory-gated TFE, venc: 150/m/s, spatial res: 3mm², temporal res: 50–55ms, RSENSE 2). The right atrium was manually defined and flow visualised with streamlines. Peak and average velocity were assessed. Contours were positioned orthogonal to the SVC and IVC to assess flow and spatial arrangement. 8 subjects underwent repeat scans for reproducibility.

**Results:** BMI, heart rate and systolic BP compared between groups. Diastolic BP was higher in the cryptogenic stroke group (93±16 vs. 81±7, p=0.06). A spectrum of right atrial flow patterns occur in the normal heart. Non-vortical patterns are more frequent in cryptogenic stroke with PFO. The relative position of the vena cava appears to be influential in their generation. The mechanistic implications of this warrants further investigation.

**Conclusion:** A spectrum of right atrial flow patterns occur in the normal heart. Non-vortical patterns are more frequent in cryptogenic stroke with PFO. The relative position of the vena cava appears to be influential in their generation. The mechanistic implications of this warrants further investigation.

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**2934 | BEDSIDE**

Lifelong endocarditis prophylaxis for congenital heart disease patients with prosthetic material?


**Background:** Risk for infective endocarditis (IE) in adult congenital heart disease (ACHD), determined in retrospective studies, is found to be increased. This is largely attributed to prosthetic material used for repair or palliation, complex defects and residue. Guidelines recommend IE prophylaxis up to six months after complete repair of congenital heart disease with prosthetic material. Whether this is sufficient has never been determined in a prospective study.

**Purpose:** To prospectively determine incidence of and risk factors for IE in a large ACHD cohort.

**Methods:** We selected all patients included in a large registry of adult congenital heart disease. Incidence of IE was determined using Poisson regression. Predictors for IE were identified using time-dependent Cox regression.

**Results:** During a cumulative follow-up of 108499 patient-years in 15284 patients (51% female, median age 34 years), 83 IE episodes occurred in 77 patients. 556 (3.6%) patients had a currently cyanotic defect, 5878 (38.5%) had prosthetic material implanted. IE incidence was 0.76 episodes/1000 person-years (95% CI: 0.61–0.94), and did not differ between before and after the new ESC IE-prophylaxis guidelines of 2009. In multivariable Cox regression, male sex (HR=1.88; 95% CI: 1.19–2.99), history of IE (1.47; 2.27–7.65) and prosthetic material (2.84; 1.77–4.57) independently predicted IE. Complex cyanotic ACHD did not (1.29; 0.52–3.23).

**Conclusions:** The incidence rate of IE in ACHD patients 0.76/1000 patient years, which is ~15 times the general risk. Prosthetic material is an important risk factor, imposing ~3 times greater risk. These findings suggest IE prophylaxis may be warranted in all ACHD patients with prosthetic material.

**Acknowledgement/Funding:** The work described in this study was carried out in the context of the Parelroener Institute (PSI).

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**THE INCREASING EVIDENCE FOR CARDIAC REHABILITATION**

**2935 | BEDSIDE**

Is cardiac rehabilitation (CR) safe and useful in octogenarians after transcatheter aortic valve implantation (TAVI) compared to surgical aortic valve replacement (sAVR) for aortic stenosis?

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**Purpose:** To compare the safety and outcome of residential CR in octogenarians after TAVI or AVR with biological prostheses.

**Methods:** From January 2010 to June 2013 58 consecutive TAVI (27% male, age 86±4, 25 Edwards, 33 CoreValve) and 52 consecutive AVR (44% male, age 82±4) aged >80 years were enrolled in a 3-week intensive CR program (walking, up to 30 minutes of cycling or treadmill session twice daily, respiratory training). Co-morbidity (cumulative illness rating state-comorbidity index) (CIRS-CI) score, Echocardiography on admission, Disability (Barthel Index) (BI), Morse Fall Scale score (MFS), Six minute walking test distance (6MWT) on admission and at discharge were assessed; a frail index (FI) at discharge was defined as the presence of at least two of the following: 6MWT <200m, BI <75, MFS ≥50.

**Results:** Compared to AVR, TAVI were older, had worse CIRS-CI and aortic prosthetic insufficiency (API) on 0–3 scale. TAVI, as AVR, could attend safely CR training but they tolerated a significantly lower workload with lower performance at 6MWT at discharge compared to AVR even if 6MWT improvement at discharge was similar in both groups. Disability, MFS and FI were higher in TAVI at discharge; yet they had significant disability improvement during CR. At follow up (range 12–36 months) death occurrence was significantly higher in TAVI (p=0.01) (Table).

**Table 1**

<table>
<thead>
<tr>
<th>Table 1</th>
<th>TAVI (58)</th>
<th>AVR (52)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIRS-CI (Ms/SD)</td>
<td>14.1±6</td>
<td>13.1±3</td>
<td>0.001</td>
</tr>
<tr>
<td>BI discharge (Ms/SD)</td>
<td>84.1±15</td>
<td>92.1±4</td>
<td>0.03</td>
</tr>
<tr>
<td>MFS discharge (Ms/SD)</td>
<td>32.1±16</td>
<td>22.1±3</td>
<td>0.03</td>
</tr>
<tr>
<td>Training load (10W or 1.5km/h twice/d (%))</td>
<td>9.1±6</td>
<td>23.4±0</td>
<td>0.002</td>
</tr>
<tr>
<td>6MWT discharge (Ms/SD)</td>
<td>1681±131</td>
<td>249±132</td>
<td>0.02</td>
</tr>
<tr>
<td>FI (%</td>
<td>16.27</td>
<td>6.11</td>
<td>0.01</td>
</tr>
<tr>
<td>API (Ms/SD)</td>
<td>1.2±0.8</td>
<td>0.6±0.5</td>
<td>0.001</td>
</tr>
<tr>
<td>Death at follow up (%)</td>
<td>19.33</td>
<td>6.12</td>
<td>0.005</td>
</tr>
</tbody>
</table>

**Conclusion:** In octogenarians after TAVI, as in patients after AVR CR is safe and useful because it leads to disability and functional capacity recovering favoring the probability of safe discharge at home. However, compared to sAVR TAVI tolerated reduced training workloads and maintained at discharge a higher FI which is expected to have influenced survival at follow up.
2936 | BEDSIDE
Secondary prevention after myocardial infarction widens health disparities between Swedish and immigrant patients
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Background and introduction: Immigrants bear a disproportionate burden of poor cardiovascular health. Secondary prevention programs are essential for patients with myocardial infarction (MI) as modification of risk factors favorably impacts their health. However, little is known about whether disparities in cardiovascular health are influenced by secondary prevention.

Purpose: The purpose of this study was to determine if secondary prevention interventions close disparities in cardiovascular health between Swedish and immigrant MI patients.

Methods: A cohort of 400 MI patients (58.6±8.0 years) was followed for two years, 292 Swedish and 108 immigrants (71% men). During the first year after MI patients participated in a secondary prevention program. The average number of six selected risk factors, before and two years post MI was evaluated and the mean change in risk burden from baseline calculated. The risk factors were current smoking, BMI ≥ 30 kg/m², total cholesterol > 4.5 or LDL > 2.5 mmol/l (in accordance with reference values at the time of the study), HDL < 1.0/1.2 (men/women) mmol/l, blood pressure > 140/90 mmHg and HSAlac > 45 mmol/mol (> 52 mmol/mol for diabetic patients).

Results: There were significant differences in risk factor exposure between Swedes and immigrants among men (p<0.005) and women (p<0.003) two years after MI. An intervention had a beneficial effect on risk factor burden in 50% of patients (p<0.001). Significant reductions were observed for BMI, total cholesterol, HDL cholesterol, blood pressure and blood sugar.

Conclusion(s): While immigrant MI patients were less likely to report tobacco cessation, implement healthy eating habits or engage in physical activity, the intervention was equally effective in closing health disparities between the two patient groups.

2937 | BEDSIDE
Optimizing patient benefit from CRT response with the addition of high intensity interval training - a randomized controlled trial
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Background: Cardiac resynchronization therapy (CRT) improves prognosis, leading to reverse remodeling with a reduction in left ventricular (LV) size, improvement in LV ejection fraction (LVEF) and systolic volume. However, 30–40% of patients who underwent CRT are non-responders. The addition of aerobic exercise to CRT may improve clinical outcomes. Moderate aerobic exercise (MAE) has been tested in CRT patients resulting in improvements in functional hemodynamics, exercise capacity and quality of life, but data on high intensity interval training (HIIT) effects are scarce. HIIT is more effective than MAE for improving functional capacity of stable patients with heart failure. It is unknown whether the beneficial effects of HIIT may be also observed in patients following CRT with less functional impairment.

Purpose: Evaluate the effect of a 6 month combining CRT and HIIT on exercise capacity, cardiac remodeling parameters and functional capacity. Responders were considered patients with ≥10% improvement in LVEF.

Methods: We conducted a nationwide survey about participation in postoperative cardiac rehabilitation (CR) in patients after heart valve surgery. Despite this CR has, since 2009, been offered to this group of patients in the Danish health care system based on recommendations for patients with ischemic heart disease.

Purpose: The aim of this study was to investigate the impact of CR on health care use and sick leave among heart valve surgery patients.

Methods: We conducted a nationwide survey among participation in postoperative cardiac rehabilitation (CR) to all patients having undergone surgery between 1 January 2011–30 June 2011 (n=667). Amongst the respondents (n=500, 75%) 12 months register-based follow-up data were analyzed for resource use categories of primary and secondary health care (outpatient visits and hospital inpatient care), prescription medication and sick leave for CR participants (n=277, 55%) and non-participants (n=223, 45%). A difference-in difference analytical strategy was undertaken. All estimates are presented as means per patient (95% confidence intervals) based on standard errors of nonparametric bootstrapping.

Results: Total costs during 12 months follow up after heart valve surgery were EUR16,064 per patient (13,730.0–18,399.4) in the CR participation group and EUR 15,182 (12,694.5–17,670.2) in the non-participation group. CR was found to lead to 5.6 (2.9–8.3) more outpatient visits per patient which was not reflected in a corresponding increase in outpatient visits among the non-participants. Additionally no statistically significant differences were observed between the groups for primary care, hospital inpatient care, prescription medication, sick leave or for the overall total costs EUR 1,330 (−4,426.9, 7,085.7).
Conclusions: CR as provided in Denmark can be considered cost neutral and with a high participation rate. CR is associated with more outpatient visits however no significant differences occurred in terms of overall total cost. Further studies should investigate the benefits of CR to heart valve surgery patients on patient reported outcomes e.g. health-related quality of life as part of a formal cost-utility analysis.

2940 | BEDSIDE
Effectiveness of cardiac rehabilitation in patients with type 2 diabetes mellitus after percutaneous coronary intervention

Introduction: Patients with diabetes mellitus are at increased risk of recurrent cardiovascular events after percutaneous coronary intervention.

Purpose: The aim of this study was to determine if cardiac rehabilitation decreases mortality and recurrence of cardiovascular events in this subgroup of patients after percutaneous coronary intervention.

Methods: We performed a retrospective cohort study of 318 consecutive patients with type 2 diabetes mellitus who underwent percutaneous coronary intervention in our hospital between September 2004 and January 2011. We classified the patients in two cohorts according to their participation (n=154) or not (n=164) in a cardiac rehabilitation programme. Events occurring in the first 2 years of follow-up were recorded.

Results: CR was associated with a significant decrease in all-cause mortality (OR 0.105 [95% CI: 0.31–0.356]; p<0.001) and cardiac mortality (OR 0.107 [95% IC: 0.24–0.468]; p<0.001) over a two year follow-up. No significant differences were observed in nonfatal myocardial infarction, stent restenosis and nonfatal stroke.

Conclusion: Participation in a CR programme after percutaneous coronary intervention is associated with a significant reduction in cardiac mortality and all-cause mortality rates in type 2 diabetic patients.

2942 | BEDSIDE
Sleep disordered breathing in cardiac rehabilitation: prevalence, predictors and influence on six-minute walk test
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Background: Identification of non-traditional risk factors is an important component of cardiac rehabilitation (CR). Yet, the prevalence and predictors of sleep disordered breathing (SDB), and its influence on exercise capacity in patients attending CR remain not well described.

Methods: Patients enrolled in a national CR center were eligible for a comprehensive screening program for SDB. Screening questionnaires for SDB, overnight sleep study, and 6-minute walk test (6MWT) were conducted.

Results: A total of 332 patients (mean age 62±10, 62.4% male) attending CR for primary (29.2%) and secondary (70.8%) prevention were recruited. Of which, 209 patients agreed and successfully completed the sleep study. SDB was diagnosed in 32.2% of the patients. SDB patients were older, had higher body mass index, neck and waist circumference than non-SDB patients. After adjusting for neck and waist circumference, age (OR −1.06; 95% CI 1.02–1.10; p=0.001) and body mass index (OR=1.19; 95% CI 1.10–1.30; p=0.001) remained independent predictors of SDB. The prevalence of excessive daytime sleepiness (Epworth Sleepiness Scale >10) was 23.9% versus 17.7% (p=0.029), high-risk for SDB based on Berlin Questionnaire (43.4% versus 35.5%; p=0.277) or STOP-BANG questionnaire (63.2% versus 53.2%; p=0.170) were similar between SDB and non-SDB groups. 6MWT scores were significantly lower in SDB versus non-SDB groups (mean difference −32m; 95% CI −57 to 7; p=0.013) (Figure). However, the relationship was no longer significant after adjusting for age, gender and waist circumference.

Change in NC volume following exercise

Conclusions: Exercise-induced plaque stabilization via reduced necrotic core (NC) and plaque burden (PB), the purpose of the study was to identify potential clinical predictors of regression of coronary atherosclerosis following aerobic exercise.

Methods: Post-hoc analysis of associations between baseline clinical variables and reductions in coronary NC and PB following aerobic exercise intervention. Plaque characteristics were measured with grayscale and radiofrequency intravascular ultrasound in 36 patients (median age 58.5 years, 7 women) with stable coronary artery disease (SCAD) or non-ST-elevation acute coronary syndrome (NSTE-ACS). Screening of variables was performed with random forest analysis followed by multivariate linear regression.

Results: The only significant variable for NC reduction was clinical presentation of disease (SCAD vs. NSTE-ACS, p<0.011). The change in NC was −4.94 (−10.33; −1.33) mm³ in patients with SCAD, and 1.03 (−4.29;3.71) mm³ in patients with NSTE-ACS (p=0.01). NC was reduced in 17 patients (94%) with SCAD and 8 patients (44%) with NSTE-ACS (p=0.01, Figure). R-squared for the model including baseline clinical presentation and baseline NC volume was 0.90. There were no significant explanatory variables for PB reduction.

Change in total core volume

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Methods: Post-hoc analysis of associations between baseline clinical variables and reductions in coronary NC and PB following aerobic exercise intervention. Plaque characteristics were measured with grayscale and radiofrequency intravascular ultrasound in 36 patients (median age 58.5 years, 7 women) with stable coronary artery disease (SCAD) or non-ST-elevation acute coronary syndrome (NSTE-ACS). Screening of variables was performed with random forest analysis followed by multivariate linear regression.

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Change in NC volume following exercise
**Sports Cardiology in Development**

2966 | BEDSIDE
High aerobic capacity is associated with increased survival. A 44 years follow-up of the study of men born in 1913

P. Ladenvall1, C. Persson2, Z. Mandalenakis1, L. Wilhelmsen1, G. Grimby2

**Purpose:** To study the predictive power of aerobic capacity regarding survival over 44 years of follow-up.

**Methods:** The study is part of "The Study of Men born in 1913", a longitudinal prospective study of men, living in a city in Sweden. A random sample of 855 men was followed from 50 to 98 years of age with repeated examinations and by linkage to the National Hospital Discharge and Cause of Death registers. In 1967, at the age of 54, 792 men participated in a bicycle exercise test of whom 1082 (83%) performed maximum exercise. Predicted VO2max was based on measurements in a subsample of participants. Risk factor levels were assessed at baseline and during follow-up.

**Results:** High VO2max during maximum exercise, no smoking, low serum cholesterol and low mean arterial blood pressure at rest were all significantly associated with survival in a Cox regression analysis (p < 0.001 for all). In multivariable analysis including body height as a variance reducer, the association between VO2max tertiles and survival was independent of established risk factors; Hazard Ratio (HR) 0.79 (0.71-0.87) (p = 0.0001) for VO2max, HR 1.01 (1.002-1.02), (p = 0.001) for mean arterial blood pressure at rest, HR 1.13 (1.04-1.22), (p < 0.005) for serum cholesterol and HR 1.58 (1.34-1.85) (p < 0.0001) for smoking. The variable impact (Wald's c2) of maximum VO2 tertiles (15.3) was secondary only to that of smoking habits (31.4). The benefit of high VO2max was confirmed throughout four decades of follow-up after exercise testing.

**Conclusion:** In a Swedish sample of middle-aged men, high aerobic capacity versus a low one, was associated with increased survival during more than forty years of follow-up. This effect was independent of traditional risk factors including smoking, blood pressure and serum cholesterol.

**Acknowledgement/Funding:** Insurance company Försäkrings AB.

2967 | BEDSIDE
Effect of gender and sporting discipline on left ventricular adaptation to exercise


**Purpose:** To assess the dose relationship between endurance exercise and coronary artery calcification in both male and female veteran athletes.

**Methods:** Veteran athletes were defined as >40 years of age, running >10 miles/wk, and having competed in multiple endurance events over a 10 year period. Coronary artery calcium (CAC) scores were obtained using a VCT XFe GE prospectively gated scanner (GE Healthcare). A significant CAC score was defined as >700 centile for age and gender.

**Results:** The relationship between the dose of exercise and coronary artery calcification in veteran athletes A. Merghani1, K. Afzakh2, K. Patel2, V. Maestri2, S. Rosmini3, A. Cox1, H. Dhuitia1, R. Narain1, J. Moon3, S. Sharma1. 1 St George’s University of London, London, United Kingdom; 2 University Hospital Lewisham, London, United Kingdom; 3 The Heart Hospital, London, United Kingdom.

**Acknowledgement/Funding:** St George University of London, London, United Kingdom.

518 The increasing evidence for cardiac rehabilitation / Sports cardiology in development

**Methods:** The study reported on 1082 healthy, elite, Caucasian athletes (41% females, mean age 21.8±5.7 years) who underwent ECG and echocardiogram as part of their cardiovascular evaluation. Sports were divided into static, dynamic or mixed as per the Mitchell classification. Left ventricular geometry was classified into 4 groups according to relative wall thickness (RWT) and left ventricular mass (LVM) (normal LVM/normal RWT, concentric hypertrophy (increased LVM/increased RWT), eccentric hypertrophy (increased LVM/normal RWT), concentric remodelling (normal LVM/increased RWT).

**Results:** Athletes engaged in 40 different sporting disciplines (62% mixed, 28% dynamic, 10% static) with similar participation rates by type of exercise between female and male athletes. Females exhibited lower LVM (83±17 vs 101±21 g/m², p < 0.001) and RWT (0.35±0.05 vs 0.36±0.05, p < 0.001) compared to male athletes. Female athletes demonstrated lower absolute (49±4 vs 54±5 mm, p < 0.001) but higher indexed for BSA LVM end-diastolic diameters (29±3 vs 27±3 mm/m², p < 0.001). The majority of athletes showed a normal LV geometry (69% males vs 71% in females, p = 0.54). There were no significant gender differences relating to the LV geometry in athletes competing in static or mixed sport. In contrast, a greater proportion of female compared to male athletes competing in dynamic sport exhibited eccentric hypertrophy. Only 4% of females compared to 15% of males demonstrated concentric hypertrophy/remodelling (p < 0.002).

**Conclusions:** Female athletes participating in dynamic sport exhibit predominantly eccentric hypertrophy. Our results indicate that although the presence of concentric remodelling or hypertrophy in male athletes engaged in dynamic sport is a common phenotype, it should raise suspicion of underlying cardiomyopathy in female athletes.
Results: We evaluated 112 veteran athletes (M=81, F=31, mean age=55.9±1.6) and 18 healthy aged matched sedentary controls (M=10, F=8). The lowest incidence of significant CAC was observed in athletes running >20 miles per week and finishing marathons in 2:45–3:15h for males and running 20–30 miles per week and finishing marathons in 3–3:30h for females (see diagram). Running more or less than those mileages and running slower or faster than these marathon times conferred unfavourable CAC. Male athletes who run faster and longer than those ranges had a 2–3 fold increase in CAC (>70th centile (39% vs 13%, p=0.037 for weekly mileage)).

Conclusion: These data indicate a U shaped relationship between the dose of exercise and coronary artery calcification in both male and female veteran athletes. Running at modest duration and intensity is more beneficial than no exercise but higher doses of exercise may accelerate atherosclerosis.

GENETICS ASPECTS OF ARRHYTHMIAS

2897 | BESIDSE
Role of electrophysiological study for risk stratification of asymptomatic patients with Brugada syndrome: a meta-analysis
S. Stavroukas, R. Lazzara. University of Oklahoma Health Sciences Center, Oklahoma City, United States of America

Introduction: Brugada syndrome (BrS) is an inherited channelopathy associated with an increased risk of sudden cardiac death. An implantable cardioverter defibrillator is recommended for patients with aborted cardiac arrest or syncope. However, controversy still exists regarding the risk stratification scheme for asymptomatic patients with BrS. We performed a meta-analysis of published trials to examine the role of electrophysiological study (EPS) for risk stratification of asymptomatic patients with BrS.

Methods: We searched MEDLINE and EMBASE databases for studies evaluating the predictive accuracy of EPS in patients with BrS. Trials which reported outcomes in asymptomatic patients were included. Among studies pertaining to the same patient cohort, only the largest study was retained to avoid duplication of data. Risk ratios (RR) with 95% confidence interval (CI) were calculated using a random effects modeling approach.

Results: Sixteen studies involving 2,997 patients with BrS were included. Of those, 1,278 (43%) patients were asymptomatic and underwent an EPS. EPS was positive in 540 of 1,278 (42%) asymptomatic patients. During a median follow-up of 34 months, 38 (3%) asymptomatic patients had an arrhythmic event. Based on the pooled estimate across the 16 studies, inducibility of ventricular tachyarrhythmia (VT) during EPS failed to predict arrhythmic events during follow up (RR 1.50, 95% CI 0.77 to 2.91, p=0.23; Figure).

Conclusion: Inducibility of VT during EPS does not predict future arrhythmic events in asymptomatic patients with BrS. The available evidence does not support a significant role of EPS for risk stratification of asymptomatic patients with BrS.

2898 | BESIDSE
Worldwide experience with the S-ICD in patients with congenital long QT
R. Weiss1, B. Knight2, S. Kaab3, P. Neuizi4, P. Sheridan5, L. Eckhardt6, R. Weiss1, B. Knight2, S. Kaab3, P. Neuizi4, P. Sheridan5, L. Eckhardt6,

Abstract 3030 – Table 1

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Overall event rate for &lt;3 h</th>
<th>Overall event rate for DA ≥3 h</th>
<th>Adjusted HR (95% CI) for &lt;3 h</th>
<th>Adjusted HR (95% CI) for DA ≥3 h</th>
<th>Interaction p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy</td>
<td>Primary outcome (CV death / MI / stroke)</td>
<td>8.0%</td>
<td>0.82 (0.64–1.04)</td>
<td>11.0%</td>
<td>0.83 (0.67–1.03)</td>
</tr>
<tr>
<td>All-causes</td>
<td>death</td>
<td>2.6%</td>
<td>0.81 (0.53–1.26)</td>
<td>4.1%</td>
<td>0.83 (0.58–1.18)</td>
</tr>
<tr>
<td>Cardiovascular (CV) death</td>
<td>2.1%</td>
<td>0.81 (0.50–1.36)</td>
<td>3.5%</td>
<td>0.89 (0.60–1.30)</td>
<td>0.79</td>
</tr>
<tr>
<td>Safety</td>
<td>Major bleeding at 7 days</td>
<td>5.9%</td>
<td>0.79 (0.60–1.05)</td>
<td>5.6%</td>
<td>1.51 (1.12–2.04)</td>
</tr>
<tr>
<td>Major bleeding at 30 days</td>
<td>8.3%</td>
<td>0.88 (0.70–1.11)</td>
<td>12.4%</td>
<td>1.22 (1.00–1.49)</td>
<td>0.037</td>
</tr>
<tr>
<td>Major bleeding at 360 days</td>
<td>11.4%</td>
<td>0.88 (0.72–1.08)</td>
<td>15.7%</td>
<td>1.33 (1.11–1.58)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Abstract 3030 | The Ohio State University, Columbus, United States of America; 7 AstraZeneca Research and Development, Molndal, Sweden; 8 Brigham and Women's Hospital, Boston, United States of America; 9 The Ohio State University, Columbus, United States of America; 10 Raphaellokinik Muenster, Department of Internal Medicine, Munster, Germany; 11 Pacific Heart Institute, Santa Monica, United States of America; 12 CMCA/Sequioa Hospital, Redwood City, United States of America; 13 Auckland City Hospital, Auckland, New Zealand

Introduction: Long-QT syndrome patients (pts) with an ICD indication are young individuals likely to survive many generator changes. Transvenous (TV) leads carry a risk of complications and increased procedure time. Subcutaneous implantable cardioverter defibrillator (S-ICD) may be an attractive option for these pts but data are scarce. We report on a worldwide experience of a large cohort with long-term follow-up in this group of pts.

Methods: Data from the S-ICD EFFORTLESS multicenter real world registry and IDE studies were pooled (N=882). All patients with a primary indication of Long-QT were included.

Results: A total of 27 pts met inclusion criteria. Age 38±13 y/o, 67% male and 13 pts (45%) were implanted for secondary prevention. Seven patients (25.9%) had a previous TV-CI (5 explanted due to infection and 2 for lead failure) and 1 patient had a concomitant pacemaker implanted prior to the SICD. During a mean follow-up of 1.8±0.8 years, there were no deaths. SICD revision occurred in 2 pts (7.4%) (1 infection, 1 repositioning). 21 of 22 pts (96%) with complete SICD testing at implant converted with ≤65J and all 100% were successful at 80J. Eight ventricular episodes in 4 patients (15%) were converted after a single shock. One patient had a VT storm with all shocks being successful. Cardiac oversensing led to device therapy in 3 (11%) patients all resolve with vector reprogramming. Converting to the non-LQT indication was different among groups with a follow up of 1080 days (13% for LQT and 16% for Non-LQT pts)

Conclusion: In the Largest cohort of Long-QT patients with the S-ICD followed to date, the SICD system was an acceptable alternative to TV-CI. All ventricular arrhythmias were successfully terminated. Inappropriate shocks were caused by oversensing and were corrected by vector reprogramming in all patients. Rates of inappropriate shocks were equivalent in the 2 patient groups.

Acknowledgement/Funding: The S-ICD IDE and EFFORTLESS studies were sponsored by Boston Scientific.

ANTITHROMBOTIC DRUGS – AN ONGOING RESEARCH

3030 | BESIDSE
Effect of time to interventional treatment on NSTE-ACS outcomes in PLATO
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Background: Ticagrelor (Ticag) has a faster onset of antiplatelet activity than clopidogrel (Clo). Early use of potent antiplatelet therapy would be expected to have benefit, although the use of another potent antiplatelet prior to angiography was seen to have no benefit and increased bleeding.

Purpose: We investigated efficacy and safety outcomes of Ticag vs Clo in the PLATO trial in NSTE-ACS pts undergoing early vs. late diagnostic angiography (DA) during the index hospitalisation.

Methods: 6792 NSTE-ACS pts underwent DA <72 hours of randomisation. Adjusted Cox proportional hazards models evaluated the interaction between timing of DA and randomisation to antiplatelet treatment “early” (<3h) or “late” (>3h) on outcomes following DA.

Results: Median time to DA was 2.7h (0.6–21.1h). There were 3486 pts in the early cohort (1749 Ticag and 1737 Clo) and 3306 in the late cohort (1697 Ticag and 1609 Clo). Initial planned treatment approach was invasive in 95% of early subjects, 73% in late subjects. In multivariate adjusted analyses, there were no significant interactions for efficacy endpoints, with similar benefit with Ticag vs Clo on CV death/MI/stroke and mortality. An interaction was observed for major bleeding, with no difference in the early DA group, but higher bleeding with Ticag at 7 days in the late DA group (Table).

Conclusion: In pts with NSTE-ACS in PLATO, the clinical benefit of Ticag over Clo was consistent in those undergoing early and late DA. In early DA pts, the benefit was consistent with outcomes at 7, 30 and 360 days, with no increase in the risk of major bleeding. In late DA pts, consistent efficacy benefit was seen with Ticag, but Ticag was associated with increased bleeding compared to Clo
3031 | BEDSIDE
Treatment and long-term results of acute coronary syndrome (ACS) in patients on chronic oral anticoagulants (OAC): data from the EPICOR (NCT01171404) study

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Background: The number of ACS patients receiving OAC as chronic medication is increasing. Triple therapy increases risk of haemorrhagic complications (Huber K et al. Am Heart J 2014;168:611–621). Patients receiving OAC may require adapted management strategies. Registries are tools to verify in real life the guidelines indications; reperfusion therapy is indicated in all patients <12h from symptom onset.

Purpose: To analyse the outcomes of ACS patients receiving OAC enrolled in the EPICOR study.

Methods: EPICOR (prospective, multicentre, observational, longitudinal cohort study) included ACS patients within 24h of symptom onset and follow-up to 2 years. The analysis was in STEMI and UA/NSTEMI groups.

Results: The study enrolled 10,568 patients at 555 sites in 20 countries. Among them, 345 (3.3%) patients were on OAC (77 [22.3%] STEMI and 268 [77.7%] UA/NSTEMI) (Table). Only 44 (65.7%) STEMI patients had pPCI and 51 (28.2%) UA/NSTEMI patients had PCI. Two-year mortality in the total OAC group was 45/453 (10.9%).

Conclusions: Interventions in ACS patients receiving chronic OAC are rarely performed. PCI in patients with STEMI on OAC is delayed. A high incidence of death, MI and stroke was observed at 2 years post-discharge.

3032 | BEDSIDE
Efficacy and Safety of Ticagrelor for Long-Term Secondary Prevention of Atherothrombotic Events in Relation to Renal Function: Insights from the PEGASUS-TIMI 54 trial

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Background: The PEGASUS-TIMI 54 trial showed that ticagrelor (T), reduces the relative risk of ischemic and bleeding events with T was similar by category of eGFR (P-trend=0.007). There was no heterogeneity in bleeding risk with T by RF (P-int=NS). Full details by T dose at ESC.

Methods: PEGASUS-TIMI 54 randomized 21,162 pts with a history of MI in the PEGASUS-TIMI 54 trial, worsening RF was associated with an increased risk of ischemic events but with similar TIMI Major bleeding risk. Pts with non-end stage renal dysfunction may enjoy a favorable benefit-risk profile with long-term T treatment, with greater absolute risk reduction for ischemic events, but a similar absolute risk increase for TIMI Major bleeding.

Conclusions: In pts with a history of MI in the PEGASUS-TIMI 54 trial, worsening RF was associated with an increased risk of ischemic events but with similar TIMI Major bleeding risk. Pts with non-end stage renal dysfunction may enjoy a favorable benefit-risk profile with long-term T treatment, with greater absolute risk reduction for ischemic events, but a similar absolute risk increase for TIMI Major bleeding.

Acknowledgement/Funding: The PEGASUS-TIMI 54 Study was funded through a grant from AstraZeneca

BICUSPID AORTIC VALVE DISEASE – NEW KNOWLEDGE AND OPEN QUESTIONS

3049 | BEDSIDE
Gender differences in the clinical history of adult patients with bicuspid aortic valves

H. Hahkka1, R.M. Suri1, O. Katan1, M.F. Eleied1, M.A. Clavel1, M.J. Maurer2, P.A. Pellikka1, D. Mahoney1, M. Enriquez-Sarano1, Mayo Clinic, Rochester, United States of America

Background: Bicuspid aortic valve (BAV), the most common congenital heart defect, affects men more than women, but long-term assessment of gender-specific outcomes is lacking.

Purpose: To determine gender-specific outcome differences in BAV adults within a community cohort, and verify gender-patterns of morbidity and mortality in large tertiary-referral groups.

Methods: Retrospective analysis of long-term outcomes in a community-cohort of 416 patients diagnosed with BAV from 1980 to 1999 (age 35±21 years, follow-up 9±6 years), and in a tertiary-referral cohort of 2824 adult patients diagnosed with BAV from 1990 to 2011 (age 51±16 years, follow-up 9±6 years). Cross-sectional analysis of a third group of 2242 adult BAV patients referred for aortic valve replacement from 1995 to 2010 (age 62±14 years).

Results: Community-cohort analysis showed no gender difference in 25-year survival (p=0.41), however, 20-year risk of BAV-related morbidity was higher in men (52±4% versus 35±6%, p=0.01), as was the 20-year risk of developing moderate aortic regurgitation (36±5% versus 14±5%, p=0.01). Overall incidence of infectious endocarditis was 13.94 (95% CI 7.25–26.79) per 10,000 patient-years (age-adjusted relative risk 1.19 [95% CI 1.47–2.74] compared to the general population, p<0.0001) with 25-year rate of 5±2% for men versus 0% for women (p=0.046). Tertiary-referral group analysis showed no gender difference in 20-year survival (p=0.79), but overall 20-year survival rate was lower than expected compared to the general population (64±2% versus 72%, p<0.0001), with age-adjusted relative death risk of 1.16 (95% CI 1.05–1.29) for men and 1.67 (95% CI 1.38–2.03) for women, p=0.001. Independent predictors of mortality were age >50 years and Charlson comorbidity index for both genders (all p<0.009), and ejection fraction for men only (p=0.004). Surgical-referral group supported observed morbidity gender-patterns.

Conclusions: The long-term outcome of adults with BAV is not benign as both men and women incur excess mortality. Risk of significant aortic regurgitation and BAV-related complications is higher in men compared to women. Infectious endocarditis incidence is higher in BAV patients compared to the general population, and affects men more frequently. Paradoxically, when compared to the general population, women exhibit higher long-term risk of death than men. These observations warrant due attention from the clinical and research communities.

Acknowledgement/Funding: AstraZeneca
**Bicuspid aortic valve disease – New knowledge and open questions / Detect to repair deficient cardiac genes**

**3050 | BEDSIDE**

BAV morphology in relation to coronary vessel dominance and outcome

W.M.C. Koernraad1, G. Tokmaj2, H.W. Vliegen1, A.J.H.A. Scholte1, H.M. Siebelink1, A.C. Gittenberger-De Groot3, B.J. Mulder2, B.J. Bouma1, M.J. Schalij1, M.R.M. Jongbloed1, 2. Leiden University Medical Center, Department of Cardiology, Leiden, Netherlands; 3. Academic Medical Center of Amsterdam, Cardiology, Amsterdam, Netherlands; 4. Leiden University Medical Center, Department of Anatomy and Embryology, Leiden, Netherlands

**Purpose:** Variable coronary anatomy has been described in patients with bicuspid aortic valves (BAVs). Prognostic relevance of coronary vessel dominance in this patient group is unclear and was never specified to BAV morphology. The purpose of this study was to evaluate BAV morphology in relation to coronary vessel dominance and outcome in patients with isolated BAV and with associated aortic coarctation (CoA).

**Methods:** Valve morphology of 189 BAV patients (141 men (79.2%), 51±14 years) was evaluated retrospectively by echocardiography. Coronary anatomy and coronary artery disease (CAD) were assessed by computed tomography or coronary angiography.

**Results:** Strictly bicuspid valves (without raphe) with left-right cusp orientation, had more left dominance than BAVs with left-right cusp orientation with a raphe (48% vs 27.3%, p=0.047). In general, strictly bicuspid BAVs more often had significant CAD (36.4% vs 21.9%, p=0.029) and coronary events (25.9 vs 40%, p=0.029) than BAVs with a raphe. Strictly bicuspid valves with left-right cusp orientation had more significant CAD than left-right oriented BAVs with a raphe (37.5% vs 20.9%, p=0.047). Patients with associated CoA more often had a strictly bicuspid valve and showed more left dominance than the non-CoA group (resp. 31.8 vs 17%, p>0.501 and 65.2 vs 24.1, p<0.05).

**Conclusion:** Strictly bicuspid aortic valves, especially with left-right cusp orientation, more often have a left dominant coronary artery system and are at risk of developing significant CAD. In patients with CoA, left dominance is more common, indicating these patients might be more at risk for developing CAD.

**3051 | SPOTLIGHT**

NOTCH1 polymorphisms as a predictor of aortic insufficiency in patients with bicuspid aortic valve


**Objectives:** To establish the contribution of NOTCH1 polymorphisms on the development of a combined BAV and CoA.

**Methods:** The study included 34 patients; the control group consisted of 200 people without CHD. We applied a targeted screening of 10 exons and the adjoining introns of NOTCH1, previously described in association with LVOT malformations and BAV.

**Results:** In 12 of 34 patients with a combination of CoA and BAV observed AR were more common (33.3%). In the control group similar exon combination practically met (1%) in patients with normal function BAV and CoA observed in a very low percentage (4.5%).

**Conclusions:** Thus, intronic NOTCH1 SNPs, probably are less associated with BAV development, but have a greater impact on remodeling type and AR.

**DETECT TO REPAIR DEFICIENT CARDIAC GENES**

**3065 | BENCH**

Proximal titin A-band truncation causes dilated cardiomyopathy in response to increased afterload in mice

I.G. Lunde1, H. Wakiimoto2, M.A. Burke3, V. Soukoulis4, W.A. Linke2, J. Gorham1, D. Conner1, G. Christensen1, J.G. Seidman3, C.E. Seidman4.

1. Harvard Medical School, Department of Genetics, Boston, United States of America; 2. Ruhr University Bochum (RUB), Bochum, Germany; 3. Institute for Experimental Medical Research, Ulevaal University Hospital, Oslo, Norway

**Purpose:** Approximately 20% of dilated cardiomyopathy (DCM) patients carry heterozygous truncating mutations in the giant protein titin (TTN). Titin spans the cardiomyocyte sarcomere from Z-disc to M-line and is important for assembly, contraction, relaxation and signaling. Truncating mutations are overrepresented in DCM patients and female mice (age 6-60 weeks) were viable, fertile and not different from wildtype (WT) in appearance, activity, or echocardiographic phenotype. Digital PCR of RNA from TTN A hearts (n=3) showed mutant transcripts levels 0.4-fold that of WT allele, and gels and immunoblot detected no mutant titin protein. TTN A and WT mice (n=5-6 per study) were stressed for ten weeks by voluntary cage-wheel running and two weeks of isoproterenol infusion, evoking no difference in echocardiographic phenotypes. Compound TTN A/LMNA mutation mice showed no exacerbation of DCM compared to LMNA mice (LVDD 4.02mm vs. 3.97mm, both p<0.05 vs. WT). By contrast, TTN A mice treated for two weeks of ANGII infusion showed hypertrophy with exacerbated diastolic dysfunction (lontitudinal strain rate 12.3±1 vs. WT: 9.6±1, p<0.05) and 3.8-fold higher BNP mRNA. Thoracic aortic constriction (TAC) exacerbated DCM in TTN A: LVDD at 1 week 3.75mm vs. 3.38mm in WT (p<0.05) and at 4 weeks 4.36mm vs. 3.77mm (p<0.05). TAC increased left atrial diameter, lung weight and BNP in TTN A vs. WT. RNAseq (n=3) analyses of TAC and ANGII treated TTN A vs. WT confirmed reduced TTN transcripts and showed differential expression (fold change >1.5 (p<0.001) of 1465 and 1434 transcripts. Pathway analyses implicated (GFD) as upregulated regulator and identified the cardiac hypertrophy and heart muscle cells. Patients with dysfunctional desmin develop progressive myocardopathy and cardiomyopathy. Frequently, cardiac complications determine life expectancy of these patients and therefore comprehensive treatment strategies are needed. In recent studies desmin deficient (DKO) mice were used as an animal model of hypertrophic cardiomyopathy.

**Aim of this study was to investigate the effect of adenovirus (AAV) mediated gene transfer of wild type desmin (DES)-cDNA on the development of cardiomyopathy in desmin deficient mice.**

M.B. Heckmann1, R. Bauer1, L. Winter2, K.H. Struckenberg3, A. Jannning1, R. Schroeder2, H.A. Katus1, C.J. Mueller1, 1. University Hospital of Heidelberg, Cardiology Department, Heidelberg, Germany; 2. University Hospital Erlangen, Institute of Neuropathology, Erlangen, Germany

Desmin is a type III intermediate filament, which is mainly expressed in muscle cells comprising 2% of the cardiac muscle’s total protein mass. Its ability to form a filamentous network is crucial to maintaining the structural integrity of skeletal and heart muscle cells. Patients with desmin dysfunction develop progressive myocardopathy and cardiomyopathy. Frequently, cardiac complications determine life expectancy of these patients and therefore comprehensive treatment strategies are needed. In recent studies desmin deficient (DKO) mice were used as an animal model of hypertrophic cardiomyopathy.

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1. Harvard Medical School, Department of Genetics, Boston, United States of America; 2. Ruhr University Bochum (RUB), Bochum, Germany; 3. Institute for Experimental Medical Research, Ulevaal University Hospital, Oslo, Norway

**Conclusion:** Transcripts encoding a titin A-band truncation are expressed but do not yield detectable mutant protein. Homozygous mice are embryonic lethal, whereas heterozygous mice show overt cardiac phenotype without stress. Increased afterload induces DCM in titin A-band truncation mice and promotes expression of cardiotoxic pathways.

**3066 | BENCH**

AAV9-mediated gene transfer of desmin restores cytoskeletal integrity and attenuates development of cardiomyopathy in desmin-deficient mice

M.B. Heckmann1, R. Bauer1, L. Winter2, K.H. Struckenberg3, A. Jannning1, R. Schroeder2, H.A. Katus1, C.J. Mueller1, 1. University Hospital of Heidelberg, Cardiology Department, Heidelberg, Germany; 2. University Hospital Erlangen, Institute of Neuropathology, Erlangen, Germany

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**Conclusion:** Transcripts encoding a titin A-band truncation are expressed but do not yield detectable mutant protein. Homozygous mice are embryonic lethal, whereas heterozygous mice show overt cardiac phenotype without stress. Increased afterload induces DCM in titin A-band truncation mice and promotes expression of cardiotoxic pathways.
22.2±9.8% on protein level yielding a typical distribution pattern characterized by cross striation and signal accumulation at the intercalated discs. Reconstitution of the desmin filamentous network also enabled syncoilin to form a proper filamentous network. AAV-DES treated mice revealed significantly reduced heart weight to tibia length ratios compared to AAV-LUC-treated animals. Cardiomyocyte number and mass were also decreased, confirming a reduced hypertrophy in AAV-DES treated animals. Masson’s trichrome stained OCT sections revealed large fibrotic areas in AAV-LUC animals which were not present in AAV-DES animals or wild type controls. Follow up echocardiography revealed a significantly smaller decrease in FS (p<0.03) and practically no increase in LV EDV. Maximal rate of pressure development was also increased compared to AAV-LUC controls (p<0.03).

In summary, our data show that AAV-mediated gene transfer of the wild type desmin cDNA is a method to restore desmin filaments in desmin deficient mice. Reconstitution of syncoilin filaments, reduced fibrosis and hypertrophy as well as ameliorated contractile function underlines the potential use of this approach for treating the cardiomyopathy associated with desminopathy.

3067 | BEDSIDE
Performance of the copy number variant (CNV) screening using next generation sequencing in a cohort of inherited cardiac disease patients

J. Palomino Doza, D. De Una, C. Gayoso, M.L. Pena Pena, J.P. Ochoa, M. Ortiz, D. Garcia, A. Graná, O. Martínez De Iriartu, L. Monserret. Instituto Investigacion Biomedica, A Coruña, Spain

Background: Inherited cardiac disease are as a group a prevalent condition usually associated with high morbidity and mortality. Previous genetic screenings in the literature report a responsible mutation in a portion of patients between 16 and 30% depending on the population and disease. The remaining patients remain genetically undetermined.

Copy number variants (CNVs) are the major type of structural variation in human genome and are important sources of human genetic and phenotypic variation. CNVs have been associated to predisposition to human diseases. Next generation sequencing (NGS), unlike traditional Sanger sequencing, allows the detection of structural variants. Our aim was to describe the performance of CNV screening in a cohort of patients with inherited cardiac disease.

Methods: One thousand and eight patients were sent to our laboratory to be sequenced using HiSeq NGS with a 214 gene panel. Analyses were focused in the genes previously associated with each pathology. CNVs were explored using comparison of sequencing coverage after normalization for total coverage in each region. Each region was analyzed using absolute coverage and deviation from the median.

Results: The two commonest phenotypes were hypertrophic cardiomyopathy (HCM) and dilated cardiomyopathy (DCM). N=338 and 171 respectively. Fifty percent of the probands were males. Mean age of diagnosis was 39±24 years. Thirty CNVs were found (2.97% of patients), 17 were considered responsible for disease (1.68% of patients). Positivity of CNV ranged from 0 in DCM or CPVT to 5.8% in ARVC (See Table 1). Four CNVs were found in ARVC probands, all considered associated with disease. CNVs represent 10% of ARVC associated mutations and 15% of disease in 7% of patients with other cardiomyopathies. Four CNVs were identified in aortic disease probands representing 5.2% of the population, 3 of them were considered associated with the disease. CNVs are 8% of the mutations associated with aortic disease and explain the phenotype in 9.3% of the probands.

Conclusion: This is the first cohort to define the performance of CNV analyses across a big cohort of cardiac inherited disease. CNVs detection using NGS coverage analysis is a reliable tool during genetic diagnosis of inherited cardiac disease. CNVs could explain 3% of the inherited cardiac disease cases. CNVs are a common cause of disease in genotype negative patients, especially in ARVC and aortic inherited disease. CNV analysis should be routinely performed during genetic test of inherited cardiac disease.

Acknowledgement/Funding: Health in Code

3068 | BENCH
The Eya4/Six1 signalling cascade is activated in acquired heart disease

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Rationale: We previously identified a mutation in the human transcriptional co-factor Eya4 as cause of familial dilated cardiomyopathy (DCM). We now provide evidence that the Eya4/Six1 signalling cascade also is crucial in acquired heart disease.

Hypothesis: We hypothesize that the transcriptional complex Eya4/Six1 regulates targets relevant in normal cardiac function. We speculate that Eya4/Six1 complex amongst others, regulates the expression of p27kip1 (p27), a known inhibitor of hypertrophy in adult cardiomyocytes, upon hypertrophic stimuli.

Methods and results: We first examined the correlation of Eya4 and p27 in regards to phosphorylation and cellular distribution in cryosections of failing and normal human hearts. Immunocytochemical analysis revealed Eya4 is mainly distributed in the cytoplasm while p27 predominantly resides in the nucleus of healthy myocardial tissue. In sections of failing human hearts, Eya4 was accumulated in the perinuclear and nuclear region; nuclear p27 levels were significantly diminished, phosphorylated p27 was evenly distributed in the cytoplasm. In a murine model of MI, immunofluorescence staining showed Eya4 is translocated to the nucleus in a time-dependent manner. 16 min after experimental MI there is a strong perinuclear accumulation of Eya4 in cardiomyocytes; translocation to the nucleus was detectable 24h post infarction compared to the cytoplasmic distribution in non MI tissue. WB analyses for p27 showed an age dependent decrease in p27 protein levels upon experimental MI compared to control littermates, respectively.

In addition, we generated transgenic mice with constitutive myocardial overexpression of Eya4 and the truncated isoform E193. As judged by MRI, histodynamic and morphometric analysis both transgenic mice models developed cardiac phenotypes compared to age-matched wildtype littermates already at basal conditions in an age dependent manner. p27 expression and downstream factors were also altered in both transgenic lines as a result of Eya4, and accordingly, E193 overexpression.

Conclusion: In summary, we provide evidence that the Eya4/Six1 signalling cascade is not only relevant in a rare version of heritable DCM but also in more common forms of acquired heart disease such as Myocardial infarction and/or postinfarction. Eya4/Six1 signalling is a feasible method to restore desmin filaments in desmin deficient mice. Reconstitution of syncoilin filaments, reduced fibrosis and hypertrophy as well as ameliorated contractile function underlines the potential use of this approach for treating the cardiomyopathy associated with desminopathy.

3069 | BENCH
Immunomodulatory microRNAs expressed in the myocardium predict individual antiviral capacity in human entero viral heart disease


Background: The impact of the human noncoding genome upon several important cardiovascular diseases is increasingly appreciated. We investigated myocardial microRNA (miR) expression patterns in a cardiomyopathy caused by the single-stranded RNA virus Cosackievirus B3 (CVB3). Here we show immunomodulatory functions of four miRs differentially expressed between patients spontaneously eliminating their virus (CVB3-ELIM) vs. those with progressive deterioration of structural variants. Our aim was to describe the performance of CNV screening in a cohort of patients with inherited cardiac disease.

Methods and results: Transcriptome mapping of CVB3 cardiomyopathy patients revealed cardiac miR patterns associated with differential clinical courses. Profiling of 754 miRs in endomyocardial biopsies (EMBs) of test cohorts was performed at initial presentation, revealing highly significant of 16 miRs in CVB3-ELIM vs. CVB3-PERS hearts. This distinctive miR pattern was confirmed in validation cohorts and multivariate ROC analysis confirmed it as highly predictive for disease course (AUC 0.89±0.01, 95% CI 0.758–1.00). Eight miRs which are undetectable in healthy human hearts, and also in CVB3-ELIM hearts, were strongly induced in CVB3-PERS (miRs 135b, 155, 190, 422a, 489, 590, 601, 1290) only. They thus constitute possible targets for antisense therapeutics drugs aiming at suppression of miRs associated with virus persistence and adverse clinical outcomes.

Further to assess therapeutic potential we used locked nucleic acid (LNA) antisense oligonucleotides (ASO)-mediated ablation of miRs 135b, 190, 422a, and 590 in human monocyes and macrophages. Strongest immunomodulating effects were observed when healthy human monocytes were infected in PMA-differentiated macrophages, with induction of FASLG (22.1-fold), IL-6 (14.5-fold), TNF (4.6-fold) and CCR5 (2.4-fold). These data suggest important immune control functions of miR-590 in macrophages: enhanced FASLG enhances cytotoxicity against PAS expressing cells, IL-6 enhances lymphocyte activation, and CCR5 enhances immune cell migration and antiviral defense via interaction with CCL5 (RANTES), CCL4 (MIP-1b) and CCL3 (MIP-1a). FASLG was also induced by miR-135b and 190a ablation (5.1- and 13.3-fold), and miR-135b ablation additionally induced chemokine receptor CCR7.

Conclusions: miR profiling is valuable to assess the risk of virus persistence and disease progression in CVB3 cardiomyopathy. Beyond this use of miRs as clinical predictive markers, the observed immunomodulating effects achieved by miR ablation in monocytes-macrophages suggest therapeutic potential via enhancement of antiviral capacity.

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3070 | SPOTLIGHT
Can differences in genetic background explain differences in extent of clinical expression of a disease causing mutation?

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Background: Single gene mutations are known to cause hereditary cardiac dis-
ease. It is unknown why there is considerable variability in the extent and severity of cardiac disease even between carriers of an identical mutation. The most common explanation is that genetic variation modifies the clinical expression of a disease causing mutation.

**Purpose:** We aimed to estimate the genomic contribution to most often used clinical traits in hereditary heart disease.

**Methods:** We compared 90 monozygotic twins (MZ) with a mutation causing dilated cardiomyopathy (DCM), hypertrophic cardiomyopathy (HCM), arrhythmogenic right ventricular cardiomyopathy (ARVC) or long QT syndrome type 1 or 2 (LQTS 1 and 2) to 132 same-sex siblings (C) with a pathogenic mutation. We compared first available data on: left ventricular ejection fraction (LVEF) and left ventricular end-diastolic diameter (LVEDD) in DCM; diastolic interventricular thickness (IVSd) in HCM; LVEF, LVEDD, right ventricular ejection fraction (RVEF) and right ventricular end-diastolic diameter (RVEDD) in ARVC; QTc-time in LQT5 1 and 2. In a LQTS 3 pedigree (118 mutation carriers and 108 non-carriers) we studied PR- and QTc-time. We estimated narrow-range heritability (h2) using Structural Equations Modeling, which decomposes phenotypic variance into additive genetic and common environmental effects and estimates which model explains phenotypic variance best.

**Results:** In DCM (18 MZ, 36 C) we estimated 34.3% h2 (95% CI 0.0–94.6%) for LVEF and 44.5% h2 (0.0–89.4%) for LVEDD. In HCM (34 MZ, 36 C), we estimated 0.0% h2 for IVSd (0.0–43.6%) and a significant environmental effect (65.6%, 20.1–83.4%). In ARVC (24 MZ, 24 C), we estimated 0.0% h2 for LVEF (0.0–68.2%) and RVEF (0.0–89.3%), and 65.1% h2 (0.0–98.8%) for LVEDD. In LQT5 1 and 2 (14 MZ, 34 C) we estimated 62.6% h2 (0.0–94.0%) for QTc-time. The best model for explaining variance of LVEDD (DCM and ARVC) and QTc-time (LQT5 1 and 2), included additively genetic effects. The best model for IVSd in HCM included common environmental effects. In the pedigree study, we estimated 33.7% h2 (8.0–57.4%) for PR-time and 18.1% h2 (0.0–38.3%) for QTc-time.

**Conclusions:** Disease causing mutations do not cause concordant cardiomyopathies in monozygotic twins, with no significant h2 for structural traits and a significant common environmental effect on IVSd variability in HCM. We found non-significant h2 for QTc-time in LQT5 1, 2 and 3 and significant h2 for PR-time in LQTS 3. Our results suggest that heritability for structural traits is low, but that additive genetic effects have an important influence on electrical trait variability.

**3071 | BEDSIDE**

**Genotype impacts survival in marfan syndrome**


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**Background:** Patients with Marfan’s syndrome often have severe cardiovascular disease leading to early death. Previous studies suggest that cardiovascular phenotype may depend on the effect of the FBN1 mutation on the fibrillin-1 protein.

**Purpose:** The purpose was to assess the impact of FBN1 mutation type upon survival and dissection-free survival in patients with Marfan’s syndrome.

**Methods:** We collected clinical and genetic data from all adults with Marfan’s syndrome who had been included in the Dutch CONCOR registry since the start in 2001. All pathogenic FBN1 mutations were classified into mutations with a dominant negative effect (DN, abnormal fibrillin-1 protein) and mutations with a haploinsufficient effect (HI, reduced fibrillin-1 protein).

**Results:** 570 patients with a mean age of 36 years (51% male, 29% prior aortic surgery, 8% prior aortic dissection) were prospectively followed for a mean duration of 8.2 years (Q1-Q3: 5–11 years). After ten-year follow-up, cumulative survival was 94% and complication-free survival was 69%. A pathogenic FBN1 mutation was known in 355 patients, of whom 130 patients were positive for a mutation causing haploinsufficiency (37%) and 225 for a dominant negative mutation (63%). Patients with a haploinsufficient mutation had a 3-fold higher risk of cardiovascular death (<0.020), a 2.7-fold increased risk of meeting the combined endpoint comprising death or dissection (p<0.001) and a 1.7-fold higher risk of any aortic complication compared to patients with a dominant negative mutation (p=0.004).

**Conclusions:** FBN1 mutation type has a major impact on survival and aortic dissection in adults with Marfan’s syndrome.

**3072 | BENCH**

**Comprehensive sequencing of dilated cardiomyopathy genes reveals additive effects of multiple genes on disease risk and severity**

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**Introduction:** Over 60 genes have been associated with dilated cardiomyopathy (DCM). However, a comprehensive assessment of rare, protein-altering variants in DCM-associated genes on DCM susceptibility or severity, accounting for the background variation rate in ethnically matched and phenotypically evaluated healthy controls, has not been performed.

**Purpose:** To robustly measure the contribution of rare coding variants in DCM genes in isolation or combination to DCM risk and myocardial phenotypes, by comparing rare variation burdens in DCM cases and phenotypically characterised healthy controls.

**Methods:** We sequenced and analysed 64 cardiomyopathy genes in 332 Caucasian DCM patients and in 319 ethnically matched healthy volunteers who underwent cardiac magnetic resonance imaging. Targeted next-generation sequencing of DCM genes was performed, and variants were called after mapping data to the Hg19 human genome reference. Burden testing for rare (minor allele frequency <0.1%), coding variants was performed for each gene, and regression modelling was used to assess the effects of genetic variation on the disease phenotype and the additive effect of multiple variant genes on disease risk and severity.

**Results:** As compared to controls, the 36 genes for which we found a nonsignificant h2 for IVSd (0.0–43.6%) in healthy controls, has not been performed.

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6.3% of LMNA subjects (patients after initiation of standard heart failure treatment, while this only occurred in Strikingly, an LVEF increase of at least 10% occurred in 50.0% of the TTN sub-

Conclusions: This study shows that truncating mutations in TTN induce a DCM that is less severe at presentation and more amenable to standard therapy than either LMNA mutation induced DCM or TTnLMNAneg DCM.

Results: After re-intervention no significant restenosis evolved.

Methods: All NCCM index patients fulfilling the diagnostic criteria for NCCM diagnosis in our medical center were included. Molecular testing was performed using next generation sequencing of a panel of 48 cardiology genes. Genetic sequence variants in the cardiology genes were classified for pathogenic effect according to the current five category diagnostic criteria.

Results: The study included 128 index patients. Pathogenic or likely pathogenic variants (class 4 and 5) were identified in 40% (49/128) of the patients, including 8% (4/49) with two or more (likely) pathogenic variants. MYH7 mutations were the most frequent, affecting 16% (21/128) of the patients. The Titin gene also appeared an important cause of NCCM with truncating variants classified as likely pathogenic in 10% (7/67) of the tested patients. In two patients (2/67) the MIB1 gene, known to regulate embryologic compaction of the ventricular wall, was involved. Variants of unknown clinical significance (class 3) were observed in 30% (38/128).

Introduction: Noncompaction cardiomyopathy (NCCM) is a genetic cardiomyopathy, characterized by hypertrabeculations with deep recesses of the left ventricular wall. We present the results of genetic analysis of a large NCCM cohort.

Methods: All NCCM index patients fulfilling the diagnostic criteria for NCCM diagnosis in our medical center were included. Molecular testing was performed using next generation sequencing of a panel of 48 cardiology genes. Genetic sequence variants in the cardiology genes were classified for pathogenic effect according to the current five category diagnostic criteria.

Results: The study included 128 index patients. Pathogenic or likely pathogenic variants (class 4 and 5) were identified in 40% (49/128) of the patients, including 8% (4/49) with two or more (likely) pathogenic variants. MYH7 mutations were the most frequent, affecting 16% (21/128) of the patients. The Titin gene also appeared an important cause of NCCM with truncating variants classified as likely pathogenic in 10% (7/67) of the tested patients. In two patients (2/67) the MIB1 gene, known to regulate embryologic compaction of the ventricular wall, was involved. Variants of unknown clinical significance (class 3) were observed in 30% (38/128).

Conclusion: Next generation sequencing detected a (likely) pathogenic variant in 40% of NCCM and variants of unknown clinical significance in an additional 30%. The improving molecular diagnostics for cardiomyopathies have a profound impact on counseling and screening of family members of NCCM patients. Further studies are needed to understand the contribution of genetic factors to this disease.

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P3070 | BEDSIDE

How common is normal renal function among patients with atrial fibrillation?

P3071 | BEDSIDE

Association between permanent atrial fibrillation and cognitive impairment: insights from a cohort of 902 patients with chronic heart failure

P3072 | BEDSIDE

How common is normal renal function among patients with atrial fibrillation?
categorized as moderate/severe. Patients with perm-AF had more frequently any degree of CI (50% vs 38%), moderate/severe CI (13% vs 7%), and showed lower scores in MMSE (24.6±4.4 vs 23.7±4.8) and Pfeiffer (1.72±3 vs 1.31±1.8) tests (p<0.05 for all). In univariable analysis, CI was associated with an older age, female gender, a history of diabetes, and perm-AF. The same variables were confirmed to be independently associated with CI in the multivariable analysis (table).

### Conclusions:
In our series of patients with CHF, perm-AF showed a discrete but independent association with CI. Other variables such as age, female gender, and a history of diabetes showed a stronger association with CI in this population.

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**P3078 | BEDSIDE**
Progression to asymptomatic atrial fibrillation as a prognostic index: the Euro Heart Study

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**Background:** Atrial fibrillation (AF) is associated with a wide variety of clinical presentations. The available data do not conclusively define whether a progression towards asymptomatic AF after clinical treatment could impact on prognosis, and what risk factors are implied.

**Purpose:** To investigate clinical and instrumental parameters predictive for developing asymptomatic AF and to determine if patients developing asymptomatic AF have a lower incidence of mortality and cardiovascular (CV) events compared to those who remain symptomatic despite therapy.

**Methods:** The Euro Heart Survey on Atrial Fibrillation included 5333 consecutive patients with documented AF on ECG or Holter recording. We compared risk of all-cause mortality and CV events between patients who develop asymptomatic AF (n=1556) and those who remain symptomatic (n=896) over one-year follow-up.

**Results:** Developing asymptomatic AF was associated with a lower risk of mortality and CV events (Table 1). AF recurrence during follow-up was associated with an increased risk of persistent symptoms despite clinical treatment (ORs 4.32, 2.41, and 2.40 for permanent, persistent and paroxysmal respectively; all p<0.01 vs no AF recurrence). Hypothyroidism (OR, 1.98; P=0.004), chronic heart failure (OR, 1.83; p<0.001), and chronic obstructive pulmonary disease (COPD, OR, 1.48; p=0.001), were also independently associated with an increased risk of persistent symptoms, whereas an AF considered cured by the clinician over 1-year was strongly associated with developing asymptomatic AF (OR 0.13; p<0.001).

**Conclusion:** This is the first study showing the relationship between left atrial dysfunction determined by echocardiography and the extent of areas with reduced atrial electrophysiological activity. Our data further support the hypothesis, that reducing AF function determined by speckle tracking echocardiography represents left atrial structural remodeling.

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**P3080 | BEDSIDE**
CHA2DS2-VASc score predicts in-hospital mortality beyond GRACE score after acute myocardial infarction

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**Background and aims:** CHA2DS2-VASc score and GRACE risk score were calculated for all-cause mortality, even when adjusted for GRACE risk score. These data suggest that CHA2DS2-VASc score has recently been suggested to predict death in patients with Atrial Fibrillation (AF). In acute myocardial in- farction (AMI), silent AF is more common than symptomatic AF and associated with poor prognosis. In patients with AMI, we aimed to assess the distribution of CHA2DS2-VASc score in patients with silent or symptomatic AF and the association of the score with mortality.

**Methods:** 849 consecutive AMI were prospectively analyzed by continuous ECG monitoring (CEM) >48 hours after admission. Silent AF was defined as symptomatic episodes lasting >30 sec. Symptomatic AF was defined as any AF occurring on ECG during the hospital stay, resulting in clinical symptoms or need for urgent cardioversion. The population was studied into three groups: No AF, Silent AF, and symptomatic AF. CHA2DS2-VASc and GRACE risk score were calculated for each patient and evaluation measurement.

**Results:** One hundred and thirty five patients (16%) developed silent AF and 45 (5%) had symptomatic AF. Compared with the no AF group, patients with AF were markedly older 80 (67–85) vs 62 (53–75) years; p<0.001, more frequently women (58 (43%) vs 198 (30%); p=0.006), and less smoker (26 (20%) vs 242 (36%); with p<0.001). Patients with silent and symptomatic AF, had higher CHA2DS2-VASc score than patients without AF (5 [4–6] and 5 [4–6] vs 3 [2–4], p<0.001). CHA2DS2-VASc score was similar in patients with silent and symptomatic AF (p=0.550). Mortality was higher in silent AF and symptomatic AF than in patients without AF (14 (10.4%) and 8 (17.8%)) vs 9 (1.3%); p<0.001. CHA2DS2-VASc score was associated with mortality in patients with AF, but not in patients without AF (OR [95% CI]: 1.32 [1.02–1.72]; p=0.036 and 1.22 [0.88–1.71], p>0.236, respectively). In the whole population, optimal threshold for predicting death for GRACE and CHA2DS2-VASc risk scores were obtained by Receiver Operating Characteristic (ROC) curve (i.e. 153 and 4, respectively). High CHA2DS2-VASc (≥4) and GRACE (≥153) scores independently stratified mortality. By multivariable analysis, high CHA2DS2-VASc score was an independent explanatory variable for death after AMI (OR [95% CI]: 3.89 [1.08–13.93]; p=0.037), beyond GRACE risk score (OR [95% CI]: 9.77 [2.74–34.80]; p<0.001).

**Conclusion:** Patients with silent AF have level of CHA2DS2-VASc score similar to patients with symptomatic AF. A high CHA2DS2-VASc score is associated with mortality, even when adjusted for GRACE risk score. These data suggest that CHA2DS2-VASc score could improve risk stratification after AMI.
P3081 | BENCH
The mean age of the study cohort was 56.5±8.9 years; 30.5% were females; 80% diabetic. All patients completed 30-day follow-up. AF occurred in 10.4% of the whole cohort. Of the whole cohort, 212 (28.6%) received ivabradine alone, 288 (38.9%) received bisoprolol alone, and 240 (32.4%) received both drugs. The 3 groups were matched for baseline characteristics and operative data (p>0.05 for all). The incidence of AF was significantly lower in group 3 (4.2%), compared with group 1 (15.5%), and group 2 (12.2%), (p<0.001).

Conclusion: The period of cardioprotection before surgery may reduce the incidence of AF at 30-day follow-up, compared with either drug alone.

EXPERIMENTAL AND CLINICAL RESEARCH IN MYOCARDIAL ISCHAEMIA

P3082 | BENCH
Pharmacological evaluation of novel adenine-hydrogen sulfide slow release hybrids designed as multi-target cardioprotective agents

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Purpose: To investigate the efficacy of peri-operative ivabradine, bisoprolol, or both for the prevention of post-operative atrial fibrillation (AF) at 30-day follow-up in patients undergoing coronary artery bypass grafting (CABG).

Methods: We enrolled 740 consecutive patients scheduled for elective CABG with or without valve surgery. Patients were assigned to one of 3 protocols: ivabradine (given for 48 hours and continued for 1 week thereafter), at a dose of 5 mg twice daily for the first 24 hours then 7.5 mg twice daily thereafter in patients who can tolerate (group 1), bisoprolol given peri-operatively at a dose of 5 mg twice daily (group 2), or both drugs given peri-operatively (ivabradine in the same previous dose plus bisoprolol at a dose of 5 mg once daily) (group 3). We excluded patients in whom the heart rate drops below 50/min during the first 48 hours. Cardiac rhythm was continuously monitored for 16 days after surgery by a transcutaneous automatic ECG recorder. Clinical follow-up for the occurrence of arrhythmias was performed for the next 14 days by office visits. The primary endpoint was the incidence of AF at 30-day follow-up.

Results: The mean age of the study cohort was 56.5±8.9 years; 30.5% were females; 80% diabetic. All patients completed 30-day follow-up. AF occurred in 10.4% of the whole cohort. Of the whole cohort, 212 (28.6%) received ivabradine alone, 288 (38.9%) received bisoprolol alone, and 240 (32.4%) received both drugs. The 3 groups were matched for baseline characteristics and operative data (p>0.05 for all). The incidence of AF was significantly lower in group 3 (4.2%), compared with group 1 (15.5%), and group 2 (12.2%), (p<0.001).

Conclusion: The period of cardioprotection before surgery may reduce the incidence of AF at 30-day follow-up, compared with either drug alone.

P3083 | BENCH
Endothelial nitric oxide synthase activation as a novel mechanism for myocardin-induced cardioprotection

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Purpose: Cardioprotection by NO donors at the end of ischemia (isc) has not been studied in detail. We sought to evaluate the contribution of the endogenous NO pathway to the cardioprotective action of nitroglycerin (NTG) and to compare this with ischemic postconditioning (PostC).

Methods and results: Adenin-hydrogen sulfide compounds were subjected to 30-min myocardial isch and 3-hour reperfusion (rep) and randomized into 15 groups: 1) Control, no further intervention; 2) PostC with 8 cycles of 30-sec isc/rep; 3) NTG treated (2 μg/kg-1/min-1) for a total time of 65 min starting 10 min prior to rep; 4) NTG plus the NOS inhibitor L-NAME; 5) NTG plus the selective iNOS inhibitor 7-NI; 6) NTG plus the selective nNOS inhibitor 1400W; 7) NTG plus the PI3K inhibitor Wortmannin (War); 8) NTG plus the adenosine receptor inhibitor SP; and 9) NTG plus the PKG inhibitor DT-2. In six additional groups, L-NAME, 7-NI, 1400W, War, SP and DT-2 were administered alone at the same time and dose as previously. The infarcted (I) to risk (R) areas were estimated in % IR. In a second series of experiments animals of the groups Control, PostC, NTG and NTG+L-NAME were subjected to the above interventions up to 10th min of rep when tissue samples were collected for determination of eNOS and Akt and of myocardial ROS by DHE fluorescence. Co-administration of L-NAME or Wor along with NTG eliminated the effect of NTG on %I/R (37.9±2.0%, and 38.3±2.6% respectively vs 23.0±3.2%, p<0.05). Inhibition of adenosine and PKG did not affect the protection afforded by NTG (12.3±1.0%, p<0.05) whilst 7-Ni itself exerted potentiation (27.05±1.6% vs 48.05±2.0% in Control, p<0.05). Inhibition of NOS did not affect the benefit of NTG on %I/R (14.4±1.3%), eNOS and Akt phosphorylation was higher in PostC and NTG groups, while ROS formation was reduced compared to Control and NTG+L-NAME groups. To further investigate the role of eNOS on NTG-mediated protection, wild type and eNOS(-/-) mice underwent isc-rep with NTG administration. NTG had no effect on %I/R in eNOS(-/-) mice compared to wild type. In order to evaluate the effect of mPTP, wild type and cyclophiline D (CypD) mice underwent reperfus with NTG administration. CypD(-/-) hearts had a lower %IR than wild type and NTG failed to confer additional protection, indicating that NTG protects through a CypD-dependent mPTP function.

Conclusion: NTG induces protection through activation of the PI3K-Akt pathway; this effect is mainly mediated by eNOS activation which further causes inhibition of mPTP.
and decreased bioavailability of nitric oxide (NO). Increased arginase activity in the myocardium and in RBCs was significantly correlated with % plaque volume (r=0.45, p<0.05), which was more prevalent in pts with IFG and/or IGT (r=0.72, p<0.001) while arginase 1 expression did not differ significantly.

Results: Basin arginase activity in the myocardium and in RBCs was significantly higher in diabetic rats than in controls. Arginase 2 expression was 1.8 fold higher in myocardium of diabetic rats vs controls (P<0.001) while arginase 1 expression did not differ significantly. Basal arginase activity in the myocardium and in RBCs was significantly increased in diabetic rats and controls (IS 65±3% and 85±3%, resp.).

Conclusion: T1DM leads to increase of arginase activity in the myocardium and RBCs and increased expression of myocardial arginase 2. Arginase inhibition protects the diabetic heart from IR injury via a NO-dependent mechanism. The described paracrine protection by arginase inhibition is comparable to that in healthy animals. Targeting arginase may be a promising therapeutic strategy for the protection against IR injury in DM.

P3086 | BEDSIDE

Inflammatory activity of pericoronary adipose tissue in predisabetic patients with NSTE-ACS

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Purpose: Paracrine activity of pericoronary adipose tissue (PCAT) may adversely affect coronary lesions formation and plaque stability. Maximal standardized uptake value (SUV) of 18-fluorodeoxyglucose (FDG) measurement by positron emission tomography has been proved to be an efficient tool to evaluate paracrine activity of different tissues. In patients with stable coronary disease it correlated with % of coronary stenosis. We sought to investigate, whether PCAT inflammation and plaque composition in Non-ST elevation Acute Coronary Syndromes (NSTE-ACS) patients.

Methods: 30 patients (98 coronary arteries: LM, RCA, LCX. LAD) have been investigated in subjects without history of diabetes mellitus with moderate/low risk NSTE-ACS (GRACE <140). SUV was measured in PCAT surrounding arteries on the sections corresponding to coronary plaques detected by grey scale intravascular ultrasound and virtual histology (VH-IVUS) during routine coronaryography. Additionally SUV was measured in subcutaneous fat (SC), visceral thoracic fat (VS), epicardial fat over right ventricle (EPI). Qualitative (calcified, fibrous, fibrofatty, or necrotic core) and quantitative analyses of plaques were performed, and further correlated with PCAT SUV. In all patients fastening blood glucose (FFG), 2 hour glucose tolerance (OGTT) test and HbA1c were analyzed. Prediabetes was diagnosed according to WHO/ADA criteria.

Results: PVAT SUV in NSTE-ACS patients was significantly greater than in other fat locations (LM SUV: 1.60; RCA SUV: 1.47; LCX SUV: 1.89; LAD SUV: 2.30 vs SC SUV: 0.59; VS SUV: 0.78; EPI SUV: 0.99, p<0.001; ANOVA). PCAT SUV positively correlated with necrotic core plaque core rate (r=0.61, p<0.05), and negatively correlated with fibrous plaque rate (r=-0.52, p<0.05), which was more prevalent in pts with IFG and/or IGT (r=-0.72, p<0.05 vs r=0.57, p<0.05, respectively). There was also positive correlation between PCAT SUV and % plaque volume (r=0.45, p<0.05).

Conclusions: Inflammatory activity of PCAT is greater than in subcutaneous, visceral thoracic, or epicardial tissue in NSTE-ACS patients; PCAT SUV correlates with necrotic core component of coronary plaque and plaque volume in patients with NSTE-ACS, especially with IFG and/or IGT.

P3087 | BENCH

Gamma-Glutamyltransferase Stimulates Tissue Factor Expression Independent of Its Enzymatic Activity in Human Mononuclear Cells

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Background: A highly consistent association links circulating Gamma-Glutamyltransferase (GGT) to incident acute coronary events to which Tissue Factor (TF), the principal initiator of the coagulation process, is known to contribute actively. GGT and TF are also co-expressed by plaques harvested from atherosclerotic patients, thus making it conceivable a direct role of the former on TF expression and activation. The aim of our study was to assess the direct effect of GGT on TF expression in human peripheral blood mononuclear cells. All experiments we run using an enzymatically inactive human recombinant (hr) GGT to exclude confounding from its enzymatic activity.

Methods: Human peripheral blood mononuclear cells were obtained from healthy donors through a discontinuous Ficoll/Hystopaque density gradient and incubated with hrGGT (0.5 ng/mL) either alone or with anti-hrGGT, a specific polyclonal antibody (2.5 μg/mL), BAY-11–7082 (10–5 M) a selective NF–κB inhibitor, and N-acetylcysteine (10–3 M) an antioxidant. TF expression was assessed by ELISA, TF mRNA by real-time PCR and PCA by a 1-stage clotting assay.

Results: hrGGT increased TF expression (from 85±59 to 536±317 pg/mL, n=13, p<0.001) and stimulated PCA (from 0.008±0.007 to 0.37±0.3 arbitrary units, n=14, p<0.001) and TF mRNA (from 0.006±0.002 to 0.048±0.034 reverses LMWH– and xaxa–mediated TF activation and PCA by 1-stage clotting assay.

Conclusions: These data represent the first demonstration of a direct effect of GGT on TF expression independent of its own enzymatic activity, a behavior consistent with a cytokine-like mechanism acting through NF–κB stimulation. This mechanism might contribute to promote acute thrombotic events, a possibility in need, however, of further evaluation.

P3088 | BENCH

Andexanet alfa reverses edoxaban-induced anticoagulation in a rabbit liver laceration model of acute bleeding


Background: Edoxaban (exdan) is an oral, direct Xa inhibitors recently approved in the US to reduce the risk of stroke in patients with nonvalvular AF. A serious risk with Xa inhibitors is bleeding, and a specific reversal agent is not available. Andexanet alfa (AnXa) is a modified recombinant Xa derivative that reverses LMWH- and Xa, ind differentiated TF activity and plasma Xa activity in human subjects, and binds direct Xa inhibitors (~11 stoichiometry). Published preclinical studies demonstrated that AnXa effectively reversed rivaroxaban anticoagulation in a rabbit liver laceration model, restored anti-Xa activity, reduced the plasma free fraction of rivaroxaban, and corrected PT and aPTT to pre-anticoagulation levels.

Purpose: Study objective was to evaluate the ability of AnXa to reverse edox anticoagulation in a rabbit liver laceration bleeding model, as assessed by coagulation markers and blood loss (BL).

Methods: Edox treatment increased BL from 9.3±3.0g in vehicle controls (N=10) to 22±8.9g in rabbits anticoagulated with edox (N=12, p<0.001), while administration of AnXa in edox-treated rabbits decreased BL to 13.8±3.7g (N=10, p<0.05). Mean unbound edox plasma concentration at the beginning of AnXa infusion was 99±16 ng/mL, and was reduced 5-fold by the end of the AnXa infusion to 20.9±6.4 ng/mL. Total mean plasma concentration of edox increased 10-fold (from ~350 ng/mL to ~3700 ng/mL, from start of to end of infusion), demonstrating that edox was redistributed rapidly from the extra- to the intra-vascular compartment. Similarly, anti-Xa activity was reduced (446±54.3 to 99±54.0, p<0.001) (N=10–12, edox alone vs edox + AnXa), as were PT and aPTT (by 66% and 18%, respectively), vs. animals treated with edox alone.

Conclusion: In active visceral bleeding due to edoxaban anticoagulation, AnXa significantly reduced BL, which correlated with a reduction in anti-Xa activity, plasma unbound fraction of the anticoagulant, PT, and aPTT. This study is consistent with human Phase 2 data in edoxaban-treated subjects in which the same coagulation markers were similarly corrected.
Conclusion:
CMR rules out LVT in a significant proportion of cases initially suspected by TTE and ongoing anticoagulation that can be safely discontinued.

Background:
Recent studies suggest that obstructive sleep apnea (OSA) is associated with impaired microvascular perfusion after primary percutaneous coronary intervention (PCI) in patients with acute ST-segment elevation myocardial infarction (STEMI). Non-invasive assessment of microvascular obstruction (MVO) and intussuspetal myocardial hemorrhage by cardiovascular magnetic resonance (CMR) provides a specific biomarker of severe microvascular dysfunction. However, the relationship between OSA and severe microvascular dysfunction has not been fully evaluated. The aim of this study was to determine whether OSA was related to the presence of severe microvascular dysfunction determined by CMR in patients with acute STEMI.

Methods:
The study population consisted of 111 consecutive patients with a first STEMI successfully treated with PCI. CMR performed within 4 days after primary PCI was used to identify the presence of reperfusion hemorrhage and contrast enhancement was used to measure MVO. Recruited patients were scheduled to undergo an overnight sleep study one week after primary PCI. Sleep apnea was classified into 4 categories based on an apnea-hypopnea index (AHI): no (AHI<5), mild (AHI<15), moderate (15≤AHI<30), and severe sleep apnea (AHI≥30). An AHI of ≥15 was considered diagnostic of OSA. We assessed the association between OSA and severe microvascular dysfunction determined by CMR.

Results:
There were 66 (5.4%), 49 (44.1%), 33 (29.7%), and 23 patients (20.7%) with no, mild, moderate, and severe sleep apnea, respectively. An increasing AHI quartile was associated with increased odds of the frequency of MVO and hemorrhagic infarction (p values for trend <0.01 and 0.027, respectively). Multiple logistic regression showed that OSA was associated with increased odds of MVO (odds ratio [OR]: 3.56, 95% confidence interval [CI]: 1.59–9.01, p=0.0022) and hemorrhagic infarction (OR: 3.84; 95% CI, 1.50–10.7, p=0.0045) compared with no OSA.

Conclusion:
Undiagnosed OSA was associated with severe microvascular dysfunction after primary PCI in patients with STEMI.
Conclusions: The presence of LV thrombi was not associated with MACE. Pain-to-balloon time emerged as a significant predictor of LV thrombi. The association of STEMI injury (late microvascular obstruction p=0.004, intramyocardial hemorrhage p=0.02) with decreased myocardial salvage, larger infarcts, and more pronounced reperfusion injury was observed.

Results: LV thrombi were detected in 33 patients (4.4%). The presence of LV thrombi was associated with larger infarcts (p<0.001), impaired LV ejection fraction (p=0.02) and more pronounced reperfusion injury (late microvascular obstruction p=0.004, intramyocardial hemorrhage p=0.02). In multivariable analysis, infarct size, anterior infarction, and time-to-balloon remained as significant predictors of LV thrombi. The prevalence of LV thrombi was significantly more frequent in patients with angiographically significant coronary vasomotor abnormalities. Acetylcholine provocation testing may be useful in these patients to determine the cause of angina and initiate appropriate medical treatment.

Methods: Between 2012 and 2014 we consecutively recruited 125 patients (mean age 64±16 years, 64 (51%) male) with angina pectoris who underwent an adenosine-stress perfusion-CMR study (including cine rest function, adenosine stress and rest perfusion and late gadolinium enhancement imaging) and invasive diagnostic coronary angiography because of suspected obstructive coronary artery disease. In all patients no relevant epicardial stenosis was found (<50% narrowing) and intra coronary ACH-testing was performed in search of functional coronary vasomotor abnormalities.

Results: Twenty-eight patients (22%) presented with effort-induced angina, 66 patients (53%) with resting angina and 31 patients (25%) had a balanced presentation of effort and rest angina. An adenosine-induced, reversible subendocardial perfusion defect was detected in 56 (45%) patients. ACH-testing revealed coronary microvascular dysfunction in 29 (47%) patients (reproduction of symptoms, ischemic ECG-changes and no epicardial spasm) while epicardial coronary spasm (<75% diameter reduction with reproduction of the patient's symptoms) was seen in 28 (23%), 38 patients (30%) had an uneventful ACH-test. Patients with a reversible stress-induced perfusion defect had significantly more often a pathological ACH-test (51/58; 88%) than those without a perfusion defect (36/67; 54%; p<0.0005).

Conclusion: Reversible perfusion defects on stress perfusion-CMR in patients with effort and rest angina are frequently due to coronary vasomotor abnormalities. Acetylcholine provocation testing may be useful in these patients to determine the cause of angina and initiate appropriate medical treatment.

P0094 | BEDSIDE Left ventricular thrombus formation in patients with acute reperfused ST-elevation myocardial infarction - insights from cardiac magnetic resonance imaging

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Background: Data on the exact incidence and predictors of left ventricular (LV) thrombus formation after primary percutaneous coronary intervention (PCI) for ST-elevation myocardial infarction (STEMI) are scarce. Moreover, data on the prognostic significance of LV thrombi on hard clinical outcomes are completely lacking.

Non-invasive investigation by gadolinium-enhanced cardiac magnetic resonance imaging (CMR) enables the detection of LV thrombi with high spatial resolution and superior diagnostic accuracy compared to echocardiography. Aim of our study was 1) to assess the incidence, determinants and clinical characteristics of LV thrombi in a large multicenter cohort of high-risk STEMI patients, 2) to assess the prognostic significance of LV thrombi at one-year follow-up.

Methods: We enrolled 746 STEMI patients reperfused by primary angioplasty (mean age 64±16 years, 64 (51%) male) with angina pectoris who underwent an adenosine-stress perfusion-CMR study (including cine rest function, adenosine stress and rest perfusion-CMR imaging) before and after PEA. LV thrombi were defined as areas with heterogeneous signal intensity persisting for more than 3.5 seconds. Twenty-eight patients (22%) presented with effort-induced angina, 66 patients (53%) with resting angina and 31 patients (25%) had a balanced presentation of effort and rest angina. An adenosine-induced, reversible subendocardial perfusion defect was detected in 56 (45%) patients. ACH-testing revealed coronary microvascular dysfunction in 29 (47%) patients (reproduction of symptoms, ischemic ECG-changes and no epicardial spasm) while epicardial coronary spasm (<75% diameter reduction with reproduction of the patient's symptoms) was seen in 28 (23%), 38 patients (30%) had an uneventful ACH-test. Patients with a reversible stress-induced perfusion defect had significantly more often a pathological ACH-test (51/58; 88%) than those without a perfusion defect (36/67; 54%; p<0.0005).

Conclusion: Reversible perfusion defects on stress perfusion-CMR in patients with effort and rest angina are frequently due to coronary vasomotor abnormalities. Acetylcholine provocation testing may be useful in these patients to determine the cause of angina and initiate appropriate medical treatment.

P0095 | BEDSIDE Long term effect of pulmonary endarterectomy on right ventricular loading conditions in patients with chronic thromboembolic hypertension by cardiac MRI

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Purpose: To study the natural history of RV adaptation to varying loading conditions in patients with chronic thromboembolic hypertension (CTEPH) from before pulmonary endarterectomy (PEA) to one year follow up.

Background: Nearly 4% of patients with pulmonary embolism develop CTEPH. Chronic thromboembolic hypertension (CTEPH) presents as a cure with excellent outcome. Cardiac magnetic resonance imaging (CMR) combined with hemodynamic measurements pulmonary arterial elastance (E-pulm), end-systolic right ventricle elastance (Ees-RV) and ventriculo-arterial coupling (Ea-pulm/Ees-RV) can be studied before and after PEA.

Methods: Sixty-five patients (mean age 41±12 years, 28 female) underwent CMR pre- and post-PEA. 44 were available for one year follow up. Ejection fraction (EF), end-diastolic (EDVI), end-systolic (ESVI), and stroke (SVI) volumes were indexed for body surface area. E-pulm was calculated as pulmonary artery mean pressure (mPAP) and ESV-RV as mPAP/ESVI.

Results: mPAP decreased from 47±12 to 25±9 mmHg, p<0.001 and PVR decreased from 646±286 to 334±285 dynes*s*ml⁻¹, p<0.05. E-pulm was increased before PEA and normalized afterwards (2.8±2.1 to 0.8±0.4 mmHg/ml/m², p<0.001). Ees-RV was depressed before and after PEA (0.72±0.27 vs. 0.68±0.3 mmHg/ml/m², p=0.13). EF improved from 25±12% to 46±10%, p<0.0001, because ventriculo-arterial coupling was restored (4.2±3 vs. 1.4±0.6, p<0.001). EDVI and ESVI improved significantly (EDVI 92±32 to 72±23 ml, p<0.001; ESVI 51±23 to 34±18 ml, p<0.001). EF 25±12 vs. 37±9%, p<0.001 and mPAP 47±12 vs. 25±9 mmHg, p<0.001 were seen in 28 (23%), 38 patients (30%) had an uneventful ACH-test. Patients with a reversible stress-induced perfusion defect had significantly more often a pathological ACH-test (51/58; 88%) than those without a perfusion defect (36/67; 54%; p<0.0005).

Conclusion: RV function is largely determined by afterload and returns to normal once afterload is normalized. This is paralleled by a significant improvement of CMR indices of right ventricular remodelling. These effects are sustained at long term follow up one year after PEA.

NEW ADVANCES IN CARDIOVASCULAR GENETICS AND GENE THERAPY

P0096 | BENCH PRKG1 mutations and thoracic aortic disease: another candidate gene for consider during genetic diagnosis approach to non-syndromic cases

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Introduction: Thoracic aortic aneurysms and dissections are major disorders affecting the thoracic aorta. These potentially lethal manifestations can be or not part of Marfan, Loeys-Dietz or Ehlers-Danlos type IV connective tissue syndromes. When they appear isolated the patients are considered affected by non-syndromic aortic disease, a monogenic condition inherited as an autosomal dominant trait with low penetrance and variable expression. Mutations in ACTA2, TGFBR1 and 2, TGFBR2, SMAD3, MYLK, MYH11 and FBN1 genes have been reiteratively described to be causal, but there are still many unresolved familial cases suggesting the need for other candidate genes to be detected.

Purpose: To identify the genetic mutation causing non-syndromic aortic disease in a 4-generation Spanish family with multiple cases of aortic disease-sudden death ≥6 alive affected family members.

Methods: Customized targeted-sequencing of aortic disease candidate genes in the proband through 5500 SOLID System followed by whole-exome sequencing of 4 affected (including the proband) and 2 unaffected family members using HiSeq 2000/2500 sequencing technology. All variants were filtered by location, minor allele frequency equal or more than 5% and affected and absent in the 2 unaffected family members. No other mutation was found in the remaining aortic disease candidate genes.

Conclusions: This new independent PRKG1-thoracic aortic disease familial case...
P3097 | BENCH
Impact of diabetes mellitus on Thymosin B4 mediated therapeutic neovascularisation
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Diabetes mellitus is one of the major risk factors for developing cardiovascular disease; especially in combination with chronic myocardial ischaemia it represents one of the most common causes of disability or death. This might be a reason, why pro-angiogenic factors like Thymosin B4 might be suitable for inducing therapeutic neovascularization in chronic myocardial ischaemia a cardio risk factor.

Methods: In wildtype and transgenic pigs displaying diabetes mellitus type I (a C484 mutation), vascularization and myocardial function were analyzed. In a second set of experiments, chronic myocardial ischaemia was induced with transgenic pigs via reduction stent graft in the circumflex circulm. Retroinouison of rAAV T4 (5x10E12 viral particles) was performed at day 28. Global myocardial function (EF, LVEDP) was obtained at day 28 and 56. In addition subendocardial segment shortening (SES) in the ischemic region and post mortem angiography (collateral growth) were examined on day 56. Histological analysis of PECAM-1 positive cells (capillaries/high power field (chpf.)) and vessel maturation (pericyte coverage, NG-2 positive cells) was performed in the ischemic tissue.

Results: Analysis of non-ischemic wt and diabetic animals revealed capillary rarefation in the myocardium (234±8 in wt vs. 163±14 chpf in diabetic hearts). Analysis of myocardial function in non-ischemic hearts detected a trend, towards loss of ejection fraction in diabetic pigs. In chronic myocardial ischaemia, rAAV.TB4 overexpression in wt animals significantly enhanced capillary density (27±8±6 vs. 148±6 chpf) and collaterals (9±1 vs. 3±1) in the ischemic area compared to control wt animals. Furthermore, rAAV.TB4 improved ejection fraction (47±4% vs. 29±3% in controls) as well as SES (at 150 beats/min: 73±5 vs. 10±6% of non-ischemic area). In diabetic pigs, blood glucose levels were elevated (305±12 mg/dL at day 28 and 355±10 mg/dL at day 56). Here, rAAV.TB4 still induced angiogenesis (190±4 chpf (T144) vs. 120±5 chpf in wildtype hearts) as well as collateral growth (4±1 (T4) vs. 2±1 in control hearts). Moreover, EF increased in rAAV.TB4 diabetic hearts (32±2% vs. 27±1% in controls)

Conclusion: Thymosin B4 transduction induces therapeutic neovascularization and thereby improves the myocardial function in the presence of type I diabetes mellitus. Therefore, rAAV.TB4 appears suitable for treatment of ischemic cardiomyopathy associated with this cardiovascular risk factor.

P3098 | BEDSIDE
Major histocompatibility complex risk haplotype predisposes to acute coronary syndrome
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Introduction HLA-DRB1*01 allele in all four populations with odds ratios varying between 1.21 and 4.43. Subjects homozygous for disease-associated BTNL2-HLA-DRA-HLA-DRB1*01 haplotype on chromosome 6p21.3 associated with acute coronary syndrome and seems to enhance immune reactions.

P3099 | BENCH
Gene transcription efficiencies, left ventricular function and fibrosis formation in mouse heart after direct intramyocardial gene transfers with aden-, adeno-associated- and lentiviral vectors
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Introduction: Gene therapy is a promising new treatment option for ischemic heart disease and viral vectors are used to deliver therapeutic genes into ischeismic tissue. Adenoviruses (Ad) are currently the most used vectors for different gene therapy protocols.

The aim of this study was to compare adeno viral vectors to adeno-associated (AAV)- and lentiviral (LeV) vectors in mouse heart regarding the transcription efficiency, effects on the left ventricular function, and fibrosis formation in order to find the most suitable and safe vector for cardiac gene therapy.

Methods: High-resolution echocardiography was used to guide the closed-chest injections of Ad-, AAV2-, AAV9- and LeV gene constructs into the anterior wall of the left ventricle (LV) of C57B1/6J mice. AAV9 was also studied by using i.v. injections of three different virus doses (1010, 1011 and 1012 viral particles). Echocardiographic measurements were performed before (d0), (d6) and (d28) days after the gene transfer. Gene expression efficiency was induced with the help of the histological morphology of the myocardium were analyzed from histological samples.

Results: Ad was the most efficient vector in delivering the transgene into the cardiomyocytes (transgene positive cardiomyocytes 43% of all myocytes in the selected area surrounding the injection site). The transduction efficiencies of AAV serotypes 2 and 9 were 22% and 24%, respectively, and LeV reached the transduction efficiency of 11%. Accordingly, the size of local scar area in the LV was the largest after Ad injection (15%), with AAV13, AAV2 7% and the smallest scar area after LeV (3%). After i.v. injection of AAV9 transgene positive cells could be seen diffusely throughout the myocardium and transduction efficiency was 16% (dose 1012 vp). However, i.v. AAV9 gene transfer also led to diffuse fibrosis in LV at d28.

Conclusions: In summary, compared to widely used Ad vector, AAV2, AAV9 and LeV were less effective in transducing cardiomyocytes, but also less harmful. Local administration of AAV9 is more efficient and safer compared to systemic administration. Further improvements could be targeted to diminish the side effects of the most effective viral vectors.

P3100 | BENCH
A deep phenotype and exome-sequencing based characterization of patients with non-compaction cardiomyopathy (NCCM)

Left ventricular non-compaction cardiomyopathy (NCCM or LVNC) is an increasingly recognized cause of heart failure, arrhythmias, thromboembolic events, and sudden cardiac death. Advanced diagnostic methods, predominantly based on modern imaging techniques, including cardiac magnetic resonance imaging (cMRI) have resulted in considerably increased detection rates, enabling a collection of larger NCCM cohorts. Hence we were able to recruit 104 subjects (67 LVNC and 37 LVNC probands, with 30 relatives) from 15 families and 11 additional healthy relatives, and performed deep phenotyping as well as whole-exome sequencing.

A common clinical presentation was heart failure (HF), which was associated with increased levels of natriuretic peptides (increased in 71.6% of the patients), but not cardiac Troponins. Of the index patients (38.8%) were in progressed New York Heart Association class (NYHA) III or IV, while 5 (7.5%) had associated left ventricular hypertrophy (LVH), and 30% patients had atrial fibrillation (AF). However, HF was not effectively treated with standard medical management (i.e. diuretics, β-blockers) and no patients reached heart transplantation due to end-stage disease. By annotating the detected variants with mutation databases (HGMD), we were able to for the first time show an overlap between the distinct causes of NCCM and other genetic cardiomyopathies. In detail, 11 mutations were previously reported to cause hypertrophic cardiomyopathy (HCM), 10 dilated cardiomyopathy (DCM) and 7 arrhythmogenic right ventricular cardiomyopathy (ARVC).

Conclusions: Our study suggests that BTNL2-HLA-DRA-HLA-DRB1*01 haplotype on chromosome 6p21.3 associates with acute coronary syndrome and seems to enhance immune reactions.
Targeted capture sequencing identifies a mutation in a substantial proportion of families and estimation of prognosis in future. We evaluated the additional yield of NGS based panel testing in PAS and CMP patients and determined if genetic testing was worthwhile in previously genotype negative – phenotype positive probands.

Methods: We examined the database of our hereditary heart disease clinic and selected patients with a clear phenotype who were genotype negative after genetic analysis of the main genes implicated in their specific phenotype. Targeted sequencing was performed on regions of 75 genes most frequently sequenced in PAS and CMP and was performed. Variant interpretation and classification was done according a stringent scoring system implementing different in-silico analyses, population frequencies and paralogous and orthologous conservation. Sanger sequencing was performed to confirm the presence of class 3 variant (of unknown significance), 4 (probably pathogenic) and 5 (pathogenic) variants. Co-segregation was done when DNA and clinical data of family members was available.

Results: 96 patients were included: 25 with LQTS, 6 with BrS, 4 with CPVT, 1 with SSS and familial sudden death, 1 with AF, 6 with idiopathic VF, 42 with HCM, 7 with DCM, 1 with restrictive CMP and 1 with ARVC. A total of 41 variants of class 3, 4 and 5 were identified. Co-segregation was performed on 20 variants. Three class 3/4 variants were downgraded to a benign variant due to lack of cosegregation. In contrast, 12 were upgraded to class 4 or 5 after critical evaluation of published functional studies or co-segregation analysis. In total we identified 22 variants of class 3 and 16 mutations (class 4/5) in 15 patients, resulting in a genetic yield of 16% (14% in CMP and 18% in PAS); The initial detection failures highlighted the difficulty in detection of a mutation in a new gene in 8 cases, allele dropout with DHPLC in 2, not reported variant by an external lab in 2, functional reclassification in 1, heterozygous calling with sequencing failed in 1 and a wrong initial diagnosis in 1.

Conclusion: Genetic testing in robust PAS and CMP cases, who were genotype negative with older scanning techniques, resulted in a genetic diagnosis in up to 16% of the cases and clearly supports genetic testing with NGS based panels.

P3102 | BENCH

Targeted versus whole exome re-sequencing for clinical application in inherited cardiac conditions

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Inherited cardiac conditions (ICC) are inherited cardiovascular diseases of the heart and circulation with a prevalence of ~1%. New sequencing technologies have enabled high-throughput sequencing of disease genes for clinical application where targeted and whole exome sequencing (WES) approaches are equally suggested for diagnostic use. Genomic DNA was extracted from patients (n=216) and three iterations of custom ICC gene panel were used to enrich 169 ICC genes using the Nextera Rapid Capture Enrichment kit. The libraries of pooled samples (n=6–12) were sequenced using Illumina Miseq paired-end 150bp reads V2 or V3 kit. Deep sequencing was performed on targeted regions and whole exome sequencing captures (ICCV1, ICCV2 and ICCV3) and we designed and validated a panel of 75 PAS and CMP susceptibility genes for clinical application.

Methods: We targeted and whole exome sequencing (WES) approaches are equally suggestive for diagnostic use. This constellation of facts entails a high-risk patient group. Our aim is to analyze the clinical profile, and prognosis of S. bovis IE episodes, and to compare them with those episodes caused by viridans group streptococci (VGS) and to compare them with those episodes caused by viridans group streptococci (VGS). Both the population and ESC guidelines suggested for diagnostic use. This constellation of facts entails a high-risk patient group. Our aim is to analyze the clinical profile, and prognosis of S. bovis IE episodes, and to compare them with those episodes caused by viridans group streptococci (VGS).
viridans group streptococci, and Group III (n=113), those episodes due to enterococci.

Results: The incidence of enterococci IE have significantly increased in the last two decades (6.4% [1996–2004] vs 11.1% [2005–2013]; p=0.005), while the incidence of IE due to S. bovis and viridans streptococci has remained stable (4% and 10% respectively). Patients with S. bovis and enterococci IE were older. Nosocomial acquisition was more frequent in Group III. Concerning comorbidity, diabetes mellitus (38.3% vs 9.0% vs 26.5%; p<0.001) was more common in Group I and Group III. Chronic renal failure was more prevalent in patients from Group III (4.3% vs 1.5% vs 19%; p<0.001). Prosthetic valve IE was more frequent in enterococcal IE. Infection upon native valves was more common in S. bovis IE. Colorectal neoplasias were found in 70% of patients from this group. Vegetation detection was similar in the three groups. However, vegetation size was smaller in S. bovis IE (7.4 mm vs 11.6 mm vs 11 mm; p=0.001). During hospitalization, in-hospital complications and in-hospital mortality were higher in enterococci episodes (Table).

Conclusions: S. bovis IE is associated with a high prevalence of colonic tumours, and affects patients without pre-existing valve disease. It is related to small vegetations and a low rate of in-hospital complications, including systemic embolisms. In-hospital mortality is similar to that of viridans group streptococci. Thus, S. bovis should not be considered a virulent microorganism.

P3105 | BEDSIDE

Dramatic decrease in Staphylococcus aureus infective endocarditis early mortality using a new strictly applied protocol

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Background: S. aureus infective endocarditis (SAIE) is still associated with high mortality despite using recommended antibiotic protocols. Objective: To assess the effectiveness and safety of a new antibiotic protocol, using the association of high doses cotrimoxazole and clindamycin (C+C) Methods: A prospective cohort of IE initiated in 2002 was used. All patients with a definitive SAIE according to DUKE criteria were included. Since 2012, combination therapy with rifampin and gentamicin was added if blood cultures were positive for cardiac surgery between those with and without new embolic events (55.2% vs 55.8%; p=0.921). The presence of preoperative cardiac surgery was associated with the rate of new systemic embiotic events (6% of incidence if absence of vegetation, 20% if vegetation size <10 mm. 74% if vegetation >10 mm; p<0.001). S. aureus infection was also more frequent in patients with new embiotic episodes (30% vs 17.2%; p=0.05). The mortality was higher in patient with new embiotic events (41.5% vs 29.2%; p=0.10). No differences were found in the need for cardiac surgery between those with and without new embiotic events (55.2% vs 55.8%; p=0.921).

Conclusions: The Preoperative Risk French Calculator including the mentioned variables was finally applied to our cohort. The accuracy of this prediction model was moderate, with an area under the ROC curve of 0.63 (95% confidence interval: 0.58 to 0.69).

P3107 | BENCH

The influence of radiological lesions on neurological outcome in endocarditis patients with preoperative stroke

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Methods: We retrospectively reviewed all charts, brain imaging, and follow-up data from patients operated for left-sided endocarditis between Jan-07 and April-13. We performed Chi-Square, multivariate, and Cox-regression analyses. Results: A total of 308 patients (age 62±13.9) underwent surgery for IE. The preoperative CVC were as follows: stroke in 91 patients (56 ischemic and 35 hemorrhagic), silent cerebral infarction in 27 patients and transient ischemic attacks in 4 patients. In-hospital mortality was higher in patients with preoperative stroke than those without it. However, the difference was not statistically significant (27.5% vs. 22.6%, p=0.38). The incidence of death because of neurological complications (massive ischemic infarction or ICB) was 2.6% (n=8) and did not differ between patients with or without preoperative stroke (3.3% vs 2.3%, respectively, p=0.70). Cox-regression analysis showed that preoperative stroke did not affect long-term survival (hazard ratio 0.78, Confidence interval 0.53–1.13). No differences were found in the need for cardiac surgery between those with and without new embolic events (55.2% vs 55.8%; p=0.921).

Conclusions: The Preoperative Risk French Calculator was useful; nevertheless a more accurate tool would be desirable.
Background: Staphylococcus aureus bacteremia (SAB) is a major cause of cardiac device infections and infectious endocarditis (IE). As socioeconomic status (SES) is known to impact the risk of infectious diseases, SES could potentially influence the risk of SAB and secondarily the risk of cardiac infections.

Methods: We aimed to investigate the association between SES and SAB risk in a nationwide adult population, and to estimate subsequent risk of endocarditis in patients who developed SAB.

Results: All residents were consecutively included at the age of ≥30 years between 1996–2012. By cross-linking nationwide registries, we obtained information on SES classified by highest attained educational level (5 groups), comorbidities and prosthetic devices. We identified patients hospitalized with primary SAB during follow-up and later risk of IE. Using Poisson regression models, we estimated incidence rate ratios (IRR) for SAB according to SES adjusted for age, calendar year, sex, comorbidities and devices.

Conclusion: Decreasing SES was associated with increasing risk of SAB in the highest relative risk found in women with basic school as highest educational attainment.

P3109 | BEDSIDE
Clinical characteristics and outcomes of nosocomial infective endocarditis in Asia

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Nosocomial infective endocarditis (NIE) is a serious, potentially preventable complication of nosocomial bacteremia that is associated with high mortality rates. The aim of our study was to compare the characteristics of NIE with community-acquired infective endocarditis (CIE) and to determine independent risk factors for in-hospital death. We retrospectively reviewed the medical records of 560 patients diagnosed with infective endocarditis between January 2000 and July 2014. Compared with patients with CIE, patients with NIE were older (mean ± standard deviation [SD], 51.30 ± 18.01 vs. 59.76 ± 14.87; p = 0.001) and suffered from under-lying diseases such as liver cirrhosis (LC), diabetes mellitus (DM), and chronic kidney disease (CKD). The in-hospital death rate of the NIE group was much higher than that of the CIE group (27.3% vs. 5.9%, p < 0.001). On multiple analysis, age, LC, cancer chemotherapy, presence of a central intravenous catheter, hemodialysis, and genitourinary tract manipulation as predisposing procedure were independent clinical risk factors for NIE. Among the patients with NIE, 33 died during their hospital admission. The independent risk factors for in-hospital death were older age (Adjusted Odds ratio [Adjusted OR], 1.04; 95% confidence interval [CI], 1.01–1.07; p = 0.037) and chemotherapy for malignancy (Adjusted OR, 3.89; 95% CI, 1.18–12.87; p = 0.026).

Impact of smoking cessation on cardiovascular prognosis: myths and reality

P3110 | BEDSIDE
Time course changes of atherosclerotic LDL complexes after smoking cessation

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Introduction: Smoking cessation is associated with increase in body weight. While long-term (over 4 years) smoking cessation certainly reduces cardiovascular events, effects of smoking cessation-associated obesity on cardiovascular risks in an early period (within one year) are largely unknown. Serum alpha-1 antitrypsin LDL (AT-LDL) and amyloid A/LDL (SAA-LDL) are oxidatively modified LDL complexes which promote atherosclerosis. We have previously reported that the serum level of the AT-LDL is higher in smokers than in nonsmokers, and that the level decreases at 3 months after smoking cessation. We have also demonstrated that larger weight gain after smoking cessation perturbs such decrease at 3 months after the cessation.

Purpose: The present study investigated time-dependent changes in AT-LDL and SAA-LDL after smoking cessation and relationships of these changes with weight gain.

Methods: In 17 patients who had continued smoking cessation for one year, we measured serum AT-LDL and SAA-LDL levels by the enzyme-linked immunosorbent assay before smoking cessation, and at 3 and 1 year after smoking cessation.

Results: Body mass index (BMI) significantly increased from baseline (pre-cessation) to 3 months after smoking cessation (from 23.0 kg/m² to 23.7 kg/m², p = 0.027). Serum AT-LDL and SAA-LDL tended to decrease at 3 months after smoking cessation (AT-LDL: from 2.1 μg/ml to 1.9 μg/ml, p = 0.008, SAA-LDL: from 9.0 μg/ml to 4.4 μg/ml, p = 0.019), and from baseline to 1 year after smoking cessation (AT-LDL: from 2.1 μg/ml to 1.6 μg/ml, p < 0.001, SAA-LDL: from 9.0 μg/ml to 4.4 μg/ml, p = 0.004).

Conclusion: BMI and levels of two atherogenic lipoproteins, SAA-LDL and AT-LDL, time-dependently change after smoking cessation. While BMI progressively increased after smoking cessation, decrease in SAA-LDL and AT-LDL levels at 3 months after smoking cessation was insignificant. In contrast, the beneficial effect of non-smoking certainly overcomes potential cardiovascular risks associated obesity at one year after the cessation.

Abstract P3109 – Table 1

<table>
<thead>
<tr>
<th>NIE</th>
<th>CIE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survived (n=88)</td>
<td>Died (n=33)</td>
</tr>
<tr>
<td>Age (year) ± SD</td>
<td>58.08±15.72</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>52 (59.1%)</td>
</tr>
<tr>
<td>Chemistry</td>
<td>20 (22.7%)</td>
</tr>
<tr>
<td>Malignancy</td>
<td>32 (36.4%)</td>
</tr>
<tr>
<td>On indication of cardiac surgery but not done</td>
<td>16 (18.2%)</td>
</tr>
<tr>
<td>Viridans group streptococci</td>
<td>5 (5.7%)</td>
</tr>
<tr>
<td>Methicillin-resistant (MRSA)</td>
<td>17 (19.4%)</td>
</tr>
<tr>
<td>Fungus</td>
<td>2 (2.3%)</td>
</tr>
</tbody>
</table>

P3111 | BEDSIDE
Effect of smoking cessation on metabolic factors and the incidence of metabolic syndrome

S. Takayama1, H. Takase1, T. Okado1, T. Tanaka1, K. Makino1, H. Hayashi2, T. Sugira3, N. Ohite1, Y. Dohi1, Enshu Hospital, Hamamatsu, Japan; 2Hamamatsu University School of Medicine, Hamamatsu, Japan; 3Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan

Purpose: Smoking is one of the major risk factors for cardiovascular disease. Although smoking cessation is essential for good health, it might increase body weight and, thereby, have undesirable influence on metabolic factors. We investigated effects of smoking cessation on the incidence of metabolic syndrome (MetS) and its components in the Japanese general population.

Methods: Participants in our health checkup program were enrolled and followed up with the endpoint being the development of MetS. Past smokers (n=1918) and participants who started smoking during the follow-up period (n=88) were excluded from the study and the remaining 5702 participants (male 49.7%, 55.1±11.5 years old) were analyzed. MetS was diagnosed according to Japanese
Both active smoking and environmental exposure to tobacco smoke appear to in- 
smoke is associated with more severe atherosclerosis of extracranial arteries.

Effects of smoking cessation on metabolic factors

<table>
<thead>
<tr>
<th>Metabolic factors</th>
<th>Never smoking</th>
<th>Habitual smoking</th>
<th>Smoking cessation</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDL-cholesterol (mg/dl)</td>
<td>62.6</td>
<td>62.1*</td>
<td>56.1</td>
</tr>
<tr>
<td>Fasting plasma glucose (mg/dl)</td>
<td>94.2</td>
<td>94.9*</td>
<td>94.4</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>82.7</td>
<td>82.5</td>
<td>82.7</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>55.3</td>
<td>55.3</td>
<td>62.8</td>
</tr>
<tr>
<td>Metabolic factors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline Follow-up</td>
<td>Baseline Follow-up</td>
<td>Baseline Follow-up</td>
<td></td>
</tr>
<tr>
<td>64.4±1.60</td>
<td>64.4±1.60</td>
<td>64.4±1.60</td>
<td></td>
</tr>
<tr>
<td>8.15±1.5</td>
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<td>8.15±1.5</td>
<td></td>
</tr>
<tr>
<td>119.74±74</td>
<td>119.74±74</td>
<td>120.74±74</td>
<td></td>
</tr>
<tr>
<td>95.5*</td>
<td>95.5*</td>
<td>95.5*</td>
<td></td>
</tr>
<tr>
<td>62.8±13.6</td>
<td>62.6±13.6</td>
<td>56.1±13.6</td>
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<tr>
<td>105.7</td>
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<td></td>
</tr>
<tr>
<td>83.6</td>
<td>83.6</td>
<td>83.6</td>
<td></td>
</tr>
</tbody>
</table>

Results: During the follow-up (median 1089 day), MetS developed in 520 sub-

Although smoking cessation is preferable, it should be noted that smoking cessation may develop MetS. Therefore, careful instruction of lifestyle modification is necessary to avoid the development of MetS after smoking cessation.

Conclusions: Our findings indicate that there is no association between smoking habit and lower rate of all-cause mortality in AMI patients.

P3114 | SPOTLIGHT
Exposure to cigarette smoke and the morphology of atherosclerotic plaques in extracranial arteries assessed by computed tomography angiography in patients with essential hypertension
P. Gac1, M. Jurdziak 2, P. Jazwiec1, G. Mazur 2, P. Poreba 2

Background: Exposure to cigarette smoke is one of the major health problems of the modern world. In recent years, an important aspect of the research is to evaluate the importance of atherosclerotic plaque morphology in the context of a variety of clinical conditions. The available literature lacks a sufficient amount of scientific evidence on the relationship between exposure to cigarette smoke and the morphology of atherosclerotic plaques in the extracranial arteries.

Methods: The study included 61 hypertensive patients diagnosed and treated pharmacologically (mean age: 69.8±9.1 years). In the group of patients based on a survey three groups of patients were distinguished, varying in their exposure to tobacco smoke: 17 active smokers (group A), 18 non-smokers, declaring environmental exposure to tobacco smoke (group B) and 26 never smokers, not declaring exposure to cigarette smoke (group C). All the patients underwent CTA of extracranial arteries. CTA images obtained were analyzed in terms of the morphology of atherosclerotic plaques in the various segments of the arteries.

Results: In the whole group of patients plaques were visualized on average in 7.70±1.65 of the 10 segments evaluated, calcified plaques in 6.44±1.60 seg-

Conclusions: We designed and conducted a prospective study to determine whether EAT and SAT cytokines were not predictive of higher/lower cytokine concentrations.

P3114 | BENCH
Association between tobacco smoking and pro-inflammatory humoral signalling in human epicardial adipose tissue: a prospective cohort study in patients undergoing major cardiac surgery
M. Orban1, M. Mach1, M. Tretina 2, H. Bedanova 1, M. Soucek 1, P. Nemec 2

Background: Epicardial adipose tissue (EAT) is a source of various pro- and anti-inflammatory cytokines. Studies to date suggest that certain EAT cytokines could act in pathogenesis of coronary artery disease (CAD). A potential relationship between known cardiovascular risk factors such as smoking or obesity and EAT humoral signalling (measured by tissue levels of cytokines) has not been fully elucidated.

Methods: Samples of SAT and EAT were harvested from patients undergoing elective cardiac surgery. Tissue concentrations of tumour necrosis factor-α (TNF-α), interleukin-6 (IL-6), adipocyte fatty acid-binding protein (AFABP), lep-

Conclusions: Smoking was independently associated with higher TNF-α and IL-6 concentrations in EAT, and higher SAT levels of TNF-α. A novel observation that pro-inflammatory cytokines are elevated in EAT in active smokers could represent an important mechanism in pathogenesis of CAD. No differences between EAT humoral signalling in non- and stop-smokers supports the results of previous epidemiological studies which demonstrated the importance of smoking cessation for cardiovascular risk reduction.

**Criteria (2005).** Participants were divided into the 3 groups (never smokers, partic-

**Methods:** We conducted a retrospective cohort study with 4,420 patients with the primary diagnosis of AMI between 2004 and 2011. We performed a propensity-

**Results:** Between the 4,420 patients of the prematched cohort, smokers (n=1,128 [25.5%]) were younger, with lower rate of hypertension, dyslipidemia, di-

**Conclusions:** Smoking was independently associated with higher TNF-α and IL-6 concentrations in EAT, and higher SAT levels of TNF-α. A novel observation that pro-inflammatory cytokines are elevated in EAT in active smokers could represent an important mechanism in pathogenesis of CAD. No differences between EAT humoral signalling in non- and stop-smokers supports the results of previous epidemiological studies which demonstrated the importance of smoking cessation for cardiovascular risk reduction.
P3115 | BEDSIDE
The combined effect of the 3872 A/G polymorphism on C-reactive protein gene with tobacco smoking on endothelial function, on inflammatory, thrombotic processes and the risk for coronary artery disease
G. Hatzis1, N. Papageorgiou1, E. Okonomou1, G. Latsios1, A. Synetos1, A. Milou1, S. Papadopoulou1, C. Antoniades1, B. Schieffer2, D. Tousoulis1.

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

Background: Tobacco smoking is an established risk factor for coronary artery disease (CAD). Recent studies suggest that the 3872 A/G polymorphism on C-Reac2 gene (rs1205) may be associated with risk for CAD, with controversial so far results. However, no data exist on the synergistic effect of this polymorphism with smoking on the risk for CAD and processes leading to coronary atherosclerosis.

Purpose: In the present study, we examined the combined effect of rs1205 polymorphism with smoking on endothelial function, inflammatory and thrombotic processes as well as on the incidence of CAD.

Methods: 646 subjects (361 non smokers) were subjected to appropriate genotyping. Endothelial function was assessed by the flow mediated dilatation (FMD) of brachial artery. IL-6 (pg/ml), Tumor Necrosis Factor-α (TNF-α) (pg/ml), high sensitivity CRP (hsCRP) (mg/l) and D-dimers (µg/l) were measured with appropriate methods.

Results: We found a significantly positive association of the G allele carriers, compared to AA homozygotes, among the smokers (AA vs G carriers OR: 0.27, CI: 0.14–0.52, p<0.001), while a significantly negative association was observed among non-smokers (AA vs G carriers OR: 3.06, CI: 1.92–4.83, p<0.001), after adjustment for all risk factors for CAD. Importantly, the G allele carriers were present to have significantly higher levels of TNF-α (4.89±2.4 vs 2.37±1.6), IL-6 (2.7±1.52 vs 1.47±0.89), hsCRP (1.92±0.95 vs 0.97±0.70) and fibrinogen (442.2±133.4 vs 365.4±76.8) in smokers (p<0.001 for all), while it was presented to down-regulate TNF-α (3.9±2.03 vs 4.7±4.11, p=0.007), hsCRP (1.69±0.78 vs 2.06±0.88, p=0.003), fibrinogen (397.3±141.3 vs 490.8±142.8, p<0.001) and D-dimers (425±5772 vs 319±4308.6, p=0.004) in non smokers. Impressively, the G allele carriers, compared to AA homozygotes, were correlated with significantly impaired endothelial function in the smoking group (4.83±2.9 vs 5.7±3.04, p=0.003), while no effect was observed among non smokers (5.01±2.9 vs 4.3±2.2, p=0.24).

Conclusions: Our results demonstrate that the genetic predisposition of the G allele of rs1205 to increase the risk for CAD in smokers is mediated by inflammatory and thrombotic processes as well as the impairment of the endothelial function.

P3116 | BEDSIDE
Smoking versus healthy diet impact on left ventricular mass and diastolic performance in essential hypertension patients
A. Angelis, C. Vlachopoulos, N. Ioakimidis, K. Aggeli, C. Chrysochoou, K. Aznaouridis, M. Abdelrasoul, I. Felekos, C. Georgakopoulos, D. Tousoulis. Hippokration Hospital, University of Athens, 1st Department of Cardiology, Athens, Greece

Background: Smoking and arterial hypertension are potent risk factors for the development of atherosclerosis. The Mediterranean diet (Med-Diet) assists in cardiovascular disease prevention.

Purpose: To investigate whether left ventricular (LV) structural changes and diastolic performance associate with smoking status and adherence to the Mediterranean type of diet in hypertensive patients.

Methods: 160 hypertensive patients (55±9 years) underwent cardiac ultrasound examination. E/A, E/E’ Doppler ratio and LV mass index (LVMi) were obtained to assess diastolic performance and myocardial systolic reserve respectively. Overall assessment of dietary habits was evaluated through a special diet score (the Med-Diet Score, theoretical range 0–55). Higher values of the score indicate healthier dietary habits.

Results: According to regression analysis, LV mass index and E/E’ ratio, were positively associated with smoking status and negatively with the Med-Diet Score (all p<0.01), independently of age and blood pressure level. E/A ratio was significantly but negatively associated with smoking habit and positively with the Med-Diet Score. Subjects were further divided into subgroups according to smoking habit (current smokers/non smokers) and high/low Med-Diet Score. Non smokers with high Med-Diet Score (n=34) had significantly lower LV mass index and E/E’ ratio and higher E/A ratio compared to all other smoking/Med-Diet subgroups (all p<0.05, figure).

Conclusions: High adherence to the Mediterranean diet confers a favorable impact on LV structure and diastolic function in primary hypertension patients. Unfortunately smoking restricts that benefit. Our data emphasize the clinical value of a healthy life style in essential hypertension population in order to maintain cardiac physiology.

MANAGEMENT OF PROCEDURAL RISKS

P3117 | BEDSIDE
Transradial access for percutaneous coronary intervention (PCI) in British Columbia, Canada from 1999 to 2013: consistently lower mortality and transfusion rates in a large unselected patient cohort
W.T. Roberts1, J. Shinn2, L. Ding3, C.H. Ng4, B. Berry5, I.J. Nadra4, A. Della Sella6, S.O. Robinson1, Victoria Heart Institute; 1 Victoria Heart Institute; 2 Royal Jubilee Hospital, Victoria, Canada; 3 Cardiac Services BC, Provincial Health Service Authority, Vancouver, Canada; 4 Royal Jubilee Hospital, Victoria, Canada

Background: Transradial access (TRA) for PCI has become more common in an effort to minimise procedural related complications such as bleeding. Despite this, significant variation remains in arterial access site used for PCI depending on operator experience and institutional practice. Using data from a large unselected patient cohort, we examined trends in the utilisation of TRA along with mortality and peri-procedural bleeding following PCI.

Methods: Data on all PCI cases from 1999 to 2013 for patients presenting with acute coronary syndrome (ACS) or stable angina (SA) from the British Columbia Cardiac Registry were linked to vital statistics mortality records. Linkage with the BC Central Transfusion Registry (CTR) was used to measure red blood cell (RBC) transfusions occurring in the 10 days following PCI as a surrogate safety marker.

Results: From June 1, 1999 and May 31, 2013, 83,659 PCI cases were performed. There was an increase in the use of TRA for PCI in patients presenting with SA (20.4% to 41.7%, p<0.001) and ACS (17.9% to 48.9%, p<0.001) including those presenting with ST elevation MI (p=0.001) and patients ≥ 80 years old (p=0.0001). Over the study period, peri-procedural transfusion rates followed a similar non-linear trend (1.5% to 1.4% from 1999 to 2012; p=0.8) but increased within the femoral group (1.8% to 3.9%, p<0.001). In a risk adjusted model, TRA independently predicted lower transfusion rates as well as 30-day mortality when adjusted for pre-procedural patient demographic and clinical characteristics including age, sex, procedural urgency, ejection fraction, cardiogenic shock, and renal dysfunction.

Conclusions: Using data from a large provincial registry, we report a sustained uptake in the use of TRA for PCI cases over more than a decade of clinical practice. Compared to patients undergoing femoral access, transradial access is associated with lower peri-procedural bleeding as well as shorter and longer term mortality. Our data strongly support recent guidelines emphasising the clinical benefits of TRA for all patients undergoing PCI.

P3118 | BEDSIDE
The European and Chinese cardiac and renal remote ischemic preconditioning study (EURO-CRIPS): a randomized controlled trial

1 Victoria Heart Institute Foundation, Cardiac Research, Vancouver, Canada; 2 Cardiac Services BC, Provincial Health Service Authority, Vancouver, Canada; 3 University Hospital San Luigi alle Scotte, Cardiology, Siena, Italy; 4 University Hospital San Luigi Gonzaga, Cardiology, Orbassano, Italy; 5 Institut Hospitalier Jacques Cartier, Cardiology, Massy, France; 6 Polyclinic Santa Maria alle Scotte, Cardiology, Siena, Italy; 7 Nanjing First Hospital, Nanjing, China, People’s Republic of China

Aims: The potential protective effect of remote ischemic preconditioning (RICP) over contrast-induced nephropathy (CIN) after Percutaneous Coronary Intervention (PCI) remains to be defined.

Methods: A double-blind, randomized, placebo controlled multicenter study was performed. Patients were allocated 1:1 to RICP or standard therapy if they were younger than 85 years old; with a renal clearance in the interval 30–60 ml/min/1.73m2 and candidate to PCI for all clinical indications except for primary PCI in ST segment elevation myocardial infarction (STEMI). Incidence of CIN was the primary end point, whilst incidence of peri procedural myocardial infarction the secondary one. Diabetes mellitus was the only pre-specified analysis.

Results: From February 2013 to April 2014 a total of 3108 patients scheduled for angiography were screened. 442 fulfilled the inclusion criteria, 223 received PCI and were randomized to sham RICP (n=107) or treatment group (n=116). The
only pre-specified subgroup of diabetic patients presented 85 (38%) cases. RIPC significantly reduced AKI incidence in the overall population (12.1% vs. 26.1%, p < 0.01, with a number needed to treat 9), in non diabetic patients (9.2% vs 25.0%, p < 0.02) whilst diabetic subgroup showed no benefit (16.7% vs. 28.2%, p = 0.21).

A trend, although not significant, was reported for periprocedural myocardial infarction (Creatinin Kinase MB more than 5 URL; 8.4% vs 16.4%, p = 0.07; troponin T more than 5 URL; 27% vs 38%, p = 0.2).

Conclusions: Remote ischemic preconditioning significantly reduces the incidence of CIN in non diabetic patients undergoing PCI. Larger sample size is presumably needed to assess effect of RIPC for patients with diabetes mellitus.

P3111 | BEDSIDE
Contrast volume to creatinine clearance ratio for the prediction of contrast induced nephropathy in patients undergoing coronary angiography or percutaneous intervention
L. Barbieri1, M. Verdoia1, F. Marino1, H. Suryapranata2, G. De Luca1 on behalf of Novara Atherosclerosis Study Group (NAS), 1 Maggiore Della Carita Hospital, Department of Cardiology, Novara, Italy; 2 University Hospital Nijmegen, Cardiology, Nijmegen, Netherlands

Background: Contrast Induced Nephropathy (CIN) is a complication of procedures that are linked to the use of contrast material. The identification of high risk patients and preventive optimal hydration are key points to reduce the incidence of CIN.

Purpose: Aim of this study was to evaluate the role of contrast volume/creatinine clearance ratio (V/CrCl) in the prediction of CIN after coronary angiography or percutaneous interventions (PCI).

Methods: Our population is represented by 2308 consecutive patients undergoing coronary angiography and/or PCI. The risk of CIN was evaluated across quartiles of V/CrCl. ROC curves were used to identify the best predictive value. CIN was defined as an absolute increase of 0.5mg/dL or a relative > 25% in creatinine levels at 24–48 hours after the procedure.

Results: The total incidence of CIN was 12.2% and was significantly higher in the fourth quartile (1st Quartile 8.8%, 2nd Quartile 8.9%, 3rd Quartile 11.6% and 4th Quartile 19.4%, p < 0.001). By the use of ROC curves we identified a V/CrCl > 6.15 as the best discriminant value for the prediction of CIN, that occurred in 25.1% of patients with V/CrCl > 6.15 vs 9.7% in patients with V/CrCl < 6.15 (OR [95% CI] = 3.12 [2.38–4.12], p < 0.001). Patients with V/CrCl > 6.15 were older, with family history of CAD, hypertension, diabetes, hypercholesterolemia and renal failure. They had more often a previous history of myocardial infarction, previous revascularization, previous cerebrovascular accident and diabetes mellitus. They were more often in therapy with statins, nitrate, aspirin, calcium antagonist and thienopyridine and renal failure. They had more often a previous history of myocardial infarction, previous revascularization, previous cerebrovascular accident and diabetes mellitus.

Conclusions: Remote ischemic preconditioning significantly reduces the incidence of CIN in non diabetic patients undergoing PCI. Larger sample size is presumably needed to assess effect of RIPC for patients with diabetes mellitus.

P3112 | BEDSIDE
Complications of percutaneous thrombin injection in patients with post-catheterization femoral pseudoaneurysm
J. Kurzawski, M. Sadowski, L. Zandecki, A. Janion-Sadowska. Swietokrzyskie Cardiology Center, Kielce, Poland

Background: Ultrasound-guided percutaneous thrombin injection (UGTI) is a safe and feasible method in the management of iatrogenic femoral post-catheterization pseudoaneurysm (pSA). However, UGTTI complications have not been reported.

Purpose: To assess iatrogenic thrombin effects during UGTTI.

Methods: A total of 347 patients with pSA underwent UGTTI and prospective screening for complications.

Results: Arterial microembolization occurred in 53 patients (15.3%) and pulmonary embolism in 1 patient (0.29%). The risk of embolization was related to the length of channel between pSA and artery with OR 1.16, 95% CI (1.09–1.125, p < 0.0001) per 1 mm, similar to the need for repeat procedure (p < 0.02). The channel length of 2 mm was the borderline value for odds of having complications.

Conclusion: During UGTTI performed for the treatment of pSA the longer the channel the smaller chances for developing complications. A repeat procedure increases the risk of complications.

P3120 | BEDSIDE
Disaster in the cath lab -cardiogenic shock induced by procedure: results from the EHS PCI registry
T. Bauer1, H. Neft1, M. Hochadel2, H. Moellmann3, U. Zeymer4, A. Gitt4, F. Weidinger5, J. Marco6, C. Hamm1. 1 University Hospital Giessen and Marburg, Giessen, Germany; 2 Heart Attack Research Center, Ludwigshafen am Rhein, Germany; 3 Klinikum Bad Neuenahr, Germany; 4 Heart Center Ludwigshafen, Department of Cardiology, Ludwigshafen am Rhein, Germany; 5 Rudolfstiftung Hospital, Vienna, Austria, 6 Cardio-Thoracic Center of Monaco, Monaco, Monaco

Background: There is a large body of literature on acute myocardial infarction complicated by cardiogenic shock (CS). However, very little is known about initially hemodynamically stable patients that develop CS in the course of PCI. The association between V/CrCl > 6.15 and an increased risk of CIN was confirmed at multivariate analysis after correction for all baseline confounders (Adjusted OR [95% CI] = 1.81 [1.19–2.76], p = 0.005).

Conclusions: This is one of the largest studies evaluating the association between V/CrCl ratio and the risk of CIN in patients undergoing coronary angiography or PCI. We found that V/CrCl ratio > 6.15 was independently associated with an increased risk of CIN.

P3121 | BEDSIDE
Radiation dose reduction in the cardiac catheterization laboratory using a novel protocol
A. Jurado Roman1, I. Sanchez Perez2, F. Lozano Ruiz-Poveda3, M.T. Lopez Lluna1, J.M. Benitez1, N. Pinilla1, P. Agudo Quilez2, A. Moreno Arciniegas1, M.T. Marina Bryssete1, J. Piqueras1. 1 Hospital General de Ciudad Real, Ciudad Real, Spain; 2 University Hospital Infanta Leonor, Cardiology, Madrid, Spain

Introduction: The cardiac catheterization laboratory is an important source of high risk were more likely to be affected by this complication. Hospital mortality rate was very high.

Table 1

<table>
<thead>
<tr>
<th>Complications</th>
<th>No complications</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheath 6F</td>
<td>66.6% (195)</td>
<td>75.9% (41)</td>
</tr>
<tr>
<td>Sheath &gt; 6F</td>
<td>33.4% (98)</td>
<td>24.1% (13)</td>
</tr>
<tr>
<td>pSA volume</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-5 mL</td>
<td>25.6% (75)</td>
<td>22.2% (12)</td>
</tr>
<tr>
<td>1-5 mL</td>
<td>45.7% (134)</td>
<td>42.6% (23)</td>
</tr>
<tr>
<td>5 mL</td>
<td>28.7% (84)</td>
<td>35.2% (19)</td>
</tr>
<tr>
<td>Channel length (mm)</td>
<td>8.3±8.6</td>
<td>2.6±4.4</td>
</tr>
<tr>
<td>One procedure</td>
<td>88.6% (257)</td>
<td>22.8% (13)</td>
</tr>
<tr>
<td>Repeat procedure</td>
<td>11.4% (33)</td>
<td>77.2% (44)</td>
</tr>
<tr>
<td>Thrombin dose per injection</td>
<td>p&lt;200 IU</td>
<td>50.2% (147)</td>
</tr>
<tr>
<td>≥200 IU</td>
<td>49.8% (146)</td>
<td>37.0% (20)</td>
</tr>
</tbody>
</table>

Logistic regression fit plot and ROC

Conclusion: During UGTTI performed for the treatment of pSA the longer the channel the smaller chances for developing complications. A repeat procedure increases the risk of complications.
P3123 | BESIDEST 
On- and off-label use of vascular closure device in Japan 
T. Kuno1, S. Kohsaka2, Y. Numasawa3, M. Sawano4, S. Takagi5, S. Noma4, K. Negishi6, Y. Maekawa7, A. Kawamura7, K. Fukuda8, Ashigaka Red Cross Hospital, Ashigaka City; 2Keio University Hospital, Department of Cardiology, Tokyo; 3Hiratsuka City Hospital, Department of Cardiology, Hiratsuka; 4Saiseikai Utsunomiya Hospital, Department of Cardiology, Utsunomiya; 5Yokohama Municipal Hospital, Department of Cardiology, Yokohama, Japan

Background: Vascular closure devices (VCD) provide immediate hemostasis after femoral approach between 2008 and 2014 at 15 hospitals in Japan. We directed patients to VCD use had similar bleeding complications rate compared with manual compression including those underwent VCD for off-label use. Post PCI puncture site bleeding 14 (1.1%) 14 (1.1%) 1.000 3 (0.9%) 4 (1.3%) 0.704
Cardiopulmonary arrest – – – 11 (3.4%) 18 (5.6%) 0.183
Post PCI complications 28 (2.1%) 28 (2.1%) 1.000 7 (2.2%) 8 (2.4%) 0.928

Table 1

<table>
<thead>
<tr>
<th>Baseline variables</th>
<th>Value</th>
</tr>
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<tbody>
<tr>
<td>Age, years</td>
<td>65±10</td>
</tr>
<tr>
<td>Gender, female</td>
<td>53%</td>
</tr>
<tr>
<td>Race, Japanese</td>
<td>87%</td>
</tr>
<tr>
<td>Height, cm</td>
<td>169±8</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>68±15</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>138±19/85±13</td>
</tr>
<tr>
<td>Diabetes</td>
<td>34%</td>
</tr>
<tr>
<td>Obesity</td>
<td>40%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>12%</td>
</tr>
<tr>
<td>Smoking</td>
<td>32%</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
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</tr>
<tr>
<td>Heart failure</td>
<td>11%</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>9%</td>
</tr>
<tr>
<td>Peripheral artery</td>
<td>12%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>14%</td>
</tr>
<tr>
<td>Smoking</td>
<td>34%</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>48%</td>
</tr>
<tr>
<td>Previous PCI</td>
<td>26%</td>
</tr>
<tr>
<td>Age &gt; 80</td>
<td>34%</td>
</tr>
</tbody>
</table>
| Cardiovascular shock | 26% |}

P3124 | BESIDEST 
Differences in prognosis between heart failure with preserved and depressed ejection fraction can be partially explained by differences in renin-angiotensin-aldosterone system (RAAS) 
N. Farre1, R. Olivero-Soldovíla2, I. Rodríguez-Costoya3, C. Enjuanes4, P. Mollner-Borja1, J. Gonzalez-Robledo5, S. Ruiz4, A. Garcia-Elias6

Abstract P3123 – Table 1

<table>
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<td>34%</td>
</tr>
<tr>
<td>Cardiovascular shock</td>
<td>26%</td>
</tr>
</tbody>
</table>
un, of the 800 hundred subjects still alive, majority (n=599) were available for re-
examinations, such as echocardiography using modern techniques. Septal E/E' could be reliably measured from 540 subjects. E/E' was divided to tertiles (1st tert <9.5, 2nd tert ≥9.5 but <12.1, 3rd tert ≥12.1), the 3rd tert indicating severe diastolic dysfunction.

Results: Several baseline variables were associated with diastolic dysfunction af-
fter over 20 years of follow-up (Table). After adjustments in the multivariable logistic regression analysis model, only systolic blood pressure (p<0.009) and shorter heart height (p=0.002) retained a significant association with the risk of developing di-
astolic dysfunction.

Conclusion: Elevated systolic blood pressure and short height are the main pred-
icators of the long-term risk of development of diastolic dysfunction in middle-
aged subjects.

P3126 | BEDSIDE
Unmasking the prevalence of silent myocardial infarction, ischaemia and microvascular dysfunction in HFpEF with CMR

P. Kanagala1, A. Singh2, J. Khan1, A. S. Singh1, S. A. Nazir1, I. B. Squire1, L. L. Ng1, G. P. McCann1, 1NIHR Biomedical Research Unit in Cardiovascular Disease, 2Department of CARDIOVASCULAR SCIENCES, UNIVERSITY OF LEICESTER, Leicester, United Kingdom; 2Kettering General Hospital, Kettering, United Kingdom

Purpose: HFpEF (heart failure with preserved ejection fraction) represents a het-
erogenous group with poor outcomes. Although CAD (coronary artery disease) has been confirmed in HFpEF, the reported prevalence is lower compared to HFNEF (heart failure with reduced ejection fraction) despite a high cardiovascular risk profile. The role of CMR (cardiac magnetic resonance) as a diagnostic tool for HFpEF is well validated.

Methods: Comprehensive CMR with adenosine stress perfusion and late gadolinium enhancement (LGE) was undertaken as part of DIAMOND HFpEF pathway for HFpEF enables better phenotyping and earlier initiation of primary prevention. A large proportion of HFpEF patients (1/5 in our cohort) have cardiovascular life expectancy less than 6 months, myocardial infarction (MI) in the preceding 6 months, severe valve disease, obstructive pulmonary disease and estimated glomerular filtration rate less than 30.

Results: A total of 181 patients were enrolled and 154 underwent CMR (n=5 did not undergo stress perfusion). Baseline characteristics reveal: mean age 72±12 years; male 51%; hypertension 90%; diabetes 49%; hypercholesterol-
amia 49%; smoking 53%; known CAD 21%; angina 18% and LVEF ≤50. Qualitative analyses revealed "silent" MI in 14 patients (9%). Reversible perfusion defects were seen in 30 (total = 29%) patients of which 19 (total = 13%) likely represented ischaemia in a CAD territory distribution and the remainder (total = 7%) were suggestive of microvascular dysfunction (MVD).

Conclusion(s): A large proportion of HFpEF patients (1/5 in our cohort) have significant previously undiagnosed CAD. Incorporating CMR into the diagnostic pathway for HFpEF enables better phenotyping and earlier initiation of primary and secondary prevention therapies which may alter prognosis.

P3127 | BEDSIDE
Acute chamber stiffening is responsible for high filling pressures during exercise in HFN EF. A dynamic pressure-volume and histological study

C. Perez Del Villar1, J. Bermejo1, K. Savastru2, P. Martinez-Legaz1, B. Lopez3, R. Yotil, A. Gonzalez-Mansilla3, F. Spillmann2, F. Fernandez-Aviles1, C. Tschoepe4, 1University of Seville, 2Charité - Campus Benjamin Franklin, Berlin, Germany; 3University Clinic of Navarra, Centre for Applied Medical Research, Pamplona, Spain; 4Department of Cardiology, Heart and Diabetes Centre, Essen, Germany; 5Department of Cardiology, Heart and Diabetes Centre North Rhine-Westphalia, Ruhr-University Bochum, Bad Oeynhausen, Germany; 6University Hospital Regensburg, Regensburg, Germany; 7Cologne University Hospital - Heart and Diabetes Centre, Kardiolinklinik Berlin, Berlin, Germany; 8Medical Center Hamburg Eppendorf, Department of Medical Biometry and Epidemiology, Hamburg, Germany; 9ResMed Science Center, ResMed Germany Inc., Martinsried, Germany

Background: Differences in prevalence and severity of sleep-disordered breathing (SDB) are observed in heart failure (HF) patients with reduced (HF-REF) and preserved (HF-PEF) ejection fraction.

Conclusion: Differences in prevalence and severity of sleep-disordered breathing (SDB) are observed in heart failure (HF) patients with reduced (HF-REF) and preserved (HF-PEF) ejection fraction.
with 238 clinical variables. To identify and rank biomarkers predicting NYHA class and outcome, orthogonal partial least square (OPLS) analysis was performed. Top-10 positive and top-3 negative predictors of outcome were analyzed by Cox regression.

**Results:** Loading scores of biomarkers and clinical variables are plotted in Figure 1. Top-10 positive predictors were significant after adjustment for NT-proBNP while the top-3 negative were not. Left atrial volume index correlated with CCL20 (r=0.32, p=0.006) and ST2 (r=0.27, p=0.020) and E/e' with CCL20 (r=-0.29, p=0.018), GDF-15 (r=-0.32, p=0.009), SPON1 (r=0.47, p<0.001), IL 8 (r=0.26, p=0.044), IL 6 (r=0.27, p=0.033), ST2 (r=0.30, p=0.017) and HGF (r=0.36, p=0.003). NYHA class correlated with log GDF-15 (r=-0.20, p=0.019), log IL 6 (r=-0.21, p=0.002) and log ST2 (r=0.042).

**Conclusions:** In HFrEF, novel biomarkers of inflammation predict HF severity and prognosis that may complement or even be more important than traditional markers such as NT-proBNP. These findings lend support to the microvascular inflammation hypothesis in HFrEF.

**P3130 | BEDSIDE**

Insulin resistance is an independent predictor of left ventricle diastolic dysfunction across the diabetic continuum

R. Ladeiras-Lopes 1, R. Fontes-Carvalho 2, P. Bettencourt 2, A.F. Leite-Moreira 2, A. Avevedo 2, 1 Gaia Hospital Centre, Department of Cardiology, Vila Nova de Gaia, Portugal; 2 Faculty of Medicine, University of Porto, Porto, Portugal; 3 University of Porto, Faculty of Medicine, Department of Physiology and Cardiothoracic Surgery, Porto, Portugal

**Background:** Type 2 diabetes mellitus (T2DM) increases the risk of heart failure but the underlying mechanisms leading to diabetic cardiomyopathy are poorly understood. Left ventricle diastolic dysfunction (LVDD) is one of the earliest cardiac changes in these patients being associated with the progression to diastolic heart failure. It is not known if this association is induced by insulin resistance or a consequence of hyperglycemia.

**Purpose:** We aimed to evaluate the association between LVDD and insulin resistance in individuals in several phases of the diabetic continuum.

**Methods:** Population-based study including a cohort of 1,063 individuals aged ≥45 years (36% male, 61.2±9.6 years). Diastolic function was assessed by echocardiography, using tissue Doppler analysis (E' velocity and E/E' ratio) according to the latest consensus guidelines. Insulin resistance was assessed using the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) score.

**Results:** Metabolic syndrome (MetS) without T2DM was present in 31% of patients and T2DM in 12%. The HOMA-IR score correlated to E' velocity (r=-0.20; p<0.0001) and E/E' ratio (r=-0.20; p<0.0001). There was a progressive worsening in E' velocity (p for trend <0.001) and in E/E' ratio (p<0.0001) across HOMA-IR quartiles. Individuals in the highest HOMA-IR quartile were more likely to have LVDD, even after adjustment for age, sex, blood pressure and body mass index (adjusted OR: 1.82; 95% CI: 1.09–3.03). From normal individuals, to patients with T2DM, there was a progressive decrease in LVDD (adjusted OR: 1.82; 95% CI: 1.09–3.03). From normal individuals, to patients with T2DM, there was a progressive decrease in LVDD (adjusted OR: 1.82; 95% CI: 1.09–3.03).

**Conclusions:** LVDD and presence of MetS were independently associated with HOMA-IR score and with the risk of LVDD. The HOMA-IR score correlated to E' velocity (p<0.0001) and E/E' ratio (<0.001) and more diastolic dysfunction (adjusted OR: 1.62; 95% CI: 1.12–2.36 and 1.78; 95% CI: 1.09–2.91, respectively).

**Figure 1**

**P3132 | BEDSIDE**

Achievement of individualized blood pressure and HbA1c targets in patients with hypertension and type-2 diabetes


1 University of Erlangen-Nuremberg, Erlangen, Germany; 2 Heart and Diabetes Center NRW, Bad Oeynhausen, Germany; 3 Novartis Pharma GmbH, Medical Department, Nürnberg, Germany; 4 Institute for Cardiovascular Pharmacology and Epidemiology, Mahlow, Germany; 5 Stiftung Institut für Herzinfarktforschung, Ludwigshafen, Germany

**Background:** Treatment targets for patients with hypertension and diabetes have recently changed to reflect the need for individualized treatment considering patient and disease specific characteristics.

**Methods:** DIALOGUE is a prospective, observational, multi-center registry in patients with diabetes and hypertension. VD was defined as the presence of CAD, prior MI, prior PCI, prior CABG, prior stroke and/or known PAD.

**Results:** Out of 8,616 patients included, 30.3% were diagnosed as having VD. BP was comparable while HbA1c and fasting blood glucose was lower. They had a significantly higher burden of hypoglycemic episodes within the 12 months prior enrollment. Differences in treatment target assignment were minor for HbA1c ≤6.5% (37.1% VD vs. 39.8% noVd; p<0.05) and systolic BP ≤130mmHg (36.1% VD vs. 39.8% no VD; p<0.01). Antidiabetic treatment strategies based on baseline diabetes and/or respectively to metformin (74.8% vs. 82.3%; p<0.0001), a lesser use of DPP-4 Inhibitors (59.9 vs. 63.3%; p<0.01) and a more frequent use of SU (19.3 vs. 16.7%; p<0.01) and Insulin (Death rates were significantly higher in the VD group in the 6 and 12 months follow-up.

**Conclusions:** VD is a frequent comorbid disease in patients with diabetes and hypertension. Treatment targets do not adequately reflect the specific comorbidity burden and the risk of treatment emergent adverse effects. Patients with VD experience more episodes of hypoglycemia, which might reflect the antidiabetic drug treatment pattern.
Background: Chronic hypoxia induces pulmonary vascular remodeling, pulmonary hypertension, and right ventricular hypertrophy. At present, little is known about mechanisms driving these responses. We performed to assess the role of sildenafil in patients with pulmonary arterial hypertension secondary to chronic hypoxic lung injury. Methods: Sildenafil treatment contributed to ameliorate the hypoxia-induced pulmonary hypertension and right ventricular hypertrophy.

Results: Compared to N, Doppler echocardiography revealed reduced pulmonary artery (PA) acceleration time and velocity time integral (~142±146 vs –0.74±0.03%, respectively) and increased PA systolic pressure (+2.0±0.08%) in CH rats, which rescued by sildenafil. Although CH resulted in a 1.7-fold increase in RV weight and in RV hypertrophy (expressed as RV/LV+Septum ratio) accompanied by a 1.5-fold increase in medial wall thickness of pulmonary arteries, these were significantly attenuated by sildenafil. This was associated with blunted proliferation of cells in response to stress, as judged by BrdU incorporation that was higher in CH than CH-sildenafil rats (BrdU+cells in lung: 48.6±9.3% vs 11.6±3.0%, respectively; BrdU+cells in RV: 25.9±4.2% vs 7.8±4.2%, respectively). Additionally, compared to N, a double IF showed an increase in the BrdU-alpha-SMA+cells in CH tissues (for lung: 0.5±0.2 vs 3.9±0.4, respectively; for RV: 3.0±1.0 vs 1.7±0.07, respectively), which inhibited by sildenafil (0.7±0.2 vs 0.2±0.04 for lung and RV, respectively). Compared to N, RT-PCR showed an mRNA up-regulation of collagen III in the lung (1.5-fold) and in the RV (2.0 fold) tissues after CH, confirmed by interstitial fibrosis, which was substantially reduced by sildenafil. Interestingly, in the lungs and RV tissues obtained from N and CH rats, the expression of L38A/B (marker of autophagy) did not alter, while it was significantly increased with sildenafil. Conclusion: Sildenafil treatment contributes to ameliorate the hypoxia-induced cardiac remodeling by reducing the proliferation of new fibroblasts and by activating autophagy as a protective mechanism to prevent excess collagen accumulation.

P3134 | BEDSIDE First quality assessment of cardiovascular drugs in 10 sub-Saharan African countries: the seven study

M. Antignac1, I. B. Diop2, B. Do3, M. S. Ikam4, R. N’gueda4, D. M. Balde5, Y. Tchabi, A. Sidi Aly6, E. Marion7, J. Xouven8 on behalf of Cardiology & Development.

Methods: Adult male Sprague-Dawley rats were exposed 2 weeks to chronic hypoxia (N: 21±2.0; n=10). CH rats received sildenafil (1.4 mg/kg/dip ip, n=10) or saline (n=10). The effects of CH on cardiovascular hemodynamics were assessed by Doppler echocardiography and RV catherization. Lungs and RV were removed and frozen for biochemical analysis or formalin-fixed and paraffin-embedded for immunofluorescence staining (IF).

Results: Compared to N, Doppler echocardiography revealed reduced pulmonary artery (PA) acceleration time and velocity time integral (~142±146 vs –0.74±0.03%, respectively) and increased PA systolic pressure (+2.0±0.08%) in CH rats, which rescued by sildenafil. Although CH resulted in a 1.7-fold increase in RV weight and in RV hypertrophy (expressed as RV/LV+Septum ratio) accompanied by a 1.5-fold increase in medial wall thickness of pulmonary arteries, these were significantly attenuated by sildenafil. This was associated with blunted proliferation of cells in response to stress, as judged by BrdU incorporation that was higher in CH than CH-sildenafil rats (BrdU+cells in lung: 48.6±9.3% vs 11.6±3.0%, respectively; BrdU+cells in RV: 25.9±4.2% vs 7.8±4.2%, respectively). Additionally, compared to N, a double IF showed an increase in the BrdU-alpha-SMA+cells in CH tissues (for lung: 0.5±0.2 vs 3.9±0.4, respectively; for RV: 3.0±1.0 vs 1.7±0.07, respectively), which inhibited by sildenafil (0.7±0.2 vs 0.2±0.04 for lung and RV, respectively). Compared to N, RT-PCR showed an mRNA up-regulation of collagen III in the lung (1.5-fold) and in the RV (2.0 fold) tissues after CH, confirmed by interstitial fibrosis, which was substantially reduced by sildenafil. Interestingly, in the lungs and RV tissues obtained from N and CH rats, the expression of L38A/B (marker of autophagy) did not alter, while it was significantly increased with sildenafil. Conclusion: Sildenafil treatment contributes to ameliorate the hypoxia-induced cardiac remodeling by reducing the proliferation of new fibroblasts and by activating autophagy as a protective mechanism to prevent excess collagen accumulation.
(miRNAs) have been proposed as novel biomarkers in patients with cardiovascular diseases. In particular, miRNA-133a has been associated with cardiovascular reverse-remodeling processes in HHD. Renal sympathetic denervation (RSD) represents a treatment option for patients with resistant HT. The primary aim of the present study was to examine the effect of RSD on HHD by analyzing the expression of miRNA-133a, as a specific miRNA for cardiovascular reverse-remodeling processes in HHD.

Methods: A total of 50 consecutive patients (mean age: 65.2 ± [10.4]) undergoing RSD were included in this study. A therapeutic response was defined as an office systolic blood pressure (SBP) reduction of ≥10 mmHg 6 months after RSD. Venous blood samples for the analysis of miRNA in serum were collected prior to and 6 months after RSD.

Results: A significant reduction in the office SBP of 24.4 mmHg (SBP baseline: 164.8 ± [7.9] mmHg; p < 0.001) was documented 6 months after RSD. At this time point circulating concentrations of miRNA-133a were significantly increased (4-fold; p < 0.001) compared with baseline values. Correlation analysis showed a significant relationship between baseline SBP values and SBP reduction (r=−0.66, p < 0.001) as well as between elevated miRNA baseline levels and the increase in miRNA levels (r=−0.48; p < 0.001) after the 6-month follow-up. SBP reduction was associated with the increase in miRNA-133a levels (r=0.36, p < 0.02) 6 months after RSD. In addition, successful SBP reduction in responders was associated with a significantly greater increase of miRNA-133a levels when compared with non-responders (p < 0.03).

Conclusion: In addition to the effective SBP reduction in response to RSD, this study demonstrates an effect of RSD on miRNA-133a reflecting cardiovascular reverse remodeling processes. These results provide information on a beneficial effect of RSD on cardiovascular reverse remodeling and HHD in high-risk patients.

NEW CONCEPTS IN ECHOCARDIOGRAPHY

3167 | BEDSIDE
Vena contracta area for severity grading in functional and degenerative regurgitation: A study based on transesophageal 3D colour Doppler in 419 patients

Background: Vena contracta area (VCA) derived by 3D colour Doppler is a new parameter for assessment of mitral regurgitation (MR). Aim of the study was to establish VCA cut-off values for grading of MR, using the EACI recommended 2D integrative approach as a reference.

Methods: Patients with at least moderate MR underwent transesophageal 3D colour Doppler echocardiography. The following 2D parameters were assessed: Biplane Vena contracta width and effective regurgitant orifice area (EROA) according to PISA method. Quantification of VCA was performed in a 3D colour Doppler dataset. In 90 patients a 3D dataset of the left ventricle (LV) and the left ventricular outflow tract (LVOT) was acquired. Velocity-time integral (VTI) in the LVOT was determined using a pulsed wave Doppler. Regurgitation volume (RV_3D) was calculated as following: (LV enddiastolic volume – LV endsystolic volume) – (LVOT area x VTI_LVOT). In addition, regurgitation volume was calculated using VCA and VTI of MR jet (RV_VCA).

Results: The patient population was divided into a group with functional MR (FMR group) and a group with degenerative MR (DMR group). The results of the echocardiographic parameters are displayed in Table 1. To define cut-off values for differentiation between moderate and severe MR, receiver operating characteristic (ROC) curves were calculated for EROA and VCA (Table 2). Regurgitation volumes calculated using VCA (RV_VCA) correlated with RV_3D (r=0.98, p < 0.001). RV_VCA values were higher when compared with RV_3D (r=0.7, p < 0.001)

Conclusion: This study delivers cut-off values for VCA in a relatively large population of patients with different types of mitral regurgitation. Regurgitation volumes derived by VCA showed a good correlation with the reference method using 3D volumetric datasets of LV.

3168 | BEDSIDE
Left atrial function across the spectrum of cardiovascular disease in the elderly- the ARIC study
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Background: Left atrial (LA) enlargement is recognized a key predictor of adverse cardiovascular (CV) outcomes; emerging evidence also suggests the importance of LA function, although it is rarely measured. We aimed to examine variation in LA function across the spectrum of CV disease burden in a large cohort of older adults living in the community.

Methods: We studied 1,210 participants in the Atherosclerosis Risk in Communities (ARIC) Study who were in sinus rhythm and free of valvular disease with acceptable quality 3D-echocardiograms. We examined the correlates of LA volumes, LA emptying fraction (LAEF), and LA global longitudinal strain (LAGLS) measured using 3D echocardiography.

Results: The mean age was 76±5 years; 59% were women. The overall mean LAEF was 53±12%; participants in the lowest quartile of LAEF (39%; IQR 33–43) were older, more likely to be hypertensive, to have heart failure (HF) and higher NT-proBNP. LAEF and LAGLS were inversely correlated with NT-proBNP (r=−0.24, p < 0.001; −0.22, p < 0.001). In multivariable analyses, participants with HF had significantly higher LA volumes and worse LA function than apparently “healthy” individuals (free of CV risk factors) or those with only hypertension. Healthy participants had smaller LA volumes than those with hypertension, but there were no significant differences in LA function between “healthy” and hypertensive adults (Figure).

were analyzed. We found a good correlation between noninvasive and invasive measurements of PVR with r=0.83, p=0.0001 (Figure - right).

Conclusion: Estimation of intracardiac relative pressure distribution is feasible by RPI and its measurements show good correlation with invasive catheter measurements.

3170 | BEDSIDE
Comparative usefulness of a novel echocardiographic measurement of pulmonary vascular resistance based on a theoretical formula among invasive methods

Background: Although pulmonary vascular resistance (PVR) is an important pathophysiologic parameter, its use has been limited because of the invasiveness of measurement by right heart catheterization. Several noninvasive methods have been proposed, but they remain empirical, lacking sufficient accuracy.

Purpose: The aims of this study were to propose a novel echocardiographic measurement of pulmonary vascular resistance based on a theoretical formula and investigate the feasibility and accuracy of this method in patients with heart failure.

Methods: Echocardiography was performed in 27 patients before right heart catheterization. Peak tricuspid regurgitation pressure gradient (TRPG), pulmonary regurgitation pressure gradient in end-diastole (PRPGed), and cardiac output derived from the time-velocity integral and the diameter in the left ventricular outflow tract (COLVOT) were measured by Doppler echocardiography. PVR based on a theoretical formula (PVRtheo) was calculated as (TRPG - PRPGed)/3COLVOT in Wood units (WU). PVRtheo was compared with PVR obtained by the methods of Abbas et al., Haddad et al., and Kouzu et al. Along with PVR obtained by catheterization (PVRcath) using the linear regression and Bland-Altman analyses.

Results: The mean PVRcath was 2.4±1.4 WU. PVRtheo correlated well with PVRcath (r=0.83, p<0.001). Bland-Altman analysis showed a homogeneous distribution with a difference of 0.79 Wood units. PVRtheo appeared to be accurate compared to earlier echocardiographically derived PVR methods (Abbas et al., r=0.52, P=0.013, Haddad et al., r=0.51, P=0.013, Kouzu et al., r=0.68, P<0.001) in this cohort of patients.

Conclusion: The new echocardiographic approach based on a theoretical formula provides a noninvasive and accurate assessment of PVR.

3172 | BENCH
Different behaviour of left atrial external work between acute left ventricular anterior and posterior ischaemia
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Background: According to our recent experimental study with speckle tracking echocardiography, left atrial (LA) external work can be measured by the LA pressure-longitudinal strain loop area, which includes two distinct phases of active contraction/relaxation (A-work) and passive dilatation/emptying (V-work).

We investigated how LA function behaved during acute left ventricular (LV) ischaemia.

Methods: Echocardiographic and hemodynamic data were simultaneously acquired in 19 open-chest dogs before and during occlusion of the left anterior descending (LADO, n=7) and proximal circumflex coronary arteries (LCxO, n=12). LA and LV external works were computed as the myocardial work.

Results: Three cases of LCxO were excluded due to ischaemia-provoked significant mitral regurgitation. Mean LA pressure was similarly elevated during LADO and LCxO (LADO: 3.2±1.7 vs. 5.0±2.1 mmHg, p=0.01, LCxO: 2.8±1.5 vs. 5.3±1.6 mmHg, p<0.01). Although two interventions induced no significant changes of LV works (LADO: 643±202 vs. 513±182 mmHg %, LCxO: 567±254 vs. 464±177 mmHg %), stroke volume maintained during LADO but significantly decreased during LCxO (LADO: 8.1±1.0 vs. 7.8±1.1 ml, LCxO: 7.8±2.2 vs. 5.7±1.3 ml, p<0.01). A-work significantly increased during LADO but not during LCxO (LADO: 5.9±4.2 vs. 13.0±12.3 mmHg %, p<0.01, LCxO: 4.4±2.0 vs. 5.5±5.0 mmHg %). V-work significantly decreased during LCxO but not during LADO (LADO: 13.3±8.1 vs. 9.1±7.3 mmHg %, LCxO: 15.1±7.3 vs. 4.7±3.9 mmHg %, p<0.01).

Conclusions: Vortex flow redirection towards the LVOT does not vary with changes in AV delay. This has implications for pacemaker and CRT optimization, where a too short AVD may negatively impact cardiac output and generate turbulent flow in the outflow tract by compromising the physiological role of vortices.

LA pressure-strain loop during ischaemia
3174 | BENCH
Long-term antihypertensive treatment improves left ventricular twisting and untwisting in hypertensives: a 3-year follow-up study
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Background: Impaired left ventricular (LV) myocardial twisting markers indicate the presence of local systolic and diastolic dysfunction. Blood pressure, arterial stiffness, LV mass, and impaired coronary microcirculation determine LV function in hypertensives. We investigated the effects antihypertensive treatment on the above parameters during a 3-year follow up.

Methods: 375 untreated patients (age 54±11 years) with essential hypertension and 50 healthy controls with similar age and sex, we measured a) blood pressure parameters by 24 ambulatory blood pressure monitoring b) Carotid to femoral artery pulse wave velocity (PWV) c) Coronary flow reserve (CFR) after adenosine infusion, LV mass/m2, twisting (Tw-deg), peak twisting (Tw-deg/sec) velocity, untwisting at mitral valve opening (unTWmVO), peak E (unTWE) and end of the E wave (unTWEd) of the mitral inflow and untwisting (unTw) velocity using conventional and speckle tracking echocardiography at baseline and after a 3-year follow up. All patients were treated with angiotensin receptor blockers. We characterized as well-controlled those with 24 systolic and diastolic blood pressure <130/80 mmHg.

Results: Compared to controls, hypertensives had lower CFR, (2.5±0.6 vs 2.9±0.6) and higher PWV (11.7±2 vs 9.2±1.5) and unTw velocity (−94±31 vs −93±31), LV mass/m2 (81±16 vs 75±16), PWV (11.7±2 vs 10.8±1.5,) and 24h BP (130/80 mmHg).

Conclusions: Long-term antihypertensive treatment improves LV twisting-untwisting in hypertensives in parallel with reduction of blood pressure, LV mass and arterial stiffness.

3175 | BEDSIDE
Combined analysis of speckle-tracking echocardiography and late gadolinium enhancement cardiac magnetic resonance improves prediction of functional recovery after acute myocardial infarction
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Background: Prediction of left ventricular recovery after acute myocardial infarction (AMI) is unknown. Weaimed to assess whether cardiovascular magnetic resonance imaging (CMR) can predict functional recovery.

Methods and results: From 2004 to 2012 we prospectively recruited 548 STEMI patients. Left ventricular (LV) ejection fraction (LVEF), infarct size (IS), edema, white matter, microvascular obstruction and myocardial salvage were quantified by CMR at pre-discharge. During a mean follow-up of 840 days, 57 ME events (10%, 23 cardiac deaths, 34 non-fatal re-infarctions) were documented. Patients with ME showed a more depressed LVEF <40% (p<0.001), slight IS (0–25% LGE), higher PWV (11.7±2 vs 10.8±1.5,) and higher 24h BP (130/80 mmHg).

Conclusions: In patients with AMI, prediction of long-term ME (cardiac death and non-fatal infarction) is unknown. We aimed to assess whether cardiovascular magnetic resonance imaging can predict functional recovery after acute myocardial infarction (STEAMI).

Methods and results: From 2004 to 2012 we prospectively recruited 548 STEMI patients. Left ventricular (LV) ejection fraction (LVEF), infarct size (IS), edema, white matter, microvascular obstruction and myocardial salvage were quantified by CMR at pre-discharge. During a mean follow-up of 840 days, 57 ME events (10%, 23 cardiac deaths, 34 non-fatal re-infarctions) were documented. Patients with ME showed a more depressed LVEF <40% (p<0.001), slight IS (0–25% LGE), higher PWV (11.7±2 vs 10.8±1.5,) and higher 24h BP (130/80 mmHg).

Conclusions: In patients with AMI, prediction of long-term ME (cardiac death and non-fatal infarction) is unknown. We aimed to assess whether cardiovascular magnetic resonance imaging can predict functional recovery after acute myocardial infarction (STEAMI).

3252 | BEDSIDE
Utility of cardiac MRI in detecting myocardial involvement and predicting adverse events in sarcoidosis: A study in 330 patients
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Background: Advances in cardiac imaging in patients with sarcoidosis have shown a wide range of cardiac abnormalities even in patients without cardiac symptoms.

Purpose: Our aim was to assess the utility of cardiac MRI in diagnosing cardiac sarcoidosis and predicting major adverse events in patients with sarcoidosis.

Methods: Consecutive biopsy-proven extra-cardiac sarcoidosis patients without known cardiac disease underwent a complete cardiopulmonary workup that included chest imaging studies, pulmonary function testing, electrocardiogram/24-hour ambulatory Holter monitoring, echocardiogram and cardiac MRI with LGE irrespective of symptoms.

Results: A total of 330 consecutive patients were enrolled. Of these, 109 patients (33%) were diagnosed with cardiac sarcoidosis based on presence of LGE (>10.3%) and IS (10.3%) on CMR. 84 (25.5%) patients fulfilled the JHCM criteria and the Mehta et al criteria respectively. During median follow-up of 58.2 months, 33 (10.3%) patients developed major adverse events. On multivariate Cox regression analysis, LGE (HR 4.84, 95% CI 1.84 to 12.73, p=0.001) along with venous re-infarctions (4%, 8%, 16%, p<0.001).

Conclusions: CMR predicts long-term ME soon after STEMI. A combined analysis of CMR-derived LVEF and IS permits a robust stratification of patients’ outcome.

Summary of Table

<table>
<thead>
<tr>
<th>Events in follow up</th>
<th>LGE-MRI (n=109)</th>
<th>JHCM criteria (n=84)</th>
<th>Mehta criteria (n=84)</th>
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<tr>
<td>Negative (n=84)</td>
<td>20</td>
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</table>

Sensitivity, specificity and predictive values of criteria for diagnosis of cardiac sarcoidosis when used to detect major adverse events:

- Sensitivity: LGE-MRI 97.2%, JHCM criteria 94.1%, Mehta criteria 97.2%
- Specificity: LGE-MRI 92.1%, JHCM criteria 92.1%, Mehta criteria 92.1%
- Positive Predictive Values: LGE-MRI 64%, JHCM criteria 57%, Mehta criteria 64%
and negative for cardiac sarcoidosis based on the JMH criteria, LGE was similarly independent predictor of adverse events (HR=10.3, 95% CI 1.51 to 70.11, p<0.017).

**Conclusion:** Presence of LGE on cardiac MRI can detect cardiac involvement in a greater percentage of sarcoidosis patients and is a better predictor of major adverse events than existing consensus criteria.

**3254 | BEDSIDE**

**Prognostic impact of unrecognized myocardial scar in the myocardium perfused by non-culprit artery detected by late gadolinium enhancement CMR in patients with acute myocardial infarction**

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**Background:** Previous report demonstrated unrecognized myocardial scar detected by LGE MRI is strongly associated with event free survival in patients with stable coronary artery disease. However, the prognostic value of CMR detection of myocardial scar in non-infarct related coronary territories in acute myocardial infarction (AMI) patients is unknown.

**Purpose:** To evaluate the prognostic impact of unrecognized non-infarct related late gadolinium enhancement (Non IR-LGE) in patients with first clinical episode of AMI.

**Methods:** We studied 248 patients with first episode of AMI who underwent cardiac MRI within two months after onset (190 men, age 66±12 y.o.). LGE and cine MR images were obtained to evaluate the presence and extent of LGE as well as global and regional LV function. MACE was defined as cardiovascular death, non-fatal AMI, unstable angina, heart failure and fatal arrhythmia. The Cox proportional hazards model was used to investigate the relationship between clinical and MR imaging variables and MACEs.

**Result:** Unrecognized Non-IR-LGE was observed in 13.7% patients with first clinical episode of AMI. During average follow-up of 27 months ranging from 3 to 95 months, 23 of the 248 patients (9.3%) reached MACE. Presence of unrecognized Non IR-LGE predicted the outcomes with hazard ratio of 4.5 (95% CI 1.4 to 14.3, P<0.001). Figure) By multivariable analyses, Non IR-LGE and BNP were significant independent predictors for MACE (p<0.01). In contrast, angiographic finding of multi-vessel disease and transmural extent of Non IR-LGE did not exhibit independent association with MACE.

**Conclusions:** Among patients with first clinical episode of AMI, unrecognized Non-IR LGE provides incremental prognostic value to MACE beyond common clinical, angiographic and functional predictors.

**ORAL ANTICOAGULANTS STILL IN THE FOCUS**

**3277 | BEDSIDE**

**Lower risk of myocardial infarction in atrial fibrillation patients treated with vitamin K antagonist than in combination with acetylsalicylic acid (ASA) or ASA alone**

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**Background:** Reducing thromboembolic risk is the main focus in atrial fibrillation (AF) patients. AF patients also have an increased risk of developing myocardial infarction (MI) and the optimal antithrombotic treatment remains uncertain.

**Purpose:** To investigate the risk of MI in AF patients treated with either acetylsalicylic acid, vitamin K antagonist or combination thereof.

**Methods:** Through the Danish nationwide registries all patients with first time non-valvular AF from 1997 to 2012 were included. Patients were divided into time varying exposure groups according to antithrombotic treatment regime. Risk of MI during the 15 years follow up period was estimated by cumulative incidence and incidence rate ratios, adjusted for sex, age, chronic heart failure, stroke, diabetes, hypertension and vascular disease.

**Results:** The study cohort included 76,133 AF patients, where 36,643 (48%) received VKA, 27,195 (16%) ASA, and 12,295 (16%) combination treatments. The median age was 71.0, 79.8, and 74.0 years in the three groups. Cumulative incidences of MI at 15 years were 7.12%, 6.13% and 7.44% in the ASA, VKA and the combination group, respectively (Fig.). The adjusted incidence rate ratios (95% confidence intervals) were 1.7 (1.6–1.8) for ASA and 1.3 (1.2–1.5) for combination treatment when compared to VKA.

**Conclusion:** Acetylsalicylic acid based antithrombotic therapy in patients with AF is associated with an increased risk of MI compared to mono vitamin K antagonist treatment.

**3278 | BEDSIDE**

**Vitamin K antagonist control in Eastern and Southeastern Asia**

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**Purpose:** To compare distribution of International normalized ratio (INR) values in patients receiving a vitamin K antagonist (VKA) for newly diagnosed atrial fibrillation (AF) in Eastern (E) and Southeastern (SE) Asia and in other countries represented in the GARFIELD-AF global registry (OGC).

**Methods:** 8445 prospective patients on VKA were enrolled in GARFIELD-AF in 2010–13. INR readings for patients on VKA at enrolment were analysed. Time in therapeutic range (TTR) of INR was estimated using Rosendaal’s method and the target INR range of 2.0–3.0.

**Results:** The UN definition of E and SE Asia includes China, Korea, Japan, Thailand and Singapore. Patients in these regions were slightly younger than patients in OGC but had similar mean CHA2DS2-VASc (3.0 vs 3.5) and HAS-BLED scores (1.3 vs 1.4). Among patients on VKA, 5066 had INR readings (845 in E and SE Asia, 4221 in OGC), amounting to 6452 readings in E and SE Asia and 62,759 in OGC. The number of INR readings per patient was 7 (interquartile range [IQR] 5–10) in E and SE Asia and 14 (IQR 8–20) in OGC. The median number of days between two consecutive readings was 28 in Asia and 14 in OGC. Compared with OGC, the distribution of INR readings in E and SE Asia was clearly shifted towards lower values. The median INR values were 1.8 (IQR 1.4–2.3) in E and SE Asia and 2.3 (IQR 1.9–2.8) in OGC. 59.3% and 28.2% of INR readings were -2 in Asia and OGC, respectively, and 9.5% and 17.7% of INR readings were -3. The median proportion of time spent in TTR in E and SE Asia was half that in OGC (30.1% vs 63.6%).

**Conclusion:** These data show a very clear difference in the distribution of INR readings between E and SE Asia and other GARFIELD-AF countries.

**Acknowledgement/Funding:** The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer Pharma AG

**3279 | BEDSIDE**

**Adherence to anticoagulant treatment with apixaban and rivaroxaban in a real-world setting**

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**Background:** The non-vitamin K antagonist oral anticoagulants (NOACs) are effective in stroke prevention in non-valvular atrial fibrillation. Although adherence
was excellent in the clinical trials with NOACs, there is scarce data on this in clinical practice.

Objectives: To compare adherence levels between the one-dose regimen of ri-
varoxaban and the two-dose regimen of apixaban among patients treated in a
well-structured atrial fibrillation clinic.

Methods: In a prospective cohort study data was collected on patients treated
with apixaban and rivaroxaban for at least three months in a well-structured nurse-
based atrial fibrillation clinic in Sweden. Information on apixaban and rivaroxaban
prescriptions and refills was obtained from pharmacies, from the time point of
the first prescription by any physician. We calculated the adherence from pharmacy
refills.

Results: Data on 593 consecutive patients (245 on apixaban, 248 on rivaroxa-
ban) were obtained during patient visits telephone calls and from the local patient
database. (50% male, median age 73 years, range: 36 - 99). There were no signifi-
cant differences between the two treatment groups in age or sex. Pat-
ients on apixaban and rivaroxaban were followed for a median (min-max) of 313
(94 - 820) and 449 (95-908) days, respectively (p-value p=0.16). The median
(interquartile range) estimated adherence was 100% (97-100) on apixaban and
100% (100-100) on rivaroxaban with 97% and 96% of patients, achieving ad-
herence levels higher than 80%. None of the latter differences was statistically
significant.

Conclusion: Our study shows high estimated adherence levels to apixaban and
rivaroxaban in clinical practice. There was no significant difference in the adher-
ence level between the two-dose regimen of apixaban and the one-dose regimen of
rivaroxaban.

ADVANCES IN HEART FAILURE THERAPY

3301 | BEDSIDE

Angiotensin receptor nephrilysin inhibition and renal function and in heart failure:
results from PARADIGM-HF

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S.D. Solomon6, K. Swedberg7, M. Zile7, M. Packer7, J.J.V. McMurray1 on behalf
of PARADIGM-HF Committee and Investigators. 1University of Glasgow,
Glasgow, United Kingdom; 2University of Iceland, Reykjavik, Iceland; 3General
University Hospital, Prague, Czech Republic; 4Novartis Pharmaceuticals
Corporation, Hanover, United States of America; 5University of Montreal,
Montreal, Canada; 6Brigham and Women’s Hospital, Boston, United States of
America; 7University of Gothenburg, Gothenburg, Sweden; 8Medical University
of South Carolina, Charleston, United States of America; 95 University of Texas
Southwestern Medical School, Dallas, United States of America

Background: ACE inhibitors often reduce glomerular filtration rate (GFR) in pa-
tients with heart failure (HF). We compared the effect of the Angiotensin Receptor
Neprilysin Inhibitor (ARNI) LCZ696 to enalapril on renal function and clinical out-
comes in the Prospective Comparison of ARNI with ACEI to Determine Impact on
Global Mortality and Morbidity in Heart Failure Trial (PARADIGM-HF).

Methods: 8399 patients with HF and reduced ejection fraction were included in
PARADIGM-HF. The primary endpoint was the composite of cardiovascular death
or HF hospitalization (CVD/HFH) in both treatment. The treatment effect of LCZ on
CVD/HFH was not modified by baseline albuminuria status (p-interaction = 0.63), as was also the
case for CVD death and all-cause death. Despite a median increase in UACR of
0.30 (95% CI: 0.10–0.50) mg/mmol in the LCZ group compared with enalapril
at 30 days after randomization, LCZ696 reduced the subsequent occurrence of the
primary outcome by 21% (95% CI: 4%-35%) in this cohort, consistent with the benefit in PARADIGM-HF overall.

Conclusion: Compared with enalapril, LCZ696 reduced clinical outcomes sub-
stantially in patients with HF-REF, despite modestly increasing urinary albumin
excretion.

Acknowledgement/Funding: PARADIGM-HF trial was funded by Novartis.

3302 | BEDSIDE

Effect of LCZ696 on urinary albumin excretion and relation to outcomes in patients
with heart failure

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PARADIGM-HF investigators. 1Popele Papa Giovanni XXIII, Bergamo,
2Brigham and Women’s Hospital, Boston, United States of America; 3Montreal Heart Institute, Montreal, Canada; 4Sahlgrenska Academy - University
of Gothenburg, Goteborg, Sweden; 5Medical University of South Carolina, Charleston, United States of America; 6Novartis Pharmaceuticals, East Hanover,
United States of America; 7University of Texas Southwestern Medical School,
Dallas, United States of America; 8University of Glasgow, Glasgow, United
Kingdom

Background: The angiotensin receptor neprilysin inhibitor LCZ696 has been
shown to reduce morbidity and mortality in patients with heart failure. LCZ696
has also been shown to increase urinary albumin excretion in patients with HF-
PEF. The prognostic importance of albumin excretion in the setting of LCZ696
therapy is unclear.

Methods: The PARADIGM trial randomized 8399 patients with heart failure and
reduced ejection fraction to LCZ696 200 bid or enalapril 10 bid in the PARADIGM
trial. Urinary albumin/creatinine ratio (UACR) was available at screening, follow-
ning LCZ696 run-in and one month following randomization in 1465 patients. We
assessed the effect of LCZ696 on UACR and the prognostic relationship between
change in UACR and outcomes.

Results: Median UACR was 1.0 (IQR 0.4, 3.2) mg/mmol at screening and 1.2
(IQR 0.5, 4.0) mg/mmol after LCZ696 run-in before randomization. Higher UACR
values at baseline and at 30 days after randomization (figure) were associ-
ated with higher risk of the primary outcome of CV death or HF hospitalization
(CVD/HFH) in both treatment. The treatment effect of LCZ on CVD/HFH was not
modified by baseline albuminuria status (p-interaction = 0.63), as was also the
case for CV death and all-cause death. Despite a median increase in UACR of
0.30 (95% CI: 0.10–0.50) mg/mmol in the LCZ group compared with enalapril
at 30 days after randomization, LCZ696 reduced the subsequent occurrence of the
primary outcome by 21% (95% CI: 4%-35%) in this cohort, consistent with the benefit in PARADIGM-HF overall.

Conclusion: Compared with enalapril, LCZ696 reduced clinical outcomes sub-
stantially in patients with HF-REF, despite modestly increasing urinary albumin
excretion.

Acknowledgement/Funding: PARADIGM-HF trial was funded by Novartis.

3303 | BEDSIDE

Beta-blocker therapy and in-hospital outcome in acute heart failure: a propens-
sity-score matching secondary analysis of the ALARM-HF registry

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G. Filippatos, A. Mebazaa, J. Lekakis, F. Follath. Attikon Hospital, 2nd University
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Background: Beta blockers (BB) constitute a life-saving therapy in heart failure,
but their use in acute heart failure (AHF) setting remains controversial. We as-
sessed short-term outcome in AHF patients receiving or not BB in a large AHF
cohort.

Methods: The Acute Heart Failure Global Registry of Standard Treatment
(ALARM-HF) was conducted during 2006–2007 and included a total of 4953
patients hospitalized for AHF in 9 countries in Europe, Latin America and Aus-
tralia. We compared in-hospital mortality between patients receiving or not BB.
Nearest-neighbour matching by propensity score was applied to produce a bal-
anced sub-sample consisting of pairs of treated and not treated patients. Mortality
was assessed by Cox regression with adjustment for age, gender, systolic blood
pressure (SBP), heart rate (HR), atrial fibrillation (AF), NYHA class, renal function
and acute coronary syndrome (ACS) at presentation.

Results: In the original sample, 2330 patients (47%) were receiving BB.
Propensity-score matching derived a sample of 2372 patients (1186 in each treat-
ment group). BB therapy was followed by reduce in-hospital mortality both in the
original [HR: 0.47, 95% CI: (0.39, 0.57)] and in the matched sample [HR: 0.51,
95% CI: (0.39, 0.67)]. The beneficial effect on mortality persisted after adjustment

Acknowledgement/Funding: Novartis Pharmaceuticals
for potential confounders before and after propensity-score matching (HR: 0.58, 95% CI: 0.47, 0.73) and HR: 0.58, 95% CI: 0.44, 0.76, respectively). Among those treated, age > 80 years, SBP>100mmHg, oliguria and ACS were associated with significantly higher risk of mortality after matching.

Conclusions: In AHF, BB therapy is associated with a significantly lower short-term mortality.

3304 | BEDSIDE
Hydrophilic versus lipophilic statin therapy on outcomes in patients with heart failure: a systematic review and an adjusted indirect comparison meta-analysis of randomised trials
K. Osei Bonsu, D.D. Reidpath, A. Kadireolu. Monash University Sunway Campus, Global Public Health, School of Medicine and Health sciences, Bandar Sunway, Malaysia

Background: Statins are known to reduce cardiovascular morbidity and mortality in prevention studies. It is unclear whether statins as a class or statin subtype (lipophilic or hydrophilic) improve outcomes in heart failure (HF). Sufficiently powered comparative trials between statin subtypes in HF are unavailable.

Purpose: To conduct an adjusted indirect comparison meta-analysis between the two statin subtypes on clinical and surrogate outcomes in HF.

Methods: We conducted a search of PubMed, MEDLINE, EMBASE and Cochrane databases until 31st October 2014 for randomized control trials (RCTs) in patients with HF evaluating statins versus placebo/standard treatment. The primary outcomes comprise all-cause mortality, cardiovascular mortality, sudden death, non-fatal myocardial infarction, cardiovascular hospitalization and hospitalization for worsening HF. We independently used a standardized abstraction tool to extract all data. RCTs with their abstracted information were grouped according to statin subtype evaluated. The abstracted data from eligible RCTs were then separately analyzed according to statin subtype. Clinical outcomes were initially pooled with the Peeto’s one-step method, producing odd ratios and 95% confidence intervals for each statin subtype. Using these pooled estimates, we performed adjusted indirect comparisons of the statin subtypes for each outcome. Data from 11, 450 patients from 23 trials were analyzed.

Results: Lipophilic statins were superior to hydrophilic statins regarding all-cause mortality (Risk Ratio [RR] 0.48; 95% CI, 0.33–0.71), cardiovascular mortality (RR 0.42; 95% CI, 0.24–0.69), sudden death (RR 0.24; 0.09–0.66), and hospitalization for worsening HF (RR 0.52; 0.37–0.72). Compared with hydrophilic statins, lipophilic statins resulted in 141 fewer all-cause mortality, 125 fewer cardiovascular deaths, 84 fewer sudden deaths, and 143 fewer hospitalization for worsening HF per 1000 patients treated. Lipophilic statins resulted in 143 fewer incidence of cardiovascular hospitalization and 38 fewer incidence of non-fatal MI compared with hydrophilic statins per 1000 patients treated but were not statistically significant.

Conclusion: Lipophilic statins lower incidence of all-cause mortality, cardiovascular mortality, sudden death and hospitalization for worsening HF compared with hydrophilic statins. This meta-analysis provides preliminary evidence that lipophilic statins offer better clinical outcomes in HF till data from head to head comparisons are made available.

3305 | BEDSIDE
Carperitide versus nitroglycerin as a first-line therapy in patients with acute heart failure: a propensity-matched comparison
N. Iwakami, T. Nagai, Y. Hirota. Ono Pharmaceutical Co., Ltd., Osaka, Japan

Background and introduction: ONO-4232, a selective agonist for EP4 subtype of prostaglandin E2 receptor, is in clinical development for the treatment of acutely decompensated heart failure (HF). At AHA 2012, we reported that ONO-4232 shows a unique left ventricular (LV) isotropic action in addition to its venous vasodilatation effect in a dog model of acute (de novo) HF. However, it was still unknown whether ONO-4232 can also improve hemodynamics (HD) in a chronic HF model, where cardiac structural remodeling and associated systolic and diastolic LV dysfunctions are evident.

Purpose: To investigate cardiac and HD effects of ONO-4232 in a dog model of chronic HF induced by chronic ventricular tachycardia pacing (CVP).

Methods: Chronic HF was induced by right ventricular CVP for 4 weeks at 250 beats/min in pacemaker-implanted dogs. Echocardiography was performed after stopping the pacing, then HD parameters were measured during intravenous infusion of saline (vehicle, 60 min), ONO-4232 (1, 3, and 10 ng/kg/min, dose escalation, 20 min each) or milrinone (0.3, 1 and 3 µg/kg/min, dose escalation, 20 min each) under pentobarbital anesthesia.

Results: ONO-4232 resulted in a significant increase in LV internal dimensions and decrease in ejection fraction, as confirmed by echocardiography. Also, in the 12 dogs that underwent HD assessment, LV end-diastolic pressure (LVEDP; 44.0±1.5 mmHg) and pulmonary capillary wedge pressure (PCWP; 35.0±1.6 mmHg) were markedly elevated, and cardiac output (CO; 1.40±0.07 L/min) was decreased prior to the drug administration. ONO-4232 dose-dependently reduced LVEDP and PCWP while increasing CO by ~23%, ~29%, and ~56% (high dose, n=4), respectively. The magnitude of ONO-4232-induced HD changes were similar to that of milrinone. Furthermore, ONO-4232 significantly shortened tau, a time constant of LV relaxation, starting from the low dose and also tended to increase LV dp/dt max at the high dose (high dose: tau; ~22%, LV dp/dt max; +20%). Of note, although milrinone shortened tau, yet significantly increased LV dp/dt max (high dose: tau; ~23%, LV dp/dt max; +40%). In ONO-4232 group, systolic blood pressure was decreased by 4 mmHg (high dose), which is considered of minimal biological relevance.

Conclusion: ONO-4232 significantly reduced both preload and afterload to a similar extent to that seen for milrinone. However, the mode of cardiac action was clearly different from the inotrope milrinone. ONO-4232 selectively improved LV relaxation. Therefore, ONO-4232 may become a new class of drug for the treatment of HF.

3307 | BENCH
Bendavia, a novel mitochondria-targeting peptide, improves contraction and relaxation of failing cardiomyocytes isolated from dogs with chronic heart failure
H.N. Sabbah, R.C. Gupta, P. Mohiy. Henry Ford Hospital, Detroit, United States

Background: Mitochondria of failed human hearts and hearts of dogs with experimental heart failure (HF) manifest structural and functional abnormalities characterized by hyperplasia, reduced organellar size and reduced respiration. These abnormalities lead to reduced rate of ATP synthesis and increased production of
reactive oxygen species (ROS) that adversely impact left ventricular (LV) systolic and diastolic function. We previously showed that chronic therapy with Bendavia (MTP-131), a novel mitochondria-targeting peptide, improves global LV function in dogs with HF without affecting heart rate or blood pressure. This improvement was associated with a reversal of mitochondrial abnormalities and normalization of mitochondrial rate of ATP synthesis. In the present study, we tested the hypothesis that the improvement in global LV function seen in dogs with HF during treatment with Bendavia results primarily from enhanced contraction and relaxation of constituent LV cardiomyocytes.

Methods: Cardiomyocytes were isolated from the LV free wall of 8 untreated dogs with chronic HF produced by intracoronary microembolizations (LV ejection fraction <30%). A standard collagenase-based enzymatic process was used for the isolation that yielded ~70% viable rod-shaped cardiomyocytes that excluded trypan blue. Extent of cardiomyocytes shortening, shortening velocity and lengthening velocity were assessed during 1.0 Hz electrical field stimulation delivered via a MyoPacer (ION Optix). Measurements were made at baseline and were repeated after one hour of gradual exposure of the same cardiomyocytes to Bendavia at a concentration of 0.1 μM.

Results: At baseline, the extent of cardiomyocyte shortening was 3.7±0.8 μm, shortening velocity was 62.8±16.9 μm/sec and lengthening velocity was −53.8±16.5 μm/sec. Exposure of cardiomyocyte to Bendavia significantly increased the extent of cardiomyocyte shortening to 5.4±1.1 μm (p <0.012), significantly increased lengthening velocity to −96.8±21.1 μm/sec (p <0.016) compared to baseline.

Conclusions: Results of this study indicate that exposure of failing isolated cardiomyocytes to Bendavia elicits significant improvements in the rate of cardiomyocyte shortening and re-lengthening indicative of improved cell contractility and relaxation. The likely mediator of the observed improvement in cardiomyocyte function is the increased availability of ATP along with reduced ROS production both secondary to improved mitochondrial function elicited by treatment with Bendavia.

3309 | BEDSIDE
Hepato-renal dysfunction on admission predicts the outcome in acute heart failure
J. Biegus, R. Zymlinski, P. Siwoloski, M. Sokolski, E.A. Jarkowska, W. Banasiak, P. Ponikowski. Centre for Heart Disease - Clinical Military Hospital - Department of Cardiology, Wroclaw, Poland

Introduction: In acute heart failure (AHF), multi-organ dysfunction is a relevant complication, which may unfavorably affect the outcomes. Surprisingly, this phenomenon has never been systematically evaluated. The MELD (Model for End-Stage Liver Disease), combines data reflecting liver and kidney function, being widely applied for prognostic evaluation in patients with liver dysfunction.

Aim: The aim of the study was to find clinical, laboratory and hemodynamic associates of the MELD and to assess its utility as prognosticator in AHF patients.

Methods: The study population consisted of 3314 AHF patients divided into derivation cohort (213 patients; mean age: 67 years, men: 70%, de novo AHF 21%) and validation cohort (136 patients; mean age: 65 years, men: 77%, de novo AHF 22%). MELD was calculated on admission using modified formula, which does not take into account the INR.

Results: In the derivation cohort the mean MELD on admission was 14.5±4 points. Patients were divided into tertiles of the MELD and those in the 3rd tertile (with the highest values) had lower blood pressure on admission (118 vs 133mmHg), lower ejection fraction (28 vs 37%), serum Na+ (137 vs 140mmol/L) and higher: AST (28 vs 23IU/L), GGTP (111 vs 54IU/L), and NTproBNP (11042 vs 4176pg/mL), all p <0.05. We did not find differences in age, hemoglobin, albumin and troponin between tertiles.

Multivariable analysis revealed independent associates of MELD: RVEDD and NTproBNP both p<0.005. Analysis of 35 patients who had invasive hemodynamic monitoring showed that MELD was correlated to cardiac index (r=−0.5), right atrial pressure (r=0.5) and PCWP (r=0.34), all p<0.05. We did not take into account the INR.

Conclusions: Results of this study indicate that exposure of failing isolated cardiomyocytes to Bendavia elicits significant improvements in the rate of cardiomyocyte shortening and re-lengthening indicative of improved cell contractility and relaxation. The likely mediator of the observed improvement in cardiomyocyte function is the increased availability of ATP along with reduced ROS production both secondary to improved mitochondrial function elicited by treatment with Bendavia.

3310 | BENCH
Hepato-renal dysfunction on admission predicts the outcome in acute heart failure
J. Biegus, R. Zymlinski, P. Siwoloski, M. Sokolski, E.A. Jarkowska, W. Banasiak, P. Ponikowski. Centre for Heart Disease - Clinical Military Hospital - Department of Cardiology, Wroclaw, Poland

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3310 | BENCH
RA123456, a novel potent and selective CaMKII inhibitor reduces diastolic Ca2+ leak and enhances SR Ca2+ content in human cardiomyocytes
M. Dryzmalski1, B. Floechinger2, L. Rupprecht2, L. Zausig3, M. Pauschinger4, J. Senges2, R. Hambrecht1 on behalf of RAID-HF study group.

Rationale: RA123456, a novel potent and selective CaMKII inhibitor reduces diastolic Ca2+ leak and enhances SR Ca2+ content in human cardiomyocytes

Introduction: RA123456 is a novel highly selective CaMKII inhibitor (CaSip). RA123456 was observed with CaMKII inhibitor AIP (1 μM, 1.4±0.14, N=25). Consistent with reduced SR Ca leak (fF/g), RA123456 reduced RyR2 phosphorylation and enhanced SR Ca content (caffeine application). Caffeine-induced dF/dF was
The Reveal LINQ is a miniaturized insertable cardiac monitor (ICM).

**Purpose:**
Hospital, Linz, Austria

The Reveal LINQ Usability study is a prospective, multicenter clinical study assessing the performance of the new Reveal LINQ ICM. We report on sensing performance over the range of body mass index (BMI) values for all study implants (N=151). Data collected at the baseline and one month follow-up visits is included.

**Conclusion:**
RA123456 reduces SR Ca-leak and enhances SR Ca content without impairing repolarization in human cardiomyocytes. Thus, CαMKII inhibitors may be useful for the treatment of HF and AF.

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

## BEST POSTERS SESSION 4

### BEST POSTERS IN SYNCOPE MANAGEMENT

#### P3312 | BEDSIDE

**Family history of syncope is associated with increased risk of adverse cardiovascular events and mortality - A Danish nationwide study**


**Background:** Previous studies suggest a familial co-occurrence of cardiovascular diseases and syncope indicating an inherited cardiac vulnerability, but it is unclear whether hospitalization of a family member with syncope is an independent risk marker for adverse cardiovascular events among first-degree relatives.

**Purpose:** To investigate the risk of major adverse cardiovascular events (MACE), all-cause mortality and early-onset cardiovascular disease in first-degree relatives of individuals admitted to hospital with syncope.

**Methods:** Using nationwide registries, we identified individuals below 60 years discharged with syncope between 1978 and 2011 and their first-degree relatives. Risk of MACE, all-cause mortality and early-onset cardiovascular disease among the cohort of relatives was estimated using Poisson regression models with the Danish background population as reference adjusting for sex, age, calendar year and comorbidities.

**Results:** In a total population of 7,318,639 consecutively included Danish residents, we identified 198,258 first-degree relatives of 102,230 syncope patients. Crude incidence rates of all-cause mortality were 1.71, 0.99 and 0.93 per 1000 person-years for siblings, maternal offspring and paternal offspring, respectively. Adjusted rate ratios for MACE were 1.45 (95% confidence interval 1.34–1.56) for siblings, 1.47 (1.31–1.65) for maternal offspring and 1.31 (1.16–1.47) for paternal offspring. Similar results were found for all-cause mortality and early-onset cardiovascular disease.

**Conclusions:** Family history of syncope was associated with an increased all-cause mortality, MACE and early-onset cardiovascular disease. These results should be taken into account in cardiovascular risk stratification of persons with a family history of syncope.

#### P3313 | BEDSIDE

**Miniaturized reveal LINQ insertable cardiac monitoring performance in different body types**

L.R.G. Dekker1, P.H. Sanders2, M. Di Bacco3, T.A. Bergemann3, J.C. Guzman1, C.A. Morillo1.

**Purpose:** The Reveal LINQ is a miniaturized insertable cardiac monitor (ICM) indicated for patients with suspected arrhythmias. This study assessed the safety and sensing capabilities of the new ICM over a wide range of body habitus.

**Methods:** The Reveal LINQ Usability study is a prospective, multicenter clinical study assessing the performance of the new Reveal LINQ ICM. We report on sensing performance over the range of body mass index (BMI) values for all study implants (N=151). Data collected at the baseline and one month follow-up visits is included.

**Results:** The mean age was 57±12 years; 33% were female. BMI was 28.1±4.4 (range 18.2–42.1). R-wave amplitudes were 0.543±0.295 mV at implant and 0.590±0.314 mV at one month Elevated BMI was associated with decreased R-wave sensing amplitude at implant (correlation = −0.30, slope = −0.029, p-value = 0.0002) and 1 month follow-up (correlation = −0.27, slope = −0.019, p-value = 0.001; figure 1). The association remained between BMI and R-wave amplitude when accounting for gender. While R-wave values decreased with increasing BMI, sensing was over the recommended amplitude of 0.2mV at implant (97.3%) and follow-up (96.6%). The ICM was inserted 8.0±4.2mm deep in the subcutaneous tissue; no major migration of the ICM was detected at 1 month follow-up (1.2±3.2mm). There was one serious procedure and device-related adverse event within one month of follow-up involving a skin perforation that resulted in device explant.

**Conclusion:** The Reveal LINQ ICM meets good performance standards, including sensing, migration and safety in patients with a wide range of body habitus.

#### P3314 | BEDSIDE

**Application of syncope guidelines in the emergency department do not reduce admission rates: a retrospective cohort study**


**Background:** Syncope comprises 1.5% of all emergency department (ED) visits and approximately 2-billion dollars (USD) in related hospitalizations. Syncope guidelines are intended to identify high-risk patients and streamline admissions and investigations.

**Purpose:** To determine if the application of syncope guidelines in the ED results in a reduction of unnecessary admissions to hospital.

**Methods:** A retrospective chart review was conducted in all syncope presentations to the ED, spanning 1 year at two major tertiary care institutions. Three different guidelines, Canadian Cardiovascular Society (CCS), American College of Emergency Physicians (ACEP) and European Society of Cardiology (ESC), were applied to determine the effect on admission rates.

**Results:** Overall a total of 1228 syncope presentations to the ED were identified (January 1, 2013 to January 1, 2014). 505 patients (41%) were admitted and 723 (59%) were discharged. Five hundred charts were randomly reviewed; of those 48 were not true syncope, 15 were not assessed by a physician and 2 charts were incomplete. Of the remaining 435 true syncope presentations, 174 (40%) were admitted as per the deciding physician and 261 (60%) were discharged from the ED. The mean age of those admitted from the ED and those discharged was 72±14 vs 55±22 (p<0.01), respectively. Medical records were reviewed 1 year following syncope presentations in both admitted and non-admitted groups and adverse cardiovascular events were 9% vs 3% (p<0.01), respectively. When compared to 174 (40%) deemed necessary admissions by the deciding physician, CCS guidelines warranted for 263 (60%, p<0.01) admissions, ACEP 189 (43%, p<0.028) admissions, and ESC 220 (50%, p<0.004) admissions.

**Conclusion:** Our study suggest that the current admitted syncope population is older and has a higher comorbidity burden, possibly explaining why adverse cardiovascular events are higher in this group. Finally, the data suggests that the application of syncope guidelines are unlikely to reduce admission rates, and that a lack of agreement exists among the different guidelines resulting in significant variation between warranted admissions.
3 years experience of diagnosing and managing postural tachycardia (PoTS) from a UK regional syncope service

Y. Zheng, C. Moyles, Y. Blackburn, E. Joy, K. Mohee, C. Morley, Bradford Teaching Hospitals NHS Trust, Cardiology, Bradford, United Kingdom

Introduction: PoTS and Orthostatic intolerance (OI) are increasingly recognised and may be very disabling, especially in patients with Joint Hypermobility Syndrome - Ehlers Danlos type III (JHS). These symptoms reflect volume (salt) depletion, hypertension, intolerance on standing or increased venous elasticity (JHS), deconditioning and possibly dysautonomia. We present a 3-phase treatment strategy for these unfortunate patients.

Definition: PoTS >30bp symptomatic HR increase or >120bp within 10 min stand.

Methods: All patients diagnosed with PoTS attending our syncope service from 2012, were included and categorised as non-JHS and JHS associated (confirmed by Rheumatology and Brighten Criteria). Drug induced, illness, endocrine and hyperadrenergic causes were excluded. Active stand and/or passive 10 min using beat-to-beat BP monitoring (Finapres) and 24 hour urine and sodium excretion were assessed.

Results: 29 Patients were included. 28 female, mean age 28 range (17–44). 18 patients were diagnosed with PoTS and JHS.

Mean 24 hour urine was 2.0L (range 0.7L–4.8L) and mean 24 hour urine sodium was 101.91 mmol/l (range 54 – 181). Mean postural increase in HR, 40 BPM (SD 11.0) and mean systolic drop was 40mmHg (SD 17.9).

Treatment (see table 1): 27 were fluid/salt repleted. 2 patients are awaiting treatment. 17 non-responders (non-JHS) were treated with Ivabradine, 2 non-tolerant and 3 with persistent/worsening OI proceeded to Midodrine, with 2 being intolerant and 3 responding. All medication tolerant patients improved with several returning to work and social activities.

Table 1. 3 Phase treatment strategy

<table>
<thead>
<tr>
<th>Phase</th>
<th>Treatment</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 1</td>
<td>Fluid and salt repletion (30–90 mmol Na daily)</td>
<td>Possible JHS or OI</td>
</tr>
<tr>
<td>Phase 2</td>
<td>Trial of Ivabradine 2.5mg bid uptitrating to 5mg bid*</td>
<td>Possible JHS or OI</td>
</tr>
<tr>
<td>Phase 3</td>
<td>Midodrine 2.5 mg increasing to 5 mg twice daily</td>
<td>All women were counselling regarding risks of pregnancy during treatment.</td>
</tr>
</tbody>
</table>

Conclusion: 1. In a regional cardiac service JHS associated PoTS was the most common diagnosis.

2. Salt depletion was universal and more prevalent than fluid depletion.

3. JHS patients may benefit from Ivabradine for PoTS and Midodrine “pill in the pocket” for OI.

4. Further research is required to determine a longer term management strategy.

P3319 | BEDSIDE

The efficacy and safety of ticagrelor in women versus men with a prior myocardial infarction: insights from the PEGASUS-TIMI 54 trial


1Biagham and Women’s Hospital, Boston, United Kingdom; 2University of Medicine, Harvard Medical School, Boston, United States of America; 3University Paris Diderot, Paris, France; 4Nottingham University Hospitals NHS Trust, Nottingham, United Kingdom

Background: The PEGASUS-TIMI 54 trial studied 2 doses of ticagrelor, the standard 90mg twice daily bid and 60mg bid, for longer term prevention of ischaemic events in patients with prior MI. Both doses reduced the rate of ischaemic events vs placebo. The pharmacokinetics (PK) and pharmacodynamics of the 60 mg bid treatment were not previously studied.

Purpose: To characterize PK and platelet inhibition with ticagrelor 60mg bid vs 90mg bid.

Methods: 180 patients who had received >4 weeks of study medication had blood sampling in the morning pre-maintenance dose and again 2h post-dose. All patients were receiving aspirin. Plasma ticagrelor levels were determined. VerifyNow P2Y12 assay and light transmission aggregometry (LTA; ADP 20µM) were performed.

Results: Plasma ticagrelor levels were approximately 1/3 lower with 60mg vs 90mg bid (post dose: 448 vs 717 ng/mL; P<0.001). Both doses achieved high levels of platelet inhibition pre and post dose, with slightly more variability with 60mg (Table). High platelet reactivity assessed by VerifyNow (PRU > 208) was rare with 60 mg pre-dose (3.5%) and absent post dose. Platelet reactivity pre- and post-dose as measured by LTA was numerically but not significantly lower with 90mg than 60mg.

Table 1. PK & platelet inhibition across both doses

<table>
<thead>
<tr>
<th>Dose</th>
<th>Placebo</th>
<th>Ticagrelor 60mg</th>
<th>Ticagrelor 90mg</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre</td>
<td>64 (10)</td>
<td>73 (12)</td>
<td>73 (12)</td>
<td>0.001</td>
</tr>
<tr>
<td>Post</td>
<td>73 (10)</td>
<td>73 (13)</td>
<td>73 (12)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Conclusions: Ticagrelor 60mg bid achieved high levels of peak and trough platelet inhibition in nearly all patients, with similar consistency of effect compared to 90mg bid. These results help explain the efficacy of the lower ticagrelor dose in the PEGASUS-TIMI 54 study.

P3319 | BEDSIDE

Differences in dual antiplatelet treatment for acute coronary syndrome patients undergoing PCI or not: a Danish nationwide population-based cohort study

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1University of Southern Denmark, Odense, Denmark; 2University of Southern Denmark, Odense, Denmark; 3University of Southern Denmark, Odense, Denmark; 4Institute of Applied Economics and Health Research, Copenhagen, Denmark

Introduction: ESC guidelines recommend 12 months’ dual antiplatelet treatment (DAPT) after an acute coronary syndrome (ACS) event, regardless of whether or not patients undergo percutaneous coronary intervention (PCI). However, contemporary nationwide real-life data on DAPT use and treatment length for the ACS population are scarce.

Purpose: To describe patients’ characteristics and type and duration of DAPT for Acute Coronary Syndrome (ACS) patients undergoing PCI or not.

Methods: This observational cohort study linked morbidity, mortality, and medication data from Danish national registries from ACS patients alive after discharge from the hospital in 2012.

Results: In total, 9700 ACS patients [8599 myocardial infarction (MI) and 1101 with unstable angina pectoris (UAP)] at discharge were identified, of whom 4864 (50%) underwent PCI. The PCI-treated patients were younger (median age, 65 years vs. 72 years) and consisted of more men (73% vs. 56%) compared with non-PCI treated patients. Approximately 31% of the ACS patients did not receive DAPT treatment. Median age of non-DAPT patients was 72 years vs. 67 years for DAPT patients. Non-DAPT patients had a higher cardiovascular risk profile (diabetes, heart failure, and atrial fibrillation) compared with the DAPT population. DAPT duration was longer in PCI-treated patients compared to the non-PCI-treated patients (mean 361 vs. 111 days).

Conclusions: Despite guideline recommendations, close to one third of all ACS patients were discharged without DAPT. For ACS patients receiving DAPT, there was a significant difference in treatment length between patients undergoing PCI.
New users of low-dose acetylsalicylic acid and risk of colorectal cancer: results using three different study designs

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Background: Evaluation of drug–outcome associations requires an appropriate and unbiased study design.

Purpose: Using data from The Health Improvement Network UK primary care database, we used three different study designs to assess the risk of colorectal cancer (CRC) among new users of low-dose acetylsalicylic acid (ASA).

Methods: The source population for each study was patients aged 40–89 years between 2000–2012 with no record of cancer or use of low-dose ASA before start of follow-up. The first design (single cohort) comprised all patients meeting these eligibility criteria. The second and third designs involved ascertaining a cohort of low-dose ASA initiators (start date was date of first ASA prescription) and either a cohort of non low-dose ASA users or paracetamol initiators, at the start date among the source population. In the second design, each day a person qualified as a new user of low-dose ASA, they were assigned to the low-dose ASA initiator cohort and matched to a person free of low-dose ASA on that day by age, sex and number of general practitioner visits in the previous year. In the third design, new users of low-dose ASA and paracetamol were identified and assigned to the first drug initiator cohort for which they qualified. In each design, patients were followed to identify incident cases of CRC. Controls were sampled among the respective study cohorts and frequency-matched to cases by age, sex and calendar year. An “As-treated” analysis was performed and current use of low-dose ASA was when use extended until index date (CRC date for cases and random date for controls) or ended 1–90 days before index date. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were calculated by multiple logistic regression.

Results: Current use of low-dose ASA (75–300 mg) was associated with a significantly reduced risk of CRC, OR 0.69 (95% CI: 0.64–0.74) in the first study design, OR 0.66 (95% CI: 0.60–0.73) in the second design, and OR 0.71 (95% CI: 0.63–0.80) in the third design. A significant reduced risk of CRC was observed with a daily dose of 75 mg (pts) in each design. When low-dose ASA was used for secondary cardiovascular disease (CVD) prevention, ORs (95% CIs) were 0.61 (0.55–0.68) in the first design, 0.60 (0.53–0.68) in the second design, and 0.62 (0.54–0.72) in the third design. Corresponding estimates for primary CVD prevention were 0.75 (0.68–0.81), 0.71 (0.63–0.79) and 0.78 (0.68–0.89).

Conclusion: A significant reduced risk of CRC among new users of low-dose ASA was shown with all three study designs and so is unlikely to be explained by selection bias.
P3324 | BEDSIDE
Relationship between Serum Electrolytes and Electrocardiographic Intervals

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Background: Hyponatremia, hypocalcemia and hypomagnesemia are assumed to be causative for an acquired long QTc syndrome, but this association is based only on a few small case series.

Purpose: Here, we aimed to evaluate the relationship between serum electrolyte concentration and changes in QTc interval and QRS complex.

Methods: This retrospective cohort study included 8,498 consecutive participants admitted to the coronary care unit at an academic tertiary care medical center from 2004 to 2013 who had at least one serum potassium and magnesium level measurement. The means of serum potassium, ionized calcium and magnesium were then categorized and the reference groups were 4.0-4.5 mEq/L, 4.8-5.0 mEq/dL, and 2.0-2.2 mg/dL, respectively. Multivariate analysis adjusted for age, sex, race, serum electrolyte, antiarrhythmics and drugs known to cause QTc prolongation was used.

Results: Serum potassium (ORs: 1.04, 1.01 and 0.99 for potassium levels of <3.5, 3.5-4.0 and ≥4.5 mEq/L, respectively) and ionized calcium (ORs: 1.02, 1.01 and 0.99 for calcium levels of <4.4, 4.4-4.6, and ≥4.6 mEq/L, respectively) were inversely associated with the QTc prolongation; only hypermagnesemia independently increased the risk of widened QRS complex. A paradoxical association between serum magnesium and QTc prolongation (ORs: 0.98, 0.99 and 1.01 for magnesium levels of <1.8, 1.8-2.0, and >2.4 mg/dL, respectively) was observed. Adjusting for duration of QRS complex, this relationship between hypermagnesemia and QTC prolongation was no longer present. However, hypermagnesemia was independently associated with a widened QRS complex (ORs: 0.95, 0.98, 1.03 and 1.10 for magnesium of <1.8, 1.8-2.0, 2.2-2.4 and >2.4 mg/dL, respectively).

Conclusions: We also observed a level-dependent relationship between hypokalemia and hypocalcemia and an increase in risk of QTC interval prolongation, but neither serum potassium nor calcium was associated with changes in duration of the QRS complex. Contrary to conventional wisdom, hypermagnesemia was associated with a prolonged QTC interval via a mechanism of widened QRS complex.

P3325 | BEDSIDE
Impact of motion correction algorithm on the image quality and diagnostic utility in patients undergoing CT angiography: a randomized controlled trial

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Background: Despite improvements in the technology in coronary CT angiography (CCTA), motion artifacts remain a limitation that cause a decline in diagnostic accuracy in up to 12%.

Aims: To investigate the diagnostic utility of motion correction algorithm SnapShot Freeze (SSF) compared to standard reconstruction algorithm (STD) in unscheduled patients randomized to receive intravenously beta-blockers (BB) or no beta-blockers (non-BB) before CCTA, and to investigate if SSF can compensate for the absence of BB.

Methods: One hundred and forty patients scheduled for CCTA and with heart rate (HR) between 60 and 85 bpm were randomized (73 patients to BB group and 67 patients to non-BB group). All images were reconstructed by SSF and STD algorithm, two blinded experienced readers evaluated the image quality according to Likert score (1:Excellent, 2:Good, 3:Adquate, 4:Non-diagnostic) and noted the presence of artifacts. Twenty five patients were excluded because of tachycardia, bradycardia or reconstruction error.

Results: Images from 64 patients in BB group (mean HR 56±4 bpm) and 51 patients in non-BB group (mean HR 67±7 bpm) were analyzed. SSF increased the number of excellent images in both groups compared to STD algorithm (BB: 59% vs 44%;P=0.002; non-BB: 25% vs. 8%;P=0.004). The number of non-diagnostic images was not significantly reduced (BB: 14% vs. 14%;P=1.000; non-BB: 37% vs. 47%;P=0.125). SSF reduced the motion artifacts (BB: 11% vs. 31%;P=0.0002; non-BB:49% vs. 75%;P=0.001). Despite this reduction, motion artifacts in non-BB were still more frequent compared to the BB group analyzed by STD (49% vs 31%).

Conclusion: The use of SSF significantly improves the image quality and reduce the motion artifacts in CCTA, but does not influence the diagnostic utility.

P3327 | BENCH
P53-induced inflammation exacerbates cardiac dysfunction during pressure overload

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The death rate related to severe heart failure is still unacceptably high. p53 is a key player in the intrinsic cellular responses to DNA damage, and activation of p53 leads to cell-cycle arrest, apoptosis, and senescence. Accumulating evidence has demonstrated the role of sterile inflammatory responses in the progression of cardiac remodeling in heart failure, however the mechanistic link between p53 and the inflammatory process in the failing heart is not known. Here we demonstrate a critical role of p53 signaling in bone marrow cells and endothelial cells in the development of cardiac inflammation in a transverse aortic constriction (TAC) induced murine pressure overload model.

Our results suggest that the activation of sympathetic nervous system-ROS-p53 signaling interacts with endothelial cells and bone-marrow cells significantly exacerbated cardiac dysfunction, inhibited the production of pro-inflammatory cytokines and ameliorated cardiac dysfunction during pressure-overload. Force expression of p53 in bone-marrow cells, worsened cardiac inflammation, and reduced systolic function. Norepinephrine markedly increased reactive oxygen species (ROS) and p53 levels in macrophages and endothelial cells. Reducing adrenergic signaling by the suppression of beta-2 adrenergic receptors in endothelial cells or bone-marrow cells inhibited ROS and p53 levels, ameliorated cardiac inflammation and systolic dysfunction upon pressure-overload.

Our results suggest that the activation of sympathetic nervous system-ROS-p53 signaling promotes the interaction between endothelial cells and bone-marrow-derived inflammatory cells by the up-regulation of ICAM-1 and integrin expression to exacerbate cardiac dysfunction. The inhibition of p53 signaling in these cells would become new therapeutic targets for heart failure.

P3328 | BENCH
Testosterone antagonizes doxorubicin-induced senescence of cardiomyocytes

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Background: Chronic cardiotoxicity of doxorubicin and other anthracyclines is less common in males than in females. Here, we hypothesized that this gender difference might be at least in part secondary to distinct activities of sex hormones on cardiomyocyte senescence, which is thought to be central to the development of long-term anthracycline cardiomyopathy.

Methods and results: Neonatal murine cardiomyocytes and H9c2 cardiomyoblasts were treated with doxorubicin alone or in combination with testosterone or 17β-estradiol, the main androgen and estrogen, respectively. As already reported, a single 3-h pulsed exposure to 0.1 μM doxorubicin resulted in extensive senescence of cardiomyocytes. This was associated with accumulation of p53 and down-regulation of telomere binding factor 2 (TRF2), two events that have previously been pinpointed as pivotal to doxorubicin-induced senescence. Distinct in senescence remained significantly more frequent in treated than untreated cells up to 21 days after incubation with doxorubicin. Testosterone, but not 17β-estradiol counteracted both immediate and delayed senescence elicited by doxorubicin. At the molecular level, testosterone stimulated the phosphorylation of Akt and nitric oxide synthase (NOS)-3 and prevented the increases in p53 and TRF2 triggered by doxorubicin. Pre-treatment with the androgen receptor (AR) antagonist, flutamide, and the phosphatidylinositol 3 (PI3) kinase inhibitor, LY294002, abrogated the reduction in senescence, as well as Akt activation and the inhibition of p53 and TRF2 levels attained by testosterone. The effect of testosterone on senescence and TRF2 was also abolished by pre-treatment with the NOS inhibitor, L-NAME.

Conclusions: Testosterone protects against cardiomyocyte senescence caused
by doxorubicin by modulating p53 and TRF2 via a pathway involving AR, PI3K, Akt, and NOS-3. This is a potential mechanism by which males are less prone to chronic anthracycline cardiotoxicity than females.

**P3329 | BENCH**
Rho-dependent kinases ROCK1 and ROCK2 and their contribution to the myofibroblast phenotype of cardiac fibroblasts

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**Background:** RhoA and its downstream effectors ROCK1 and ROCK2 are known to play a pivotal role in the pathogenesis of myocardial fibrosis. However, their specific function in cardiac fibroblasts (CF), the major contributor to cardiac fibrocytes, and cardiac cytoskeletal remodelling processes is poorly understood. Remodelling of the diseased heart results in the transition of fibroblasts to a myofibroblast phenotype exemplified by an increased proliferation, migration rate and synthesis of extracellular matrix (ECM) proteins. Therefore, the aim of our study was to test whether RhoA-ROCK protein signalling intermediates have an impact on cellular characteristics, intracellular protein expression and mechanical properties in CF and engineered tissues.

**Methods:** Neonatal cardiac fibroblasts were isolated from wild type rats and RhoA/ROCK knockdown was achieved by lentiviral transduction or transfection. Wild type fibroblasts were treated with 10 μM Fasudil or 300 mM H1152 for 48 μM. The ROCK1/ROCK2 ratio was assessed by Western blotting of Rho, ROCK1/ROCK2 protein expression and modification was determined by immunoblot analysis, CF morphology and the localisation of cytoskeletal proteins by immunofluorescence analysis, cell proliferation by automated nucleic counting and cell migration by cell life cell imaging.

**Results:** The downregulation of RhoA or ROCK1 and ROCK2 was associated with changes in cell morphology accompanied by a disorganization of higher order actin structures including stress fibres and geodesic domes. The knockdown of ROCK1 and ROCK2 in fibroblasts significantly increased adhesion density and decreased proliferation capacity. Interestingly, the knockdown of RhoA and ROCK2, but not of ROCK1 led to a significantly decreased migration velocity and distance suggesting a specific role for ROCK2 in fibroblast migratory behavior. Moreover, ROCK2 isoforms were shown to influence viscoelastic and contractile properties of homogeneous and heterogeneous engineered tissues. Destructive tensile strength measurement to assess properties and function of the ECM in engineered cardiac fibroblast tissue (ECFT) showed that rigidity was significantly reduced in ECFT treated with ROCK inhibitors. Isometric force measurement in response to calcium of engineered heart muscle (EHM) treated with ROCK inhibitors showed a decreased resting force, whereas force of contraction was increased. **Conclusion:** This study demonstrates that RhoA-ROCK signalling controls myofibroblast characteristics of CF via remodelling of the cytoskeleton and the ECM.

**P3330 | BENCH**
Phosphodiesterase 3A1 protects the heart against isoproterenol-induced cardiac injury via anti-oxidative mechanism

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**Background:** Oxidative stress plays an important role in the pathology of cardiac remodelling and heart failure. Sustained stimulation of β-adrenergic receptor signaling induces the production of reactive oxygen species in the situation of heart failure. Phosphodiesterase 3A1 (PDE3A) inhibits β-adrenergic receptor (βAR)/protein kinase A axis by metabolizing cAMP. Therefore, we hypothesized that overexpressed PDE3A has anti-oxidative effects against isoproterenol-induced cardiac injury.

**Methods and results:** Isoproterenol (30 mg/kg/day) was continuously infused using osmotic mini-pump for 7 days in wild-type (WT) mice and transgenic (TG) mice with cardiac-specific expression of exogenous PDE3A. Isoproterenol-induced fusion increased heart weight/body weight ratio by 33% in WT mice compared with WT mice given vehicle (5.3±0.2 vs 4.4±1.0 mg/g, p<0.05), whereas by only 12% in TG hearts after isoproterenol (5.9±0.3 vs mg/g. 5.3±0.2 mg/g, ns). Echocardiography revealed that isoproterenol lead to cardiac hypertrophy in WT mice, whereas in PDE3A transgenic mice (WT vs PDE3A, +48±17 vs 86±22%, ns). In contrast, β-OHDA, a marker of oxidative stress, positive area was increased by isoproterenol stimulation in WT hearts compared with vehicle hearts (14.9±3.7 vs 7.4±1.1, p<0.05), but not in TG mice (0.98±0.04 mm vs. 0.93±0.05 mm, ns). The 8-OHdG, a marker of oxidative stress, positive area was increased by isoproterenol stimulation in WT hearts compared with vehicle hearts (0.05±0.01 vs 0.02±0.01, p<0.05), but not in TG hearts (0.04±0.01 vs 0.03±0.01, ns). Interestingly, protein expression of the pro-apoptotic protein BNIP3 was increased in WT mice compared with vehicle mice (0.11±0.04 vs. 0.13±0.04, p<0.05). In contrast, the expression of the pro-apoptotic protein BNIP3 was not increased in TG hearts compared with WT hearts in both basal (1.9±0.2 AU vs 1.0±0.1 AU, p<0.01) and after isoproterenol infusion (2.8±0.2 AU vs 1.3±0.2 AU, p=0.01), suggesting that PDE3A upregulated Sirt1-related signaling. **Conclusions:** We conclude that PDE3A inhibits isoproterenol-induced cardiac oxidative stress via regulating the interaction between βAR and Sirt1 signaling.

**P3332 | BEDSIDE**
Circulating endothelial microparticles are elevated in bicuspid aortic valve disease and are associated with aortic root dilatation

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**Background:** The mechanisms involved in ascending aorta dilatation in bicuspid aortic valve (BAV) patients are not well known. The circulating endothelial microparticles (EMP) have emerged as new biomarkers of endothelial dysfunction and have been related to aortic valve disease. However, the relationship between EMPs, BAV, and aortic dilatation has not been previously analyzed.

**Methods:** We performed this study in 4 steps: 1) comparing circulating EMPs levels between BAV patients (<55 y.o. and without significant left ventricle remodelling, n=60) and tricuspid aortic valve (TAV) controls (matched by age/sex); 2) analysing the variables related to circulating EMPs in BAV patients (<55 y.o. without other restrictions; n=70); 3) comparing circulating EMPs levels between BAV (n=25) and TAV (n=16) patients with a dilated aortic root (>21 mm2) and similar aortic diameters, and; 4) describing the time course of circulating EMPs in BAV patients depending on the requirement of aortic valve/ascending aorta surgery.

**Results:** 1) we observed higher levels of circulating EMPs in BAV patients with respect to controls (2.39±0.4 and 3.98±0.2 per log EMPs/mL respectively, p=0.001; β=0.38, p=0.001), and 2) we identified the aortic root diameter and dilatation as the main factors related to the increased EMPs levels within BAV patients (β = 0.132 ± 0.0001). The dilatation of the aortic root (Aortic diameter = 2.39±0.4 and 3.98±0.2 per log EMPs/mL respectively, p=0.001; β=0.38, p=0.001). 2) we identified the aortic root diameter and dilatation as the main factors related to the increased EMPs levels within BAV patients (β = 0.132 ± 0.0001). 3) Comparing circulating EMPs levels between BAV and TAV patients, no significant differences were found. 4) Finally, we observed that after aortic valve/ascending aorta surgery the circulating levels of EMPs decreased drastically (4.2±0.6 to 1.75±0.3 EMPs/mL, p=0.002), especially in those patients undergoing aortic root replacement. In contrast, the time course effect was observed those BAV patients who did not require aortic valve/ascending aorta surgery.

**Conclusions:** The pattern of elevation of circulating EMPs observed links BAV, endothelial aortic root damage and aortic dilation, suggesting the implication of the anomalies flow generated by BAV. Circulating EMP may emerge as new biomarkers of aortic root dilatation in BAV disease.

**P3333 | BEDSIDE**
Association of bicuspid aortic valve morphology with ascending aortic dimensions and growth

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**Background:** Bicuspid aortic valve (BAV) is associated with thoracic aortic pathology, but presence and progression rates of dilation vary widely among patients. Conflicting evidence exists on the association of valve morphology and aortic dilation and growth. **Purpose:** To investigate whether an association between BAV morphology on aortic dimension and aortic progression rate of dilatation exists.

**Methods:** A retrospective, observational study in a European tertiary care centre. Echocardiographic images were screened for presence of BAV. Two observers independently confirmed presence and morphology of BAV. If needed, consensus was reached by involving a third observer. Only cases with serial echocardiographic images were included in the analyses. Mixed linear model analyses were used to identify independent factors associated with ascending aortic dilation. **Results:** A total of 392 patients had confirmed BAV with sufficient image quality to assess valve morphology and thoracic ascending aorta dimensions. At base-line, mean age was 48±17 years, 69% of patients were men, and dilatation of any segment of the ascending aorta was present in 30% (dilatation of the tubular ascending aorta in 26% and aortic sniut dilation in 10%). Age was associated with aortic stenosis, sinusotubular junction (STJ), and tubular ascending aorta dimensions. Aortic valve morphology was associated with left ventricular outflow tract (LVOT), aortic sinus and tubular ascending aortas dimensions. Sex was associated with dimensions of LVOT, aortic sinus and STJ. BSA was associated with LVOT and tubular ascending dimensions. Severity of aortic valve stenosis was associated with aortic sinus, sinus tubular dimensions and STJ. **Conclusions:** We observed a significant progression rate (0.17 mm/year [95% confidence interval (95-CI) 0.12–0.23], p<0.000), and 0.33 mm/year [95-CI 0.25–0.44], p<0.000). However, BAV morphology did not...
predict growth in both segments (aortic sinus p<0.670, and tubular ascending aorta p=0.658).

Conclusions: In this large single centre cohort, several factors were independently associated with dimensions of diverse parts of the thoracic ascending aorta. During follow-up, the aortic sinus and the tubular ascending aorta showed significant progressive growth, which could not be predicted by BAV morphology.

P3333 | BEDSIDE

Detachment of commissure is a major cause of aortic regurgitation in acute type A aortic dissection

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Background: Significant aortic regurgitation (AR) frequently complicates acute type A aortic dissection (AD). Avulsion of an aortic valve commissure is thought to be one of the causes of AR in type A AD. Purpose: We sought to determine the mechanisms of AR in acute type A AD by transthoracic echocardiography (TEE).

Methods: 251 patients with acute type A AD were enrolled in this study. TEE images were recorded every 4 days to assess aortic valve architecture in the 251 patients. Results: Avulsion of the aortic valve commissures was found in 189 (189/301 (63%), 79 (79/189 42%) had avulsion of one commissure, 102 (54%) had avulsion of two commissures and 7 (4%) had all commissures avulsed. Avulsions of both commissures between non-coronary cusp (NCC) and right coronary cusp (RCC) and between NCC and left coronary cusp (LCC) were observed in 93 (49%). Avulsion of commissure between RCC and LCC alone was observed in 74 (39%). Avulsion of commissure between NCC and LCC alone was observed in 5 (3%). Of the 87 who had moderate or severe AR, 76 had eccentric jets and 11 had central jets. Eccentric jets were directed toward the opposite side of the avulsed aortic valve in 74, which means avulsion of the aortic valve commissure is the cause of AR.

Conclusions: Avulsion of commissure is commonly observed in type A AD. Detachment from the aortic wall at one commissure, which leads to the simultaneous detachment of 2 cusps and can cause aortic regurgitation. We verify almost all eccentric AR jets in type A AD to oppose site of avulsed commissure. Avulsion of the aortic valve commissure is a major cause of AR in Type A AD.

P3335 | BEDSIDE

Predictors of aortic complications in patients with bicuspid aortic valve


Background: Bicuspid aortic valve (BAV) is the most common congenital heart disease (1.3% of the global population, M:F 3:1). It is a valvuloaortopathy. The bicuspid aortopathy (BA) is the dilatation of any thoracic aortic segment from the root to the arch (prevalence in patients with BAV between 20% and 84%). The dilatation rate (0.2–1.9 mm/year) is higher both in adults and in children with BAV than in that with tricuspid aortic valve. The most important predictors of progression of the aortopathy towards the aortic aneurysm are: dilatation of the aorta, advanced age, male sex, systemic arterial hypertension (IPA), valvular stenosis-insufficiency and RL pattern. The worst complication of BA is the aortic dissection (AD), even if it is quite rare (Toronto cohort 5/642, 0.78% cases; Olmsted County cohort 2/416, 0.48% cases, incidence 3.1/10000/year).

Purpose: To identify predictors of aortic complications in patients with bicuspid aortic valve in our population.

Methods: In a population of 389 consecutive patients from 1994 to 2015 with an echocardiographic diagnosis of BAV and an average follow up of 11.1 years we investigated the BA natural history using aortic root or ascending aorta aneurysm (AA, diameter ≥5 cm) and aortic dissection (aortic complications) as end points.

Results: The mean dilatation rate of aortic root and ascending aorta were respectively 0.36 mm/year and 0.57 mm/year in <50 years old (y.o.) patients; 0.65 mm/year and 0.37 mm/year in ≥50 y.o. patients. During follow-up 12 patients developed an AA (3.08% of the population, mean age 43.1 years, 11 M and 1 F). The univariate analysis reveals that the most powerful predictors are the basic diameter of the aorta and arterial hy- pertension: root or tubular portion of the ascending aorta diameters (D) ≥35 mm p 0.005, RR 7.016. D ≥40 mm p 0.001, RR 7.64 and for arterial hypertension p 0.005, RR 5.97. In multivariate analysis the most powerful predictor was the diameter ≥40 mm (p 0.002). 6 cases of acute aortic dissection occurred (1.5%, incidence 1.96/1000/year). In univariate analysis the best predictors of AD were basal aortic diameters (diameters ≥35 mm p 0.006, ≥40 mm p 0.012) and arterial hypertension (p 0.002).

Conclusions: Basal aortic diameter and the arterial hypertension are the main predictors of aortic complications in patients with bicuspid aortic valve. Therefore, it would be highly recommended a strict follow up both in cases with baseline diameters ≥40 mm and in cases with arterial hypertension. The incidence of aortic dissection is higher than in general population.

P3337 | BEDSIDE

Yellow dust and particle pollution are independently associated with increased risk of hospital admission for ischemic heart disease in South Korea

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Background and introduction: Although air pollution has been associated with increases in acute morbidity and mortality, its effect is not well known in East Asian countries, where was affected by yellow dust phenomenon.

Purpose: To identify predictors of an increase in acute myocardial infarction (AMIs) admissions in a heavily industrialized region.

Methods: By random sampling method, total 2515 cardiac admissions were selected. Admissions for IHD were associated with same-day concentrations of PM 10 (μg/m3) (RR 1.004, 95% CI 1.003–1.005) per 10 μg/m3 increase of yellow dust (RR 1.846, 95% CI 1.505–2.265) but not with concentrations of NO2, CO and ozone. There was no seasonal variation in admission rate despite of distinctive four seasons in Korea. The concentration of PM 10 and yellow dust had independent relationship with IHD admission after adjusting each other (RR 1.002, 95% CI 1.001–1.003 per 10 μg/m3; RR 1.402, 95% CI 1.057–1.859, respectively).

Conclusions: To our knowledge, this is the first study identifying nation-wide influence of air pollution and yellow dust on IHD. The results suggest that fine particulate matter and yellow dust are independent risk factors for hospital admission due to IHD in South Korea.

P3338 | SPOTLIGHT

Air pollutants and acute myocardial infarction in a heavily industrialised region. Is there any relationship?

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The objective of the study was to examine the relationship between hospital admissions for acute myocardial infarction (AMI) and environmental pollution in the heavily industrialised Siberian region.

Materials and methods: The main indicators of environmental pollution and number of AMI admissions in the our Cardiology Center were assessed for the period between December 2010 and November 2014. Additionally, the annual number of days with unfavorable meteorological conditions and their impact were considered. The regression analysis was used to assess the relationship between the parameters and to build the equations of correlation for continuous variables. The number of AMI admissions was considered as a dependent variable; the % of days with unfavorable meteorological conditions and their impact were considered. The results were presented as regression coefficient, B, and correlation coefficient, R. Differences were considered statistically significant if p<0.05.

Results: It was found that there were associations between the increased number of hospital admissions for primary acute myocardial infarction and the elevated levels of nitrogen oxide and dioxide in winter time in comparison with summer time. It was found that, throughout the follow-up period, the elevation of nitrogen oxide concentration by 10% of MACDa results in the increase of AMI admissions of 1.4 cases and the elevation of nitrogen dioxide concentration, in the increase of 0.9 cases of AMI admissions. In winter season, the 10% elevation of average monthly concentration of nitrogen oxide was associated with the increase in AMI admissions of 2.9 cases. Then the relationship between the concentra-
tions of air pollutants and AMI extent was examined. A 10% elevation of nitrogen oxide concentration results increased the number of hospital admissions for Q-wave AMI of 1.7 cases throughout the follow-up period and of 2.4 cases in winter. When analysing the relationship between the concentrations of air pollutants and admissions for non-Q-wave AMI, it was found that, as the levels of nitrogen dioxide, carbon monoxide and fine particulate matter (PM2.5) increased, the number of non-Q-wave AMI increased by 0.4, 0.9 and 1.2 cases, respectively. Therefore, there is the association between the incidence of hospital admissions for primary acute myocardial infarction and environmental pollution. This association is especially evident during winter season.

P3339 | SPOTLIGHT
Particular matter and hemorrhagic stroke: a systematic review and meta-analysis
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Background and objectives: Ambient particulate matters (PM) are inconsistently associated with the risk of hemorrhagic stroke (HS) incidence and mortality. The purpose of this study is to assess their relationships between PM and HS using a meta-analytic approach.
Methods: We evaluated the odds ratio (OR) and 95% confidence interval (CI) of stroke in incidence and mortality associated with per 10 μg/m3 increase of the concentration of PM, suspended PM (SPM), PM10 (PM with aerodynamic diameter ≤10 μm), or PM2.5 (PM with aerodynamic diameter ≤2.5 μm) as effect scale, and a sensitivity analysis for the results was conducted.
Results: Thirteen studies were identified. There was a statistically significant association between PM concentration and HS incidence (OR per 10 μg/m3 = 1.037, 95% CI: 1.009–1.065). In subgroup analyses of HS incidence, the relationship between PM total and HS was also associated with a higher mortality of HS (OR per 10 μg/m3 = 1.075, 95% CI: 1.001–1.149) but not in SPM and PM10. Furthermore, higher PM concentration was associated with a higher mortality of HS (OR per 10 μg/m3 = 1.016, 95% CI: 1.003–1.029). In subgroup analyses of HS mortality, the relationship seemed similarly significant (PM OR per 10 μg/m3 = 1.020, 95% CI: 1.005–1.035) but not in PM2.5. Sensitivity analysis showed that the results were robust.
Conclusions: PM is associated with risk of HS incidence and mortality. Different PM subtypes had different effects on HS.

P3340 | SPOTLIGHT
Ambient particulate matter air pollution and temperature levels: impact on blood pressure in high-risk cardiac patients
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Background: and objectives: Ambient particulate matters (PM) are inconsistent associated with the risk of hemorrhagic stroke (HS) incidence and mortality. The purpose of this study is to assess their relationships between PM and HS using a meta-analytic approach.
Methods: We evaluated the odds ratio (OR) and 95% confidence interval (CI) of stroke in incidence and mortality associated with per 10 μg/m3 increase of the concentration of PM, suspended PM (SPM), PM10 (PM with aerodynamic diameter ≤10 μm), or PM2.5 (PM with aerodynamic diameter ≤2.5 μm) as effect scale, and a sensitivity analysis for the results was conducted.
Results: Thirteen studies were identified. There was a statistically significant association between PM concentration and HS incidence (OR per 10 μg/m3 = 1.037, 95% CI: 1.009–1.065). In subgroup analyses of HS incidence, the relationship between PM total and HS was also associated with a higher mortality of HS (OR per 10 μg/m3 = 1.075, 95% CI: 1.001–1.149) but not in SPM and PM10. Furthermore, higher PM concentration was associated with a higher mortality of HS (OR per 10 μg/m3 = 1.016, 95% CI: 1.003–1.029). In subgroup analyses of HS mortality, the relationship seemed similarly significant (PM OR per 10 μg/m3 = 1.020, 95% CI: 1.005–1.035) but not in PM2.5. Sensitivity analysis showed that the results were robust.
Conclusions: PM is associated with risk of HS incidence and mortality. Different PM subtypes had different effects on HS.

P3341 | SPOTLIGHT
Fine particulate matter (PM2.5) air pollution and extreme levels of ambient temperature (T) have been linked to changes in blood pressure (BP). However, few studies have evaluated their joint hemodynamic effect among subsets at high risk for late bleeding is essential in order to identify the optimal PM2.5. 50%)

Background and objectives: Ambient particulate matters (PM) are inconsistent associated with the risk of hemorrhagic stroke (HS) incidence and mortality. The purpose of this study is to assess their relationships between PM and HS using a meta-analytic approach.
Methods: We evaluated the effects of ambient PM2.5 and outdoor T levels during the prior 1 to 7 days on resting BP among 2078 patients entering cardiac rehabilitation at the University of Michigan (from January 2003 to August 2011). We used multiple linear regression analyses, controlling for age, sex, body mass index, and the same-day alternate environmental factor (i.e., PM2.5 or T). Results: Mean ± standard deviation (SD) of PM2.5 and T levels was 12.6±8.2 μg/m3 and 10.3±1.4 °C, respectively. Each SD increase in PM2.5 levels during lag days 4–6 was associated with significant increases in systolic (2.1 to 3.5 mm Hg) and diastolic (1.7 to 1.8 mm Hg) BP (Figure). Conversely, a SD increase in outdoor T levels during lag days 4–6 was associated with reductions in both systolic (−3.6 to −2.3 mm Hg) and diastolic (−2.5 to −1.8 mm Hg) BP (Figure). Overall, no consistent pattern of effect modification by other covariates (e.g., demographics, seasons, medication usage, resting BP) was observed.

Conclusions: Short-term elevations in ambient PM2.5 - even within air quality standards - were associated with detrimental hemodynamic effects, while higher ambient T was linked to decreased BP. Both ubiquitous environmental factors have clinically-meaningful consequences on resting BP among high-risk cardiac patients.

Acknowledgement/Funding: This study was funded in part by a grant from the U.S. Environmental Protection Agency (RD83479701)
Results: Of 2776 with type 1 DM (58% male), mean age was 57 years (SD 11), mean diabetes duration 35 years (SD 14, range 0–76) and mean HbA1c 67 mmol/mol (SD 14). Mean follow-up time was 7.2 years (SD 2.2). The most common indications for coronary angiography were stable coronary artery disease (31%), non-ST-elevation myocardial infarction (38%) and ST-elevation myocardial infarction (10%). Patients with three- compared to one-vessel disease had longer DM duration (39 vs. 33 years) and lower onset age of DM (21 vs. 23 years) while actual HbA1c was similar (67.2 vs. 66.8). Mortality was comparable in those with normal and one-vessel diseases while those with two-vessel almost had similar mortality rate as those with three-vessel disease.

Conclusion: In type 1 DM mortality is increased by numbers of affected coronary vessels. Duration of DM seems more important than actual HbA1c for numbers affected coronary vessels abnormalities and modification of antiplatelet therapy (APT) regimen.

Methods: The PESTO study was a prospective national multicenter registry involving 29 French catheterization labs. Patients referred with acute coronary syndromes (ACS) were prospectively screened for definite ST and analyzed by OCT after culprit lesion deocclusion. ST were classified as acute (AST), sub-acute (SAST), late (LST) and very late (VLST), according to the Academic Research Consortium criteria. Baseline clinical, biological and angiographic characteristics were collected for each subject. Three independent operators unaware of patients’ characteristics reviewed OCT data to identify the ST etiologies.

Results: A total of n=120 patients (mean age 61.6±1.1 y, 89% male) were included in the study. VLST was the clinical presentation in 75%, LST in 6% and SAST+AST in 19% of the patients. Bare metal stents (BMS) were involved in 39%, drug-eluting stents (DES) in 59% and biolimus eluting stents (BVS) in 2%. The delay between initial PCI to ST was shorter (1.8±0.7 vs. 5.3±0.6 y, p<0.001) and left anterior descending was more frequently involved (69% vs. 40%, p<0.006) in patients under DAPT than under SAPT.

Conclusions: Progressive PSS might be one of the risk factors for MACE and VLST in 1st generation DES, but not in 2nd generation DES, although the follow-up period was shorter than the previous studies. The Kaplan-Meier curves are shown in the figure.

Figure 1. Event free survival in 1st generation DES

P3345 | BEDSIDE
Association between progressive peri-stent contrast staining, major adverse cardiac events, and very late stent thrombosis: a comparison between 1st and 2nd generation drug-eluting stent

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Background: Peri-stent contrast staining (PSS) is reported to be associated with subsequent target lesion revascularization (TLR) and very late stent thrombosis (VLST).

Methods: We performed percutaneous coronary intervention (PCI) in 13155 lesions between November 2002 and December 2013 using 8 types of DES. We performed follow-up coronary angiography (CAG) at 6 to 8 months (mid-term) and 18 to 20 months (late-term) after PCI. PSS is defined as vessel enlargement, with contrast medium staining outside the stent, and over 20% of the stent diameter, as previously reported. We found PSS in 328 lesions (2.5%) at follow-up CAG. We observed the temporal change of PSS with serial follow-up CAG and performed clinical follow-up for more than 1 year after late-term follow-up CAG in 199 lesions (1st generation DES, 124; 2nd generation DES, 75). We divided them into 2 groups: progressive PSS and non-progressive PSS. We examined the difference in the cumulative rates of major adverse cardiac events (MACE: all-cause death, myocardial infarction, and TLR) and VLST between the 2 groups in each generation DES.

Results: The patients were 159 men and 40 women, and the mean age was 67.0±11.2 years. The mean follow-up period after late-term follow-up CAG were 4.35±1.94 years in 1st generation DES and 2.11±0.64 years in 2nd generation DES (p<0.001). The Kaplan-Meier curves are shown in the figure.

Figure 1. Event free survival in patients with PSS

Conclusions: Progressive PSS might be one of the risk factors for MACE and VLST in 1st generation DES, but not in 2nd generation DES, although the follow-up period was different between the 2 groups.

Best Posters in PCI: long-term outcome / Best Posters in new treatment modalities and treatment implementation

P3347 | BEDSIDE
Efficacy of short courses of low-frequency electric myostimulation in patients hospitalized for decompensated chronic heart failure (CHF) in early terms of hospital treatment

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Aim of the study: To evaluate efficacy and safety of short courses of low-frequency
frequency lower limb muscle electric myostimulation (EMS) in patients with decompensated chronic heart failure (CHF) in early terms of hospital treatment.

Methods: 51 patients (67.7% male, 65.3±3.8 years old) were enrolled in the study. Patients were randomized into two comparable groups: 1- effective EMS (n=28) and 2 - sham EMS (n=23). In 2-3 days after admission to hospital patients underwent low-frequency stimulation of anterior and posterior muscles of thigh and shin. We used electromyostimulator “Stimulator-01” generating bipolar symmetric square-wave electric impulses with pulse duration of 1±0.5 ms at a frequency of 25±1 Hz in cyclic regimen (t0±1 s – stimulation, t0±1 s – rest).

Average duration of EMS was 50.0±20.0 minutes daily. In first group amplitudes of the impulses was adjusted individually up to maximally tolerated, in group of sham – amplitude was minimal. Physical tolerance and quality of life were evaluated using visual-analogue scale (VAS), 6-minute walk test (6-mwt), Duke Activity Status Index (DASI) and Minnesota Living with Heart Failure Questionnaire (MLHFQ) at baseline, after 2–3 weeks of treatment (just before discharge from the hospital) and after 1, 3 and 6 months after discharge.

Results: Patients from EMS group showed reliable improvement p<0.05 for all comparisons) of well-being according to VAS (from 3.6±0.6 to 7.2±1.0; Δ 3.5±1.1), quality of life according to MLHFQ (from 53.6±8.5 to 34.0±18.0; Δ 21.6±5.3), improvement of physical activity according to DASI (from 12.1±5.6 to 6.2±4.2 and 6-mwt (from 206.1±3.1 to 253.9±11.9 m; Δ 88.8±56.2). Patients from group 2 demonstrated reliable improvement according to VAS (from 3.0±1.8 to 7.0±0.7; Δ 3.6±0.6) and MLHFQ (from 58.5±7.1 to 48.7±8.1, Δ 7.9±4.3; p<0.05 for both). According to DASI there was no statistically significant difference in sham group and according to 6-mwt there was a tendency for improvement of physical tolerance (from 211.4±51.6 to 236.8±54.7 m; p=0.056). In 1, 3 and 6 months after discharge there was no dynamics in investigated parameters for both groups thought patients from the EMS group demonstrated better indices of life quality and physical tolerance compared with sham group.

Conclusions: Functional electric stimulation of lower limb skeletal muscles leads to significant improvement of physical tolerance and can be safely used in patients with CHF early after decompensation when physical training is not possible. Longer cycles of EMS are required for fixation of positive effect.

P3349 | BEDSIDE
Impact of standardised medication titration forms and incentive payments on medication titration in heart failure: should we pay for more?

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Background: Angiotension converting enzyme inhibitors (ACEI), angiotension receptor blockers (ARB) and beta blockers (BB) are prescribed at lower doses in real-world practice compared with the doses achieved in the randomised controlled trials that demonstrated their efficacy.

Purpose: We undertook a series of quality initiatives to determine whether we could improve medication titration in newly referred patients with heart failure and a reduced ejection fraction (HFREF) following hospital discharge.

Methods: We conducted three audits of consecutive eligible HFREF patients (LVEF≤50%) who were newly referred to the multidisciplinary heart failure services at three hospitals and followed-up in our health district between July to December 2009 (N=126), 2010 (N=103) and 2011 (N=106). A standardised medication titration form was introduced (2009/2010), followed by incentive payments to heart failure services for each medication titration form used (2011). Data were collected by independent reviewers through hospital chart audit and general practitioner surveys. To compare differences between groups, one-way ANOVA were used for continuous normally distributed variables and Chi-squared tests for categorical variables.

Results: Patients enrolled during the three time periods were similar (Mean age 71 years, 31–35% male, Mean LVEF 31–32%) with high prescription rates at hospital discharge (ACEI/ARB 93–97%, BB 92–94%). Comparing the three time periods, a progressively higher proportion of patients received the medication titration form (28%, 47%, 65%, P<0.001) and a higher proportion achieved target doses by six month post-hospital discharge: ACEI/ARB (37%, 48%, 55%, P=0.051); BB (38%, 33%, 51%, P=0.045). The higher titration rates at six months post-hospital discharge were achieved in the patients who were not prescribed target doses when discharged from hospital: ACEI/ARB (24%, 35%, 41%, P<0.011); BB (29%, 25%, 45%, P=0.036). Patients who received a medication titration form were more likely to achieve target doses for ACEI/ARB (54% vs. 34%, P<0.001) and BB (54% vs. 38%, P<0.013).

Conclusion: The use of a standardised medication titration form was associated with improved medication titration in HFREF. The introduction of incentive payments was associated with increased utilisation of the medication titration form.
tion between PARF and percentage of patients attaining different NT-proBNP targets aged <75 vs. >75 is depicted in the Figure. PARFs of the NT-proBNP targets did not differ significantly between age groups. Attainment was significantly lower for elderly patients for every NT-proBNP target (21% vs. 32%, p < 0.001 for <1500; 40% vs. 33%, p = 0.001 for <3000; 57% vs. 69%, p < 0.001 for <5000; 87% vs. 91%, p < 0.001 for <15000).

Conclusion: In ADHF patients, the proportion of mortality that would be prevented by attaining a NT-proBNP target is similar between young and elderly patients. However, attainment of targets is lower in elderly patients. Instead of age-dependent NT-proBNP targets, future studies need to investigate why less elderly patients attain NT-proBNP targets.

BEST POSTERS IN HYPERTENSION MONITORING AND TREATMENT

P3353 | BENSIDE

Accuracy of different types of blood pressure measuring devices at high altitude. Data from HIGHCARE-ALPS

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Objective: Blood pressure (BP) measuring devices may become inaccurate at high altitude due to low barometric pressure. Aim of this study was to assess the changes in the accuracy of different types of BP measuring devices between sea level and high altitude, taking auscultatory measurements with mercury sphygmomanometer as reference.

Design and methods: In the frame of HIGHCARE-ALPS project, we obtained multiple BP measurements in 39 healthy, normotensive volunteers (age: 36.4±8.5y, M/F:21/18), using a mercury (MER, reference), an aneroid (ANE), and two validated oscillometric devices [one for home (OSC-HBP; AND UA-767PC) and one for ambulatory (OSC-ABP; AND TM2430)] BP monitoring, at sea level and during acute exposure to high altitude (4559mm, barometric pressure 437–439 Torr). BP measurements with the different devices were performed sequentially on the same arm in random order, consistent under both study conditions.

Results: Mean systolic (S) and diastolic (D)BP were higher at high altitude than at sea level (MER: 117.6±80.3 vs. 110.9±74.1 mmHg, p < 0.001) The mean differences in SBP between MER (reference) and the remaining devices at baseline and high altitude were 1.7±6.5±6.0±7.1 (OSC-ABP), −3.1±5.7–3.8±3.3 (ANE) and −1.2±7.0–5.0±6.7 (OSC-HBP) respectively. The corresponding differences for DBP were −3.9±5.9–4.5±5.6 (OSC-ABP), −2.2±5.1–5.3±3.6 (ANE) and −4.8±7.6–2.1±7.2 (OSC-HBP), (mmHg, p < 0.01 vs. MER). The over- or under-estimations of basic values by tested devices as compared with MER were consistent and similar at sea level and high altitude, except for a greater underestimation of SBP by OSC-HBP (p<0.01), and of DBP by ANE (p=0.03) at altitude and for a greater underestimation of DBP by OSC-HBP (p=0.02) at sea level. Although statistically significant, the absolute changes in the size of error between sea level and high altitude never exceeded 4 mmHg. The distribution of mean between-device differences within the group was consistent between sea level and high altitude never exceeded 4 mmHg.

Conclusions: Accuracy assessment of blood pressure measuring devices is a critical issue to monitor patients admitted in high altitude. The distribution of mean between-device differences within the group was consistent between sea level and high altitude, with about 50% of subjects displaying between-devices differences always smaller than 5 mmHg.

P3354 | BEDSIDE

Cardiovascular diseases registry (RECVASA): focus on antihypertensive treatment and outcomes in hypertensive patients with cardiac comorbidities

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Purpose of the study was to evaluate concomitant cardiovascular (CV) pathology, antihypertensive treatment and outcomes in hypertensives using a registry of patients with arterial hypertension (AH), ischemic heart disease (IHD), chronic heart failure (CHF) and atrial fibrillation (AF) in the Ryazan Region.

Methods: The total of 3648 patients with AH (age 66±12.9 years; 72% women) applied for general practitioners or cardiologists of 3 outpatient clinics were enrolled in the registry. End points at 12 months follow-up were evaluated for 3593 (98.5%) of patients. Cox model was used to estimate the hazard ratio (HR), 95% confidence interval (CI) for prediction of all cause mortality (MTo), CV mortality (CVM), stroke and myocardial infarction (MI).

Results: Only 741 (20.3%) of patients had AH without other CV diseases (CVD). Most of the patients (79.7%) had cardiac comorbidities: AH, IHD - 200 (5.5%); AH, CHF - 377 (10.3%); AH, IHD, CHF - 1809 (49.6%); AH, IHD, CHF, AF (CVD) - 494 (13.5%); other - 27 (0.8%). The mean number of CVD was 2.6±0.9 and 63.8% of patients had three or four CVD. History of stroke (HSTR) and MI (HMI) was observed in 348 (9.5%) and 418 (11.4%) patients. The following antihypertensive drugs (AHD) were prescribed: ACE inhibitors (50.1%), β-blockers (41.8%), thiazide diuretics, TD (34.1%), sartans (26.6%), calcium channel blockers (22.0%), other - 5.0%. HMI were not prescribed in 13.8% of cases. The mean number of AHD was 1.7±0.9. Incidence of target blood pressure (BP) level in hypertensives was 19.9%. During 12 months follow-up we identified: 168 cases of death (11.4%) based on the central analysis according to ESH-ABPM guidelines. Despite 784 patients in the whole group were monitored, antihypertensive therapy remained unchanged in 322 patients (41%).

In the subgroup with established CV disease the respective values for control rate and change of antihypertensive therapy in uncontrolled patients were as shown in the Table.

Table 1

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<th>Nephropathy</th>
<th>Additional medication in uncontrolled patients</th>
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<td>80%</td>
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<td>78%</td>
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<td>81%</td>
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<td>80%</td>
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<td>79%</td>
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Conclusions: ABPM identified a high rate of uncontrolled patients with type-2 diabetes and established cardiovascular disease. The total cardiovascular risk was grossly underestimated by GPs as compared to central analysis. Despite the high risk of our patients with cardiovascular disease we observed a lack of therapeutic decision making in uncontrolled patients.
CATHETER ABLATION AND SUPRAVENTRICULAR ARRHYTHMIAS

P3356 | BEDSIDE
Long-term natural history of adult Wolff-Parkinson-White syndrome patients treated with and without catheter ablation
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Objective: There are a paucity of data regarding the long-term natural history of adult Wolff-Parkinson-White (WPW) syndrome patients in regard to risk of mortality and atrial fibrillation (AF). In addition, it is unclear if curative catheter ablation interrupts the natural history of AF.

Results: Three groups of patients were studied: a WPW population separated by treatment with ablation (Ablation: 872, No Ablation: 1461) and a 1:5 control population (n=11,175). AF was diagnosed by ICD codes and system wide review of the electrocardiogram and ambulatory event monitor database. Patients were followed for long-term mortality and AF. Results: WPW patients that underwent ablation were younger, less likely to have hypertension, diabetes, renal failure, or coronary artery disease compared to non-ablated patients. The average follow-up for the WPW group was 2987±12166.3 (median: 2502) days and was similar between the ablation and non-ablation groups. Long-term death rates were similar between the WPW group versus the control group [adjusted HR=0.96 (95% CI: 0.83-1.11), p=0.56]. However, non-ablated WPW patients had a higher long-term death risk compared to WPW ablation patients [adjusted HR=2.10 (95% CI: 1.50-20.93), p<0.0001]. Incident AF risk was higher in the WPW group compared to the control population [HR=1.55 (95% CI: 1.29-1.87), p<0.0001]. Non-ablated WPW patients had lower risk than ablated patients [HR=0.39 (95% CI: 0.28-0.53), p<0.0001].

Conclusion: Long-term mortality rates in WPW patients are low and similar to an age- and gender-matched control population. Catheter ablation patients have lower mortality rates compared to WPW patients not treated by catheter ablation. AF rates are high long-term and ablation does not reduce this risk which is suggestive of an underlying inherited atrial myopathy.

Acknowledgement/Funding: None

P3357 | BEDSIDE
Management of refractory atrial appendage tachycardia: repetitive catheter ablation or thoracoscopic atrial appendectomy?
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Background and Introduction: The outcome of different management for patients with refractory atrial appendage tachycardia (AAT) (after initial radiofrequency catheter ablation (RFCA) is unknown.

Purpose: We tried to compare the mid/long-term outcome of video-assisted thoracoscopic (VAT) atrial appendectomy and re-do RFCA in treating patients with refractory AAT (initial RFCA failure).

Methods: Nineteen consecutive patients with initially failed RFCA for AAT were enrolled. Five of them were resorted to video-assisted thoracoscopic VAT atrial appendectomy (short-term appendectomy cohort) and 14 received re-do RFCA (RFCA cohort). The combination of acute treatment failure and AAT recurrence was the endpoint of observation. We investigated the mid/long-term outcomes of the two cohorts by survival analysis.

Results: After a mean follow-up of (353±217) days, no patients experienced recurrence in atrial appendectomy cohort, while 8 out of 14 patients (57.1%) in the RFCA cohort experienced recurrence. Log-Rank analysis observed significant differences between two cohorts (P=0.049). No major complications were reported in either cohort. Larger earliest 10 ms activation area in the endocardial atrial appendage and more antiarrhythmic drug resistance indicated recurrence for patients who underwent redo-RFCA.

Conclusion: VAT atrial appendectomy may be a reasonable option for patients with relapsed AATs after the initial RFCA.

P3358 | BEDSIDE
Serum levels of YKL-40 before and after therapy in patients with supraventricular arrhythmias
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Background: The inflammatory glycoprotein YKL-40 (chitinase-3-like protein 1) has emerged as a potential biomarker in cardiovascular disease including atrial fibrillation (AFib). Its role, however, in other supraventricular arrhythmias besides AFib is not known, while evidence on its predictive value in AFib remains controversial.

Methods: We measured serum levels of YKL-40, C-reactive protein (CRP) and interleukin (IL)-6 in 70 patients with AFib, atrial flutter (AFl), atrioventricular node reentry tachycardia (AVNRT) or other supraventricular tachycardia (SVT) before, immediately after therapy and 1 week later in comparison with 20 healthy controls. Patients were followed for 6 months for arrhythmia recurrence.

Results: Baseline YKL-40 was significantly higher in AFib (99.5±202.5 ng/mL versus 47.2±38.9 ng/mL in controls, p<0.001), but not in patients with other supraventricular arrhythmias and correlated positively with left atrial volume index (Spearman's rho=0.853, p<0.001). YKL-40 levels dropped significantly 1 week post-treatment only in AFib (p<0.009 versus baseline). Arrhythmia recurrence at 6 months occurred in 13 patients (19%), including 11 with AFib and 2 with AFl. Baseline YKL-40 was independently associated with AFib recurrence [adjusted odds ratio=1.02, 95% confidence interval=1.00–1.04, p=0.016], CRP and IL-6 remained practically stable throughout the study and were not associated with AFib recurrence.

Conclusion: Serum YKL-40 was elevated only in AFib and not in other supraventricular arrhythmias. In AFib, YKL-40 levels were responsive to therapy and predicted long-term recurrence.

P3359 | BEDSIDE
Characterization and significance of accessory pathway dormant conduction in patients with WPW syndrome
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Background: Adenosine can be used to provoke re-occurrence of accessory pathway (AP) conduction after successful ablation. However, the mechanisms of adenosine-induced AP re-occurrence (dormant vs. residual conduction) remain unknown.

Methods and results: This study comprised a total of 49 patients (38±18 y, male=30) with WPW syndrome (overt pre-excitation). Catheter ablation, exclusively performed using RF energy, eliminated the AP in all patients (left AP: n=23, right AP: n=26). After ablation, all patients were challenged to adenosine with the aim to induce AV block or re-occurrence of AP conduction. In all patients with adenosine-induced AP re-conduction, ablation was continued until re-administration of adenosine resulted in complete AV block. Adenosine-induced re-occurrence of AP conduction was observed in 12 (24%)
Methods: evaluate safety, efficacy and learning experience of electrophysiologists during AVNRT was recently reported in small series of patients. This study aims to complete elimination of fluoroscopy (No-X-Ray approach-NXRA).

Results: A total of 756 procedures of AVNRT CA were analysed from which 347 procedures were performed with NXRA. No significant in-hospital complications occurred and only 0.5% of failed procedure were reported in each subgroup. Fellows performed procedures in 267 patients (age: 36±26; range 7–73 years; 80% of women, 25% with NXRA). During the same period of time, 489 patients (age: 31±56; range 10–85 years; 60% of women, 57% with NXRA) were treated by experts only. Conversion to fluoroscopy in NXRA occurred in 3% procedures in similar incidence in both groups. NXRA was associated with longer total procedure and total X-Ray exposure time in fellows rather than in experts (5±20 vs 5±20 and 0.7±2.7 vs 0.4±0.4 min; both p<0.05). NXRA procedures as compared to those without NXRA had similar procedural time and total time of X-Ray exposure in fellows and experts groups (5±24 vs 5±24; p=NS and 5±8±5.2 vs 5.5±4.5 p=NS, respectively). Only in experts' group significant decrease in total procedure time were observed between the first and the last quarter of procedures in both groups. In average the time in patients when 3D-EAM was available all AVNRT were ablated by experts with NXRA.

Conclusions: Simplified, NXRA for CA of AVNRT can be implemented for EP fellows trained and performed as standard approach by experts as safe and effective method of CA. NXRA could be successfully implemented for training of new generation of EP fellows as well as routine approach for experts.

P3362 | BEDSIDE
Anatomical features determining the difficulty of ablation in atrioventricular nodal reentrant tachycardia

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Purpose: Thanks to a high success rate, ablation of the slow pathway (SP) has become the treatment of choice for atrioventricular nodal reentrant Tachycardia (AVNRT). However long procedures with prolonged X-ray exposure and risk of complications remain present. The purpose of this retrospective study was to define anatomical features of the right atrium (RA) that could influence the efficacy of the ablation, using a 3D rotational angiography (3DRA).

Methods: We studied 51 consecutive patients undergoing AVNRT ablation and for whom a per procedural 3DRA was performed. Dimensions of the triangle of Koch (ToK) and the cavotricuspid isthmus (CTI) were measured and correlated to difficulty of ablation determined by the total number of radiofrequency applications (RFA). An ablation was considered to be “easy” if it was successful with ≤2 RFA and “difficult” if ≥2 RFA were applied.

Results: Acute procedure success was reached with 2±5 RFA. Dimensions of the ToK and the length of the CTI were not statistically different for patients with an “easy” vs “difficult” ablation. However, the presence of a Eustachian valve (p<0.001) and a concave CTI morphology (p=0.05) were significantly more frequent in patients with a “difficult” ablation.

Conclusions: The difficulty of SP ablation was not correlated to the dimensions of the ToK but to the presence of a Eustachian valve and a concave CTI morphology. This is probably due to the proximity of the CTI and the SP region, target for ablation of the SP. Purple dot is the registration of the most proximal His bundle potential.

Conclusion: The difficulty of SP ablation was not correlated to the dimensions of the ToK but to the presence of a Eustachian valve and a concave CTI morphology. This is probably due to the proximity of the CTI and the SP region, target for ablation (figure 1).

Fig. 1. 3D reconstruction of the RA with 2D overlay in Right Anterior Oblique (RAO) and Left Anterior Oblique (LAO) view. Black arrow shows the Eustachian valve. The yellow ring represents the region target for ablation of the SP. Purple dot is the registration of the most proximal His bundle potential.

P3363 | BEDSIDE
Clinical course of paroxysmal atrioventricular nodal reentrant tachycardia in children

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Purpose: The aim of the study was to assess the clinical course of paroxysmal atrioventricular nodal reentrant tachycardia (AVNRT) in children.

Methods: Data were obtained from prospective standardised multicenter CA registry from January 2012 to January 2015. Consecutive unselcted patients with final diagnosis of AVNRT were recruited. All procedures were performed using simplified approach with 2 catheters from femoral access and the same electrocardiographic system. Three-dimensional electro-anatomical mapping system were used. Simplified pacing maneuvers and techniques were used to prove mechanism of arrhythmias. No lead-aprons were used by medical staff in EP-lab till fluoroscopy was needed. Procedural data were compared between three advanced electrophysiologists (experts) and three fellows (mid-advanced).

Results: A total of 756 procedures of AVNRT CA were analysed from which 347 procedures were performed with NXRA. No significant in-hospital complications occurred and only 0.5% of failed procedure were reported in each subgroup. Fellows performed procedures in 267 patients (age: 36±26; range 7–73 years; 80% of women, 25% with NXRA). During the same period of time, 489 patients (age: 31±56; range 10–85 years; 60% of women, 57% with NXRA) were treated by experts only. Conversion to fluoroscopy in NXRA occurred in 3% procedures in similar incidence in both groups. NXRA was associated with longer total procedure and total X-Ray exposure time in fellows rather than in experts (5±20 vs 5±20 and 0.7±2.7 vs 0.4±0.4 min; both p<0.05). NXRA procedures as compared to those without NXRA had similar procedural time and total time of X-Ray exposure in fellows and experts groups (5±24 vs 5±24; p=NS and 5±8±5.2 vs 5.5±4.5 p=NS, respectively). Only in experts' group significant decrease in total procedure time were observed between the first and the last quarter of procedures in both groups. In average the time in patients when 3D-EAM was available all AVNRT were ablated by experts with NXRA.

Conclusions: Simplified, NXRA for CA of AVNRT can be implemented for EP fellows trained and performed as standard approach by experts as safe and effective method of CA. NXRA could be successfully implemented for training of new generation of EP fellows as well as routine approach for experts.

Fig. 1. 3D reconstruction of the RA with 2D overlay in Right Anterior Oblique (RAO) and Left Anterior Oblique (LAO) view. Black arrow shows the Eustachian valve. The yellow ring represents the region target for ablation of the SP. Purple dot is the registration of the most proximal His bundle potential.

Conclusion: The difficulty of SP ablation was not correlated to the dimensions of the ToK but to the presence of a Eustachian valve and a concave CTI morphology. This is probably due to the proximity of the CTI and the SP region, target for ablation (figure 1).
P3364 | BEDSIDE
Feasibility and accuracy of non-invasive mapping and ablation of different atrial tachycardias
Introduction: We prospectively examined the feasibility and accuracy of a novel, 3D non-invasive mapping System as a tool for atrial tachycardia (AT) characterisation.
Methods: Various consecutive focal and macroreentrant ATs were mapped in 18 patients (10-male, median age=51, IQR's 25/75=46/63) using a non-invasive mapping system. AT mechanisms and localizations mapped by non-invasive potential and activation sequences were confirmed with a traditional invasive mapping system. Ablation was performed with an irrigated tip catheter in the manifest atrial pathway ERP (1,410±3.1 ms vs. 1,190±3.0 ms, p<0.001). Significant decrease in AVNRT ERP was followed by the reduction of maximal AV node conduction rate (167.7±29.4 vs. 186.6±26.9 impulses per minute; p<0.05), and an increase in the time from ERP washing-out to the first depolarisation of the accessory pathway (293.3±34.2 ms vs. 246.6±35.7 ms; p<0.03).
Conclusions: AVNRT clinical course is progressive in 52.3% of cases, is followed by atrial fibrillation in 4.7% of cases, and has a spontaneous remission in 10% of cases with the possibility of recurrence in early adulthood. The age of 12–15 years is critical to the occurrence and advancement of AVNRT.

P3365 | BEDSIDE
The use of non-invasive mapping and 3D image integration to avoid transbaffle access in patients after total cavopulmonary connection surgery: a single centre experience
Introduction: Remote magnetic navigation-guided ablation with 3-dimensional (3D) image integration can provide maximum benefit in patients with complex anatomy due to surgical correction of congenital heart disease. We reviewed our experience on patients with total cavopulmonary connections (TCPC) from July 2008 to December 2013.
Methods and results: A total of 24 pts with TCPC (15 m, mean age 27±3 yrs), including 14 tricuspid atresia (TA), 8 double inlet left ventricle (DILV), 3 double outlet right ventricle (DORV) with atrioventricular septal defect (AVSD) +/- atrial isomerism and common AV valve, one mitral atresia and one pulmonary atresia presented with sustained arrhythmias and were admitted for catheter ablation. For all patients, the procedure was carried out with CARTO RMT (either XP or 3) and 3D image integration using either CMR or CT and was performed completely remote-controlled without the switching back to conventional mapping & ablation or need for transbaffle punctures. Using femoral venous access, a multipolar transbaffle access in patients after total cavopulmonary connection (TCPC) served as a timing reference (ParaHis). As a default, femoral arterial access was gained to allow retrograde access to the native aorta via the suture line.
A total of 32 arrhythmias were inducible (1:3/patient, range 1 to 4), 15 re-entrant (44%) including 4 typical flutter, 8 focal (24%), 3 AVNRT implicating transient AV node block were less frequent than spontaneous major AE (0.4%) (5/1186 vs 23/1770, p<0.015). Multivariable analysis, only greater age (OR per one year increase in age=1.02, CI: (1.01–1.04), p<0.001) was independently associated with a higher risk of ablation complication.
Conclusions: SVT-related adverse events occurred in 19% of patients. However, life-threatening arrhythmias were rare (1%). Most of them are drug-related. Advanced age, male gender and presence of heart disease are predisposing factors for adverse events. Ablation, significantly associated with a lower risk of immediate major complications should be recommended in these patients.

P3366 | BEDSIDE
Feasibility and accuracy of non-invasive mapping and ablation of different atrial tachycardias
Introduction: We prospectively examined the feasibility and accuracy of a novel, 3D non-invasive mapping System as a tool for atrial tachycardia (AT) characterisation.
Methods: Various consecutive focal and macroreentrant ATs were mapped in 18 patients (10-male, median age=51, IQR's 25/75=46/63) using a non-invasive mapping system. AT mechanisms and localizations mapped by non-invasive potential and activation sequences were confirmed with a traditional invasive mapping system. Ablation was performed with an irrigated tip catheter in the manifest atrial pathway ERP (1,410±3.1 ms vs. 1,190±3.0 ms, p<0.001). Significant decrease in AVNRT ERP was followed by the reduction of maximal AV node conduction rate (167.7±29.4 vs. 186.6±26.9 impulses per minute; p<0.05), and an increase in the time from ERP washing-out to the first depolarisation of the accessory pathway (293.3±34.2 ms vs. 246.6±35.7 ms; p<0.03).
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P3367 | BEDSIDE
The use of a new high resolution mapping system in the validation of linear lesions
Background: Linear lesions are crucial for the treatment of macro re-entry tachy-
Catheter ablation and supraventricular arrhythmias / Catheter ablation of supraventricular and ventricular arrhythmias

P3368 | BEDSIDE

Short PQ interval on ECG in children: etiology of the phenomenon and its clinical significance

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Purpose: The aims of the study were to assess the atrioventricular (AV) conduction characteristics in children with short PQ interval on ECG, the risk of spontaneous tachycardia initiation and the danger of sudden cardiac death (SCD).

Methods: 300 children (210 (70%) boys and 90 (30%) girls) with short PQ interval on ECG without paroxysmal tachycardia were examined (the value of PQ interval was normal age-dependent limit and with absence of delta wave). Exclusion included: ECG, 24-hour Holter monitor, treadmill test, echocardiogram, transesophageal pacing study (TEPS) and intravenous adenosine drug test.

Results: Mean age at the moment of the first examination was 13.3±3.6 years (3–17 years). Follow-up period was 1773.9 patients-years (3.7±3.8 years: from 1 year to 9.2 years). 57 (13%) children were lost from follow-up. There were no SCD cases during the follow-up, and 1 child deceased secondary to oncological etiology. 5 children (2.1%) developed paroxysmal tachycardia 5.2±3.9 years (2–10 years) following identification of the short PQ interval on ECG. 3 children were diagnosed with atrial nodal reentrant tachycardia (AVNRT), and 2 children were diagnosed with orthodromic AV reentrant tachycardia (AVRT) with left-sided accessory pathways. The mean age of children at the time of the first episode of tachycardia initiation was 13.2±2.1 years (11–16 years). During TEPS arrhythmia was induced in 7 (2.3%) children without spontaneous paroxysmal tachycardia: 2 – with AVNRT, 2 – with AVRT, 3 – with non-sustained atrial fibrillation or flutter. 42.3% of children had enhanced AV nodal conduction (maximal AV node conduction more than 200 impulses per minute). In 18 (7.4%) children (mean age 18.1±6.5 years) the duration of the PQ interval on at least 3 ECGs normalized during the follow-up period. In these children PQ interval was initially longer than in those with stable short PQ interval (112.6±13.8 ms vs. 104.9±3.5 ms respectively; p<0.01). 13 children underwent adenosine drug test. During the study AV block (AVB) of I–III degree developed in all of the children (first-degree AVB in 4, second-degree AVB in 8, third-degree AVB in 1 child), which confirms the absence of accessory pathways in these patients.

Conclusions: Children with short PQ interval on ECG have a good prognosis: they rarely develop paroxysmal tachycardia and are not at risk for SCD. Short PQ interval is not secondary to the presence of accessory pathways and instead is likely due to AV nodal conduction peculiarities.

P3369 | BEDSIDE

Performance of the SA-VA difference to differentiate atrioventricular nodal reentrant tachycardia from orthodromic reentrant tachycardia in a large cohort of patients

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Background: Pacing stimulus and the last entrained atrial electrogram minus the tachycardia ventriculoatrial interval (SA-VA interval) represents a simple diagnostic maneuver to distinguish between atrioventricular nodal reentrant tachycardia (AVNRT) and orthodromic reentrant tachycardia (ORT) during electrophysiological study. However, its usefulness has largely been studied in selected patient subgroups.

Methods: Consecutive patients with inducible supraventricular tachycardia and successful entrainment through pacing trains from right ventricular apex during an electrophysiological study were prospectively included. Atrial tachycardias were excluded. The following intervals were calculated for each patients: SA-VA difference; his potential and atrial electrogram (HA) during entrainment minus HA during tachycardia (ΔHA); and the corrected return cycle.

Results: A total of 456 patients fulfilled the inclusion criteria, of which electrophysiological study revealed 265 typical AVNRT, 38 atypical AVNRT, 54 and 108 ORT through a septal and free-wall accessory pathway, respectively. An SA-VA difference >99 ms identified AVNRT in all patients with sensitivity, specificity, positive and negative predictive values of 97.7%, 96.9%, 98.3% and 95.7%, respectively.

Conclusions: This study confirms the high ability to distinguish AVNRT from ORT using the SA-VA difference, not only in selected patient subgroups, but as whole when a cutoff of >99 ms is used.

P3370 | SPOTLIGHT

Novel method of alcohol ablation using endovascular intramyocardial injections

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Aim: Anatomic variability of the coronary artery supplying the hypertrophied obstructive septum can limit transcatheter septal ablation. The purpose of this study was to examine the efficacy and safety of endocardial alcohol ablation as prospective treatment option for hypertrophic cardiomyopathy.

Methods and results: We studied endocardial septal ablation in 5 anesthetized mini pigs. Electro-magnetic navigational system Noga XP and catheter for intramyocardial injections MyostarTM were used. There were no any complications during or after endocardial ablation. After intervention animals were observed in vivarium during 6 months. At 6 months follow-up, LVEF volumes were unchanged (63±4% vs. 61±7% (p=0.05)). At the end of the observation period heart retrieval was performed for further histological study of the injection zones. Heart weight was 68±12.2 g. Mean infarction size was 2.76±1.2 g, corresponding to 42% of LV mass. There was a 32% reduction in thickness of the septum. Average percentage of sclerosis (correlation between the sclerotic tissue and initial myocardiun) was 91±7%. There was no evidence of infarction-related damage of myocardium outside the target area.

Conclusions: Our preliminary results from animal study demonstrates the feasibility of endocardial alcohol ablation for cardiac procedures. Although further study is needed to make a definitive statement. In our opinion these results have important implications for advancing technology needed for ablation of hypertrophic cardiomyopathy.

P3371 | BEDSIDE

Ablation of frequent PVC in primary prevention patients meeting criteria for ICD implant. Safety and appropriateness of withholding the implant

D. Penela1, J. Acosta1, L. Aguinaga2, L. Tercedor2, J. Fernandez-Armenta3, P. Sanchez1, J. Brigada1, L. Mon1, A. Berreuzo3. Arrhythmia Section, Cardiology Dept. Thorax Institute. Hospital Clinic, Universitat de Barcelona, Spain

Catheter ablation and supraventricular arrhythmias / Catheter ablation of supraventricular and ventricular arrhythmias

Abstract P3368 – Table 1. Diagnostic accuracy of pacing maneuvers

<table>
<thead>
<tr>
<th>Cut-off</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>ROC (95% CI)</th>
<th>Patient subgroup</th>
</tr>
</thead>
<tbody>
<tr>
<td>SA-VA</td>
<td>&gt;99ms</td>
<td>97.7%</td>
<td>96.9%</td>
<td>98.3%</td>
<td>95.7%</td>
<td>0.994 (0.987-1.0)</td>
</tr>
<tr>
<td>Subgroup 1: SA-VA (atypical AVNRT &amp; septal AVRT)</td>
<td>&gt;85ms</td>
<td>99.7%</td>
<td>82.1%</td>
<td>91.2%</td>
<td>99.3%</td>
<td>0.994 (0.987-1.0)</td>
</tr>
<tr>
<td>Subgroup 2: SA-VA (VA &lt;100ms)</td>
<td>&gt;100ms</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>1.0 (1.0-1.0)</td>
</tr>
<tr>
<td>Corrected PPI-TCL</td>
<td>&gt;10ms</td>
<td>97.4%</td>
<td>92.0%</td>
<td>96.5%</td>
<td>96.9%</td>
<td>0.978 (0.965-0.990)</td>
</tr>
<tr>
<td>ΔHA+</td>
<td>&lt;0ms</td>
<td>98.6%</td>
<td>94.5%</td>
<td>95.9%</td>
<td>98.1%</td>
<td>0.997 (0.991-1.0)</td>
</tr>
</tbody>
</table>

*Subgroup of patients.
P3373 | BEDSIDE
Isolated epicardial RVOT scar: a typical substrate for VT in endurance athletes without evidence for inherited cardiomyopathy
J. Venlet, S.R.D. Piers, G.F.L. Kapel, M. De Riva Silva, M.J. Schalji, K. Zeppenfeld. Leiden University Medical Center, Cardiology, Leiden, Netherlands
Background: Early arrhythmogenic right ventricular cardiomyopathy (ARVC) usually involves the subtricuspid RV. Endurance training in ARVC has been related to disease progression. Endurance training may however result in specific structural RV changes detectable by electroanatomical mapping in the absence of inherited, inflammatory or cardiomyopathic disease.
Methods: Consecutive patients undergoing endo/epicardial mapping for ventricular tachycardia (VT) of RV origin and genetic testing for desmosomal and PLN mutations were enrolled. Evaluation included family and endurance training history, ECG, imaging and biopsies, if appropriate. Electroanatomical (EA) voltage maps were reviewed for scar distribution (bipolar -1.5 mV, unipolar -5.5 mV, fragmented/late potentials).
Results: A total of 33 patients (50±16 years, 82% male) were inducible for 3 VTs/pat (IQR 1.0–3.5). The EA scar was located in the subtricuspid RV inflow-tract (group A) in 27 patients (53±15 years, 85% male) with additional involvement of the RVOT in 8, the RV apex in 3 and the lateral free wall in 2. In 6 patients (37±13 years, 67% female), the scar was restricted to the epicardial, subpulmonary RVOT (group B). In 16/27 group A patients a desmosomal or PLN mutation was found, 8 had no mutation and 3 patients had sarcoidosis. Three of eight patients with no mutation were competitive athletes with normal ECGs, the remaining 5 (3/5 ECG abnormalities and whether ICE visualization offers additional information during VT ablation.
P3374 | BEDSIDE
Catheter ablation of ventricular tachycardia in patients with arrhythmogenic right ventricular cardiomyopathy: Insights from a French monentric registry
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Background: Few early studies assessing mostly endo-epicardial ablation of ventricular tachycardia (VT) among patients with arrhythmogenic right ventricular cardiomyopathy (ARVC) have reported considerable VT recurrences during long-term follow-up. None of them have identified predictive factors of radiofrequency catheter ablation (RFA) efficacy.
Purpose: To determine whether RFA outcomes were similar to those previously reported and to investigate predictors of long-term benefit from RFA.
Methods and results: The study population comprised 32 patients (age 47±12 years, 28 male) with ARVC according to revised Task Force Criteria, in whom all underwent a total of 55 RFA (53 endocardial, 2 combined epicardial and endocardial procedures). Between 1999 and 2014, VT recurrences and VT burden were assessed after the first procedure or after the whole RFA treatment. Over a mean follow-up of 74±51 months, VT-free survival rates after the 55 procedures were 37.1%, 21.6%, and 18.9% at 1, 5 and 10 years respectively. VT burden was significantly reduced after a single procedure (31 versus 16 VT episodes/year, p<0.02) or after the whole RFA treatment (15 versus 3 VT episodes/year, p<0.01). After a mean follow-up of 58±34 months, clinical response rates to the whole RFA treatment defined as freedom from sudden cardiac death from VT requiring hospitalization and from heart transplantation were 80.6%, 64.6%, and 59.2% at 1, 5 and 10 years respectively. Younger age, no amiodarone treatment, familial history of ARVC, no heart failure, inducible VT at RFA with isoproterenol and 0.35 cm, voltage was preserved. In one patient in whom api- cal extent of the scar was significantly more epicardial (depth 0.6 cm), VT exit was mapped to the border zone of the Sound scar and could not be successfully ablated. In cases where scar extends more midventricularly or epicar- dially with preserved endocardial to Sound scar distance >0.35 cm, bipolar voltage may not reflect closeby scar and epicardial access may be needed.
Conclusion: Sound scar assessment is consistent with scar delineated by bipo- lar voltage mapping. In cases where scar extends more midventricularly or epicar- dially with preserved endocardial to Sound scar distance >0.35 cm, bipolar voltage may not reflect closeby scar and epicardial access may be needed.
Purpose: To evaluate whether intraoperative echocardiography may facilitate understanding of cardiac substrate contributing to ventricular arrhythmias during cardiac ablation.
Methods: In patients undergoing VT ablation, full CARTOSound (Sound) maps were made of the endocardial left ventricular (LV) surface, intracavitary structures including the valves and papillary muscles, and epicardial regions suggestive of ventricular scar. Complete voltage maps were then made and VT was induced and mapped with either pace-mapping when hemodynamically not tolerated or with activation and entrainment mapping when well tolerated. Bipolar voltage recordings were made with voltage >1.5 mV considered normal tissue. Voltage-assessed scar area was then compared against Sound assessed scar area.
Results: In 8 patients, complete LV maps were created. Average Sound scar area was 9.2±3.4% of the overall LV and voltage scar area was 8.2±3.1% (p>NS). Average depth of Sound scar was 0.7±0.2 cm. In 3 patients, the scar was oblong extending midmyocardially and/or epicardially with preserved endocardial tissue based on ICE at the border zones. Average depth of endocardial surface to Sound scar was 0.35±0.1 cm. In areas where endocardial scar to surface distance was >0.35 cm between scar and endocardial surface, bipolar voltage abnormality was seen. At depths >0.35 cm, voltage was preserved. In one patient in whom api- cal extent of the scar was significantly more epicardial (depth 0.6 cm), VT exit was mapped to the border zone of the Sound scar and could not be successfully ablated. In cases where scar extends more midventricularly or epicar- dially with preserved endocardial to Sound scar distance >0.35 cm, bipolar voltage may not reflect closeby scar and epicardial access may be needed.
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Catheter ablation of supraventricular and ventricular arrhythmias

P3376 | BEDSIDE

The transseptal or transaortic approach for pediatric left sided accessory pathway ablation in era of NavX/Ensite? Comparison of four approaches

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The ablation of left sided accessory pathways (LSAPs) can be performed via transseptal (AO) or transaortic (TS) approach. Both technique can be achieved with non-fluoroscopic approach, however this significantly increases the procedural duration.

The aim was to assess the safety and feasibility of 4 strategies for LSAP ablation: standard RTG approach with AO (RTG+AO) or TS (RTG+TS) access and low fluoroscopic NavX/Ensite approach with AO (NX+AO) or TS (NX+TS) access. RTG+AO and RTG+TS were performed with 2-electrodes (fixed 4 and deflectable 10 poles). In the NX+AO group procedure was started from RA, CS and location His bundle. Aorta was reconstructed before passage to the left ventricle. Short fluoro was used during TS. We analyzed the procedural (duration of GA and procedure), X-ray (fluoroscopy (FT), air-karma dose (DJ) and ablation parameters (time to 1st and the last application (1stAP_L, the AP), the number of applications (N_AP), total RF duration (RF_T) and success rate. We included 176 pts with LSAP (age 13.3±3.4 years, 73% with SVT (76%), WPW (96) or palpitations. In 118 pts the NavX was used. In 102 of them short fluoro was needed. Ablation was completed with AO in 109 and TS in 77 pts. There were 38 patients in RTG+AO group, 16 in RTG+TS, 58 in NX+AO and 56 in NX+TS. TS vs AO ablation: There were no difference in procedure duration (70±30 vs 73±32 min) between groups. There were lower FT and D in TS group (9±11 vs 13±11 min. and 32±45 vs 66±168mGy) as well as the time to 1stAP and L_AP and lower N_AP and RF_T (24±13 vs 31±13 min., 44±29 vs 53±28 min., 7.8±12 vs 10.1±9.4, 243±189 vs 274±232 sec.). The NavX significantly reduced the RTG parameters without change to ablation parameters. The shortest procedure duration was for NX+TS (65±23 min.), with shortest FT (5.4±3.3 minutes) lowest D (22±41 mGy). The RF+TS approach was technique with shortest 1stAP and L_AP, with lowest N_AP and total RF_T (22±11 min., 36±21 min., 4.9±4.3 and 192±132 sec.). The success rate for RTG+AO was 86%, RTG+TS 86%, NX+AO=100% and NX+TS=94%.

Conclusion: Non-fluoroscopic NavX/Ensite approach for catheter ablation of atrial tachycardia (AT) is feasible and is safe, even in children with the shortest procedure duration.

P3377 | BEDSIDE

Electroanatomic mapping system allows zero fluoroscopy in cryo and radiofrequency ablation of accessory pathways in children

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Purpose: Fluoroscopic catheter ablation of cardiac arrhythmias in pediatric patients is challenging and associated with potential adverse events because of body and heart size and radiation sensitivity and longer life expectancy. We evaluated the feasibility, safety and efficacy of accessory pathway (AP) cryo and RF ablation guided by 3D electroanatomic mapping (EAM) system aiming to reduce fluoroscopy exposure.

Methods: We included 63 patients (mean age 13.1±3.3 years). An electrophysiological study with a 3D EAM reconstruction was performed in every patient with a venous transseptal direct right atrium approach or an arterial transseptal retrograde approach to reach the mitral annulus. In 2 patients with left-sided AP the ablation was performed via a patent foramen ovale. Our approach was done with RF and in 13 with cryoenergy (all Kent bundles: 5 para-Hisian, 4 right postero-septal, 2 right antero-septal, 1 right anterior and 1 left postero-septal). All ablation procedures were performed without the use of fluoroscopy and without complication. At a mean follow-up of 15.0±11 months we observed 9 recurrences, 5 of them successfully reablated without fluoroscopy. In 1 case cryoablation of the para-Hisian AP was ineffective. The primary success was 97.7%.

Results: Conclusion: Zero fluoroscopy approach for catheter ablation of tachycardy-mias in children is safe and feasible and could be used in order to decrease potential harmful effect of fluoroscopy on patient and clinic staff.

P3379 | BEDSIDE

Electrocardiographic estimation of successful ablation site in patients with manifest posterior accessory pathway

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Introduction: Posterior accessory pathways (APs) have a wide distribution. For this reason, the mapping and radiofrequency ablation of such APs are difficult. Electrocardiographic (ECG) identification of AP location may guide the endocardially and/or epicardially approach and ablation procedures.

Purpose: We aimed to estimate successful ablation site based on ECG in patients (mean age: 25.8±9.0; 126 males) with posterior AP.

Methods: 137 consecutive patients with manifest posteroseptal preexcitation (QRS>110 ms) and single AP located at the posteriorseptal region assessed by electrophysiologic study were retrospectively analysed (Table).

Results: Right endocardial posterior APs were discriminated from left endo...

Clinical characteristics

<table>
<thead>
<tr>
<th>Total (n=137)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Male gender (n, %)</td>
</tr>
<tr>
<td>Right endocardial PS AP (n, %)</td>
</tr>
<tr>
<td>Left endocardial PS AP (n, %)</td>
</tr>
<tr>
<td>Epicardial PS AP (n, %)</td>
</tr>
<tr>
<td>Common disease (n, %)</td>
</tr>
<tr>
<td>Documented PSVT (n, %)</td>
</tr>
<tr>
<td>Preceded AF (n, %)</td>
</tr>
<tr>
<td>Unexplained palpitation or syncpe (n, %)</td>
</tr>
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</table>

AF: atrial fibrillation; AP: accessory pathway; PS: posterior; PSVT: paroxysmal supraventricular tachycardia.
cardiac APs with a R/S ratio <1 (sensitivity 96%, specificity 72%, p=0.001) and negative delta wave in lead V1 (sensitivity 74%, specificity 84%, p=0.001). Epicardial posteroseptal APs were differentiated from endocardial APs by a negative delta wave in lead II (sensitivity 57%, specificity 79%, p=0.03), and R/S ratio >1 in V1 (sensitivity 57%, specificity 79%, p=0.04).

Conclusions: Delta wave polarity and R/S ratio in lead V1 differentiate right enocardial posteroseptal APs from left endocardial APs. Delta wave polarities in leads II, AVR and V1, and R/S ratios in leads II and V1 estimate epicardial po- teroseptal APs.

P3380 | BEDSIDE
Long-term outcome of intra-atrial reentrant tachycardia catheter ablation in adults with congenital heart disease
University Hospital La Paz, Madrid, Spain

Purpose: Radiofrequency catheter ablation (RFCA) has evolved as a feasible curative treatment modality for intra-atrial reentrant tachycardia (IART) in adults with congenital heart disease (CHD). However, data on long-term outcome are scarce. The aim of this study was to determine the long-term outcome of RFCA for IART in adults with CHD and predictors of IART recurrences.

Methods: Seventy patients (41 male, mean age 40±12 years) undergoing RFCA of IART, which completed a follow-up of at least 1 year after the procedure, were studied. CHD was tetralogy of Fallot in 21 P (30%), atrial septal defect in 16 (23%), TGA in 10 (14%), pulmonary stenosis in 7 (10%), single ventricle physiology in 6 (9%) and others. Complete acute success was defined as termination of all IART circuits and partial success as termination of the spontaneous IART. We analyzed the influence of clinical factors (age, sex, type of CHD, age at surgical repair, systolic function of systemic and pulmonary ventricle, pulmonary hypertension and right atrial dilatation), electrophysiological factors (type, number and cycle length of induced IART) and procedure related factors (complete or partial success, use of irrigated tip catheter and use of electroanatomic mapping system) in the development of IART recurrence.

Results: Complete acute success was obtained in 52 P (74%) and partial suc-
cess in 10 (14%). Median follow up was 53 months (IQR 18–104). IART recur-
rence was noted in 22 P (31%). A new RFCA was performed in 15 P. In 12 P the circuit of the clinical IART was the same as that observed during the first proce-
dure. Thirteen P developed atrial fibrillation during the follow up (7 paroxysmal, 2 persistent and 4 permanent). One patient died suddenly and 2 P underwent heart transplantation. An ICD was implanted in 3 P and a pacemaker in 4. At the end of follow-up, 61 P (87%) were in sinus rhythm. At multivariate analysis, the use of electroanatomic mapping (HR 0.4, IC 95% 0.2–0.65, p=0.001) and irrigated tip catheter (HR 0.49, IC 95% 0.32–0.75, p=0.001) was associated with the lack of recurrences whereas the presence of moderate to severe right atrial dilatation was independent predictor of IART recurrence (HR 1.7, IC 95% 1.13–2.55; p=0.001).

Conclusion: Despite recurrent IART and development of atrial fibrillation, sinus rhythm at the end of a long-term follow-up is present in the majority of P with IART undergoing RFCA. The use of electroanatomic mapping and irrigated tip catheter reduced the recurrence of IART after RFCA, whereas right atrial dilatation is associated with a higher risk of IART recurrence.

P3381

ABSTRACT WITHDRAWN

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P3382 | BEDSIDE
The Historic - AF Trial: European, prospective multicenter study of hybrid thoracoscopic and transcatheter ablation of persistent atrial fibrillation
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Background: The treatment of persistent atrial fibrillation (AF) still presents a major challenge in current clinical practice: pharmacological as well as trans-
catheter strategies have shown limited efficacy at short-term duration. Novel, less-invasive surgical approaches for AF ablation demonstrated promising results especially when utilised along with catheter-based approaches in hybrid fashion.

Purpose: The Hybrid Staged Operating Room and Interventional Catheter Ablation for Atrial Fibrillation trial is a prospective, multicenter study designed to evaluate the outcomes of staged endoscopic and transcatheter ablation in patients with stand-alone, long-standing persistent AF (LpAF). Primary end-point of the study was the clinical outcome and efficacy of the procedure defined as a freedom from AF>60% according to HRS criteria at 6, 12, 24 months follow-up.

Methods: From June 2012 to January 2015, 89 consecutive patients with LpAF were enrolled: all surgical procedures were performed via a minimally invasive thoracoscopic approach to perform an epicardial, left atrial isolation (‘box’ lesion set) with a uni-bipolar radiofrequency energy device. Achievement of at least exit and/or entrance block were mandatory intraoperative end-points. Rhythm as-
281essment was carried out by means of 72-hrs ECG-Holter or implantable loop recorders. In presence of AF recurrence, a staged EP evaluation and ablation was performed. Results: All endoscopic procedures were successfully performed without ma-
389jor perioperative complications. Postoperative PM implantation occurred in 2 pts (2.2%), while hospital mortality was 0%. A staged EP evaluation was required in 8 pts (8.9%) with AF recurrences following the 3 months blanking period: transcatheter ablation mostly targeted CFAEs and cavo-tricuspid isthmus isthmus ablation. No ablation of the mitral isthmus was performed in the current study population. At 6 and 12 and 24 months follow-up a stable restoration of sinus rhythm was achieved in 90.7% (59/65), 88.8% (49/55) and in 93.3% (14/15) of patients respectively; according to HRS guidelines, the percentage of patients in sinus rhythm and with-
74-out antiarrhythmic drugs were 78.4% (51/65) at 6 months, 77.8% (35/45) at 12 months, 80% (12/15) at 24 months.

Conclusions: Early outcomes of the HISTORIC AF trial demonstrated that epica-
drial thoracoscopic and transcatheter left atrial isolation in patients with long-
79-standing persistent AF is associated with excellent and stable results up to 24 months follow-up. Staged EP transcatheter ablation was required only in a minor-
355ity of patients with AF recurrences.

P3383 | BEDSIDE
Feasibility and safety of uninterrupted peri-procedural apixaban administration in patients undergoing radiofrequency catheter ablation for atrial fibrillation: results from a multicenter study
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Introduction: Periprocedural anticoagulation management with uninterrupted
warfarin with a ‘therapeutic INR’ represents the best approach reducing both thromboembolic and bleeding complications in the setting of catheter ablation for atrial fibrillation (AF). The purpose of this study was to evaluate the safety and feasibility of uninterrupted apixaban administration in this setting.

Methods: We performed a prospective multicenter registry of AF patients undergoing radiofrequency catheter ablation at 4 Institutions in USA and Europe with an uninterrupted apixaban strategy. These patients were compared with an equal number of patients, matched for age, gender and type of AF, undergoing AF ablation on uninterrupted warfarin. The apixaban group comprised consecutive patients who were on twice daily 5 mg Apixaban for at least 30 days prior to ablation. The last dose of apixaban was taken the morning of the procedure. A subset of 29 patients underwent dMRI to detect silent cerebral ischemia (SCI) in the apixaban group.

Results: A total of 103 patients (200 patients in each group) were included in the study. The average age was 65±9.9 years with 286 (71.5%) male and 334 (83.5%) patients having no paroxysmal AF. There were no differences in major (1% vs. 0.5%, p=1.0), minor (3% vs. 2.5%, p=0.56) and total bleeding complications (4.5% vs. 3.0%, p=0.43) between the apixaban and the warfarin group respectively. There were no symptoms of thromboembolic complications. All the dmRIs were negative for SCI in the apixaban group.

Conclusions: Uninterrupted apixaban administration in patients undergoing AF ablation, appears to be feasible, and effective in preventing clinical and silent thromboembolic events without increasing the risk of major bleeding.

P3384 | BEDSIDE
Rivaroxaban a new alternative to warfarin for atrial fibrillation ablation: a meta-analysis of embolic and bleeding complications
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Introduction: Rivaroxaban (R) is being used more commonly pre and post-atrial fibrillation ablation, appears to be feasible, and effective in preventing clinical and silent thromboembolic events without increasing the risk of major bleeding.

Methods: We conducted a meta-analysis of all published papers (n=3) and abstracts (n=5) to date that compared complication rates for peri-AF ablation use of FTI or CF.

Results: The 95% CI for R vs W was 0.89–1.44 in the FTI group (n=50), RF was delivered until FTI reached target lesion depth (4mm posterior wall, 6mm anterior wall). In FTI group, FPTI values were used to optimise the ablation lesion. In FTI group, FPTI values were used to optimise the ablation lesion. In FTI group (n=50), radiofrequency (RF) was delivered until FTI reached at least 35 Gy*cm². Optimized fluoroscopy can reduce safely the radiation dose to lower than 5 Gy*cm².

Conclusions: Current medical radiation exposure during PVI in Germany is 35 Gy*cm². Optimized fluoroscopy can reduce radiation dose to lower than 5 Gy*cm². Befiting introducing novel expensive technologies for fluoroscopy reduction optimizing of conventional fluoroscopy is mandatory.

P3385 | BEDSIDE
Rivaroxaban a new alternative to warfarin for atrial fibrillation ablation: a meta-analysis of embolic and bleeding complications
D. Musat1, N. Garkipati2, M.W. Preminger1, T. Sichrovsky3, S. Mittal1, J.S. Steinberg1.
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P3386 | BEDSIDE
Site of atrial fibrillation rotors may overlap gangionated plexi in left atrium
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Introduction: The cardiac autonomic nervous system plays an important role in atrial fibrillation (AF). Recent advances in mapping human AF report localised sources (rotors) treatable by focal ablation. We hypothesised that such rotors may colocalise with gangionated plexi (GP).

Methods: We studied 78 consecutive patients with AF (61.2±9.1 years, 73% present; recorded by 64 pole contact catheters (Constellation, BSCI) and phase mapping of AF singularities (GP) at EP study. Electroanatomic shells were analysed independently by 4 blinded observers for overlap with superior/inferior left GP and anterior/inferior right GP.

Results: AF sources arose in 77/78 (99%) patients for 2.3±1.1 each (left atria, LA 1.6±0.8 right 1.0±0.7). Of all patients, 75 had LA sources. Of these, 68 (89%) had at least 1 rotor that colocalised with a GP, either definitely (32 patients, 41%) or possibly (31 patients, 40%). Of out 122 LA rotors identified, only 30 were not related to any GP. Of the rotors identified at GP sites, 31 rotors were at SLGP, 26 at ILGP, 27 at ARGP and 18 were at IRGP. The figure shows 2 targeted rotors overlapping GP sites. Patients who had rotors colocalising at the SLGP site tended to have paroxysmal AF (vs persistent AF, p=0.015).

Conclusions: Fibrillatory rotors in human left atria commonly occur at sites of GPs, offering a possible physiological basis for source formation and targeted ablation. Future studies should define how patient specific GP locations may sustain AF.
were unblinded off-line. Follow-up (without blanking period) consisted of clinical examination and Holter-ECG at 1, 3, and 6 months in all patients.

**Results:** Demographic, cardiovascular and anatomic characteristics were similar in both groups. Isplatal PV was obtained in 100% of cases (n=200). Compared to FTI, FPTI was associated with a higher rate of first encirclement isolation (98% vs 85%, p < 0.001), a higher rate of PV resistant to adenosine (97% vs 83%, p = 0.01), shorter mean RF time per ipsilateral circle (1068±231 s vs 1665±447 s, p < 0.0001) and shorter mean procedure time (143±27 min vs 194±42 min, p < 0.0001). At 6 months follow-up, 8/30 (16%) had AF recurrence in FTI group versus none in FPTI group (p = 0.0001). Repeat ablation was performed in 4 FTI patients. Analysis of the index procedure showed that PV reconnection (12 gaps) occurred where lesions did not overlap (n=7) or did not reach adequate depth (n=5).

**Conclusion:** Our findings suggest a benefit of FPTI in guiding CF-guided PV. FPTI-guidance produced fast, complete and adenosine proof ipsilateral PV isolation in 98% of cases. At 6 months follow-up, FPTI-guidance was associated with improved clinical outcome.

**P3388 | SPOTLIGHT**

**Intra-operative mapping procedure for diagnosis of the substrate of atrial fibrillation**


**Introduction:** Multi-site, high resolution mapping of the atria can be used to identify the left-sided PV ostia than the right-sided PVs (LSPV: 28%, LIPV: 24%, RSPV: 22%, RIPv: 26%). Furthermore, sites of chronic PV reconnection were found more frequently in the inferior parts of the LA as compared to the superior parts for the PV-LA conduction of all four pulmonary veins (PV-LA conduction of all four pulmonary veins). There was a significant difference in the number of PV-EAMs in patients who did not have a successful isolation of the PVs (17/30) minutes in patients treated with RF vs. 1.7 (1.3/2.2) hours and fluoroscopy time was n.s.). Phrenic nerve palsy occurred in 1 patient in the CBA-Group.

**Aims:** The new Cryoballoon generation (CBA) shows superior 2 year success rate in a LA area below 23cm² compared to RF- Ablation in pts suffering of persistent AF.

**Methods:** Intra-operatively mapping procedure during cardiac surgery (P3389).

K. Kettering, F. Gramley. University Hospital, Frankfurt, Germany

**Catheter ablation of atrial fibrillation: long-term outcome of radiofrequency catheter ablation for redo procedures after pulmonary vein isolation with the cryoballoon technique**

K. Kettering, F. Gramley. University Hospital, Frankfurt, Germany

Catheter ablation has become the first line of therapy in patients with symptomatic, recurrent, drug-refractory atrial fibrillation. Cryoballoon ablation has been shown to be a safe and effective technique for pulmonary vein isolation. However, the arrhythmia recurrence rate of 2 year follow-up is higher after cryoballoon procedures and there are no established strategies for redo procedures in these patients. Therefore, we have summarized our experience with two different strategies for redo procedures using radiofrequency catheter ablation (including an analysis of pulmonary vein re-isolation and re-connection patterns).

**Methods:** One hundred and ten patients (paroxysmal AF: 78 patients, persistent AF: 32 patients) had to undergo a redo procedure after initially successful circumferential PV isolation with the cryoballoon technique (Arctic Front Balloon, CryoCath/Medtronic). The redo ablation procedures were performed using a segmental approach or a circumferential ablation strategy (CARTO; Biosense Webster) depending on the intra-procedural findings.

**Results:** During the redo procedure, a mean number of 2.5 re-conducting PVs were identified (using a circular mapping catheter: 1 PV: 15 patients, 2 PVs: 46 patients, 3 PVs: 33 patients, 4 PVs: 16 patients). There was a higher incidence of chronic PV reconnections related to the left-sided PV ostia than to the right-sided PVs (LSPV: 28%, LIPV: 24%, RSPV: 22%, RIPv: 26%). Furthermore, sites of chronic PV reconnection were found more frequently in the inferior parts of the LA as compared to the superior parts for the PV-LA conduction of all four pulmonary veins (PV-LA conduction of all four pulmonary veins). There was no major complications in both redo groups.

**Conclusion:** In patients with an initial circumferential PV ablation using the cryoballoon technique, a repeat ablation procedure can be performed safely and effectively using radiofrequency catheter ablation. In most cases only a few re-conducting PV fibers were found and therefore, a segmental re-ablation approach seems to be sufficient in the majority of patients.

**P3389 | BEDSIDE**

**Reduction of fluoroscopy exposure during atrial fibrillation ablation using a novel fluoroscopy image integrated 3-dimensional electroanatomical mapping system**

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**Background:** We explored whether a novel fluoroscopy image integrated 3-dimensional electroanatomical mapping (F-EAM) system could result in a reduction of overall fluoroscopy time and radiation doses during the whole procedure of atrial fibrillation (AF) ablation.

**Methods and results:** Eighty patients (44 men, age 63±10 years, who underwent catheter ablation due to paroxysmal AF, were recruited consecutively in the current study. All patients were randomized 1:1 into two arms for AB ablation, using a conventional 3-dimensional electroanatomical (EAM) system or the F-EAM system, respectively. Fluoroscopy time (10.42 (IQR 8.45–12.46) vs. 1.45 (IQR 1.05–2.22) min; p = 0.001) and doses (2440 (IQR 1593–3091) vs. 652 (IQR 326–1440) cGy cm²; p = 0.001) in the EAM group were statistically significantly greater than those in the F-EAM group. The majority of fluoroscopy exposure was achieved after transseptal puncture, which was nearly zero-fluoroscopy exposure. In total, approximately 84% of fluoroscopy time and 73% of radiation doses have been reduced during AF ablation procedure using the F-EAM system, compared to using the conventional EAM system. However, procedure time did not differ significantly (1:39 (IQR 1:18–2:10) vs. 1:37 (IQR 1:17–1:50) min; p = 0.362).

**Conclusions:** AF catheter ablation using the novel fluoroscopy image integrated 3-dimensional electroanatomical mapping system was safe and resulted in a significant reduction of radiation exposure for patients and staff without complicating the workflow of the procedure. A near non-fluoroscopic catheter ablation could be performed without compromising acuity efficacy and safety.
Background: Transesophageal echocardiography (TEE) is routinely performed before atrial fibrillation (AF) transcatheter ablation to exclude left atrial (LA) or left atrial appendage (LAA) thrombi.

Purpose: To evaluate whether AF ablation can be performed without TEE in patients with LAA thrombi.

Methods: The prevalence of LAA thrombi was analyzed in 1,790 consecutive patients undergoing catheter ablation for persistent atrial fibrillation (pAF). The database included 1,790 consecutive patients undergoing catheter ablation for persistent atrial fibrillation (pAF) between January 2012 and December 2014. The prevalence of LAA thrombi and their incidence during the follow-up period were determined.

Results: The prevalence of LAA thrombi was 3.9% (72/1,790). The incidence of LAA thrombi during the follow-up period was 0.8% per patient-year. The incidence of LAA thrombi during the first year after ablation was 0.5% per patient-year, and it decreased to 0.1% per patient-year thereafter.

Conclusion: The prevalence of LAA thrombi before AF ablation is low, and the incidence during the follow-up period is also low. Therefore, TEE can be omitted in patients with LAA thrombi before AF ablation without increasing the risk of complications.

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rate in patients with PsAF and heart failure. The isolation of the coronary sinus is often required in these patients in addition to PV to increase long term freedom from atrial arrhythmias. We sought to evaluate safety and feasibility of coronary sinus isolation in patients with AF and CRT-D undergoing atrial fibrillation ablation.

Methods: Data of 64 consecutive patients with heart failure and CRT-D undergoing PV and coronary sinus isolation were prospectively collected. In all cases ablation occurred at least 5 months after CRT-D implant. In all cases a duodécapolar catheter via the internal jugular vein to map the right atrium and the coronary sinus to assess the presence of the LV lead. In all cases a 3.5 mm open irrigated catheter was utilized for ablation. In all cases a challenge test with high dose of isoproterenol was used to detect non PV triggers. Procedural and long term outcome were collected and analyzed and compared with a control group of 64 patients matched for sex, age and AF type that had CRT-D and underwent PV ablation alone.

Results: The study population had a mean age of 63.9±13.5 years, 53 (82.8%) patients were male and all patients had non-paroxysmal AF. Mean LA size was 4.8±5.8 cm and moderate to severe left atrial scar was present in 67% of patients. Non-PV triggers were detected in 48 (75%) patients and in all of them coronary sinus triggered sustained and non sustained arrhythmies. The mean power utilized to isolate the coronary sinus was 33±2 watts. No LV lead dislocation/damage occurred. One (1.6%) pericardial effusion not requiring surgical intervention occurred. After 15±6±7 months follow up, 42 (65.6%) patients under going CS isolation were recurrence free while 13 (20%) were recurrence free in the control group (log-rank test, p-value <0.001).

Conclusions: Coronary sinus isolation in addition to PV is feasible and safe in patients with CRT-D and AF and does not damage the LV lead. In addition it increases the freedom from AF at follow up in patients with AF and heart failure.

P3397 | BEDSIDE

Meta-analysis of Outcome of Catheter Ablation of Persistent Atrial Fibrillation Using Termination Mode as a Procedural Endpoint

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Background: Catheter ablation of persistent atrial fibrillation (PsAF) is an established therapeutic option for rhythm control in symptomatic patients. The efficacy and safety of pulmonary vein isolation among patients with paroxysmal atrial fibrillation is a well-defined procedural endpoint. In patients with PsAF, there is no consensus regarding the best procedural end-point. There is no consensus if termination of persistent AF by ablation is associated with lower risk of recurrence arrhythmia compared to procedural failure to terminate AF with the need for electrical cardioversion at the end of procedure. We performed a meta-analysis to assess safety and outcome of PsAF in patients based of AF termination mode (directly in SR, evolving into regular atrial tachycardia (AT) and subsequently into SR, after direct current (DC) cardioversion if AF persists after catheter ablation).

Methods and results: A systematic review was conducted in MEDLINE/PubMed and CochraneLibrary. In this meta-analysis were included randomized controlled trials including clinical trials and observational studies including patients with PsAF in which AF termination mode were detectable. Ablation using a stepwise ablation approach (pulmonary vein isolation, electrogram-guided and linear ablation) with the desired procedural endpoint being AF termination. Fourteen studies were selected, including 2786 patients. Mean follow-up was 25 (95% confidence interval 12-60) months. Overall complication rate was 3.9 (3.1-4.7%). Success rates were as follows. Overall (p<0.001): DC cardioversion, 23.5-26.2%; sinus rhythm 73.7%; sinus rhythm after AT, 67.0%. Single ablation: DC cardioversion, 21.4%; sinus rhythm, 68.8% (OR 1.54, 95% CI 1.06-2.24, P=0.02). Reablation: DC shock 29.0%; sinus rhythm, 77.2% (OR 1.53, 95% CI 1.07-2.20, P=0.02). There were no differences in the termination mode between sinus rhythm and evolving into regular AF and subsequently into SR.

Conclusions: In patients with PsAF, an ablation strategy aiming at AF termination is associated with freedom from arrhythmia recurrence in the majority of patients.

P3398 | BENCH

Anatomical and functional determinants of preferential rotor locations and stability in atrial fibrillation


Introduction: Rotor have been shown to drive atrial fibrillation (AF) and targeting these sites has emerged as an ablation strategy. However, factors that influence the stability and local triggers and observational studies including patients with PsAF in which AF termination mode were detectable. Ablation using a stepwise ablation approach (pulmonary vein isolation, electrogram-guided and linear ablation) with the desired procedural endpoint being AF termination. Fourteen studies were selected, including 2786 patients. Mean follow-up was 25 (95% confidence interval 12-60) months. Overall complication rate was 3.9 (3.1-4.7%). Success rates were as follows. Overall (p<0.001): DC cardioversion, 23.5-26.2%; sinus rhythm 73.7%; sinus rhythm after AT, 67.0%. Single ablation: DC cardioversion, 21.4%; sinus rhythm, 68.8% (OR 1.54, 95% CI 1.07-2.20, P=0.02). Reablation: DC shock 29.0%; sinus rhythm, 77.2% (OR 1.53, 95% CI 1.06-2.24, P=0.02). There were no differences in the termination mode between sinus rhythm and evolving into regular AF and subsequently into SR.

Conclusions: In patients with PsAF, an ablation strategy aiming at AF termination is associated with freedom from arrhythmia recurrence in the majority of patients.

P3399 | BEDSIDE

One Shot technologies to Pulmonary vein isolation (SPV) project: a standard clinical practice

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Background: Catheter ablation (CA) is used to treat asymptomatic atrial fibrillation (AF). “One Shot” (OS) catheters have been introduced to simplify CA procedure; the 2 most diffused approaches are cryoballoon ablation (CBA) and phased radiofrequency ablation (PRF).

Purpose: Aim of our research was evaluating in a large real world cohort, demographics, procedural data and outcomes.

Methods: 941 patients (76% male, median age 60) suffering from AF; underwent pulmonary vein isolation (PVIs) CA were prospectively followed; patient’s data were collected in ClinicalService® One Shot TO Pulmonary vein isolation (SPV) project. The cohort was divided in 2 groups according to energy source used: 794 (85%) patients treated with CBA and 146 (16%) with PRF.

Results: 70% of patients were affected by paroxysmal, 26% by persistent and 4% by long standing AF; at time of procedure 65% of the population was affected from >24 months AF; 4% of the cohort was treated as first line without trying any anti arrhythmic drugs (AADs); 31% underwent CA after only 1 AAD while the remaining patients received >2 AADs. Procedural details and acute success rate are reported in table. Overall, procedural complications were 4%, without any major complications, as well, at 12 months, 80% of patients were free from AF; AF related symptoms decreased from 87% at baseline to 21%.

Cryobalation

<table>
<thead>
<tr>
<th>Number of vein (mean)</th>
<th>Target: 3.9 Procedure: 144 minutes</th>
<th>Treated: 3.8 Fluoroscopy: 37 minutes</th>
<th>Acute Success: 97.6% LA Catheter: 72 minutes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 1</td>
<td>Balloon 23mm/28mm: 48/721</td>
<td>Achieve 15 mm / 20mm / NO: 50/605/113</td>
<td></td>
</tr>
<tr>
<td>Phased RF</td>
<td></td>
<td>1.8</td>
<td></td>
</tr>
</tbody>
</table>

Overall application (mean) 4.8

Success rate 2: 1–5

Conclusion: Among OS technologies, CBA is the most widespread ablation technique; Procedure times, acute and mid-term success rate as well as procedural related complications confirm that both technologies are safe and effective, with positive effect on AF related symptoms.

P3400 | BEDSIDE

Impact of continuous monitoring of the pulmonary venous pressure on the acute results of cryoablation in atrial fibrillation


Background: A new technical development, the cryoballoon ablation (cryoablation...
P3402 | BEDSIDE
Prevention of phrenic nerve palsy during cryoballoon ablation in patients with atrial fibrillation: comparison between percutaneous and endovascular electromagnetic monitoring technique
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Introduction: Right phrenic nerve palsy (PNP) is the most common complication of cryoballoon ablation (CBA). Diaphragmatic electromyography (DE) can predict PNP. DE techniques have used the CMAP amplitude to compare the efficacy and safety of a percutaneous and an endovascular monitoring technique (PMT, EMT).

Methods: The study includes 21 patients (13 males). The CBA was performed using the Circular Multi-Electrode Ablation System (MEA). During right diaphragmatic CBA with PMT and EMT is feasible. Right nasal pharyngeal CBA, the PN was paced at 60 beats per minute. The diaphragmatic compound motor action potential (CMAP) amplitude was measured simultaneously using a PMT and EMT. To record right diaphragmatic CMAPs percutaneously, 2 standard surface electrodes were positioned on the thorax and spaced 16 cm apart, one 5 cm above the xiphoid process and the second along the right costal margin. The endovascular measurement was performed via a quadrupolar catheter positioned in a subdiaphragmatic hepatic vein. The CMAPs were recorded continuously during CBA. If a 30% drop in CMAP amplitude was observed, the procedure was discontinued.

Results: Reliable recording of CMAP amplitude was feasible in 20 patients. At any 30% reduction of CMAP amplitude, EMT could be applied in another patient as a result of failed catheter placement in the hepatic veins. The mean values of CMAP amplitudes were comparable during PMT and EMT (1.10 vs. 1.07 mV pre CBA, 0.97 vs. 0.96 mV post CBA, p = ns). In contrast the CMAP amplitude variation was significantly different during CBA. In contrast, respiratory movements did not influence CBA. Unlike surface recording, overlay of CMAP amplitudes with ECG didn’t occur using EMT. In 2 patients 30% reduction cutoff was reached and CBA was discontinued. The reduction of CMAP amplitude was detected simultaneously with PMT and EMT. Nevertheless, one patient suffered from PNP, however recovered completely within 2 days. The second patient had no impairment of diaphragmatic movement. No complication related to phrenic nerve monitoring were observed.

Conclusions: Recording of CMAP during PMT and EMT is safe and feasible during CBA. The CMAP amplitude does not vary during respiration and is not superimposed by the ECG using EMT. The assessment of an optimal cut-off to discontinue CBA needs further investigations. CMAP monitoring should be used in daily routine to prevent permanent PNP.

P3403 | BEDSIDE
Acute procedural and clinical outcome comparison using the first- and second-generation cryoballoon: inside a large cohort of data from derived real world multicentric experience
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Background: Limited data are available on safety and efficacy of second-generation cryoballoon compared to first-generation cryoballoon (CB1). Purpose: We aimed to evaluate in a large cohort of patients treated in real world clinical settings, demographics, procedural data and outcomes comparing CB2 to first-generation cryoballoon (CB1).

Methods: Between April 2012 to December 2014, 581 patients (74% male, 59±10 years, 78% paroxysmal AF, mean left atrial diameter, 41±6 mm) suffering from AF were enrolled. Four RCTs were reviewed for an overall of 830 patients included of which, 709 (85.4%) had paroxysmal AF and 121 (14.6%) persistent AF. The per-95% confidence interval absolute risk difference of any AT recurrence in the MEA group was 3%, meeting criteria for non-inferiority (risk difference −3%; 95% CI −10% to 3%; relative risk 0.92; 95% CI 0.92–1.09; I2=0%). Procedural time was significantly reduced during MEA procedures (weighted mean difference −54.3 minutes; 95% CI −83.7 to 25.3; p < 0.001; I2=95%). Non-significant reductions in fluoroscopy time (weighted mean difference −6.42 minutes; 95% CI −13.8 to 0.96; p = 0.09; I2=95%) and adverse events (RR 0.47; 95% CI 0.21 to 1.08; p = 0.07; I2=0%) were detected during MEA procedures.

Conclusion: In patients with primarily PAF, duty cycled pulmonary vein isolation was non-inferior and appears to be superior to conventional RF ablation of PAF recurrences from AF. Multi-electrode ablation is associated with a favorable safety profile, and is comparable to CPVI. Further larger RCTs are needed to determine which technology is associated with the lowest recurrence and adverse event rate.
freedom from AF at 12 months FU for patients with paroxysmal indication, con-
sidering a blanking period (BP) of 3 months, was 67.8% (CI: 53.1–78.8%) in CB1
group and 77.8% (CI: 68.6–84.7%) in CB2.

Conclusions: The novel cryoballoon Arctic Front Advance (CB2) has proven to
achieve, in a large clinical standard setting, significantly faster PVs times in com-
parison with the first-generation balloon, results also in lower acute procedural
complication rates and a 78% 1-year freedom from AF.

Conclusion:

Control group (p=0.19).

duration was identified in 1/13 in Voltage guided ablation group and 5/20 in the

control group (p=0.19). Associated with an increase in bleeding complications.

However this was not

As heparin dosage was led by the values of the ACT, patients with apixaban
generated TPT as compared to rivaroxaban. However this was not

in aPTT and ACT already before application of heparin. In contrast the effect of

on global coagulation assays. This has to be taken into account considering a blanking period (BP) of 3 months.

P3404 | BEDSIDE
Voltage guided pulmonary vein isolation: preliminary results of short
term outcome
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Maximum voltage guided ablation has been described to identify putative muscle
circles in the cavotricuspid isthmus. Similarly, we postulated that voltage
mapping of pulmonary veins and their respective antral regions will help identify
critical sites to achieve PV isolation.

Aim: To investigate the intra procedural efficacy of voltage guided CPVA strategy
with short-term follow-up.

Methods: We included 33-age/ sex-matched cohorts from our centre that under-
went PV procedure. Thirteen patients, (6 female) had voltage guided PVI where RF started at the highest voltage area recorded at the antrum. This group was randomized to 20 controls, (7 female) which underwent circumferential pul-
monary vein isolation using standard (CSI) technique. Each patient had at least 3
secual lesions encircling each antrum. A 3-dimensional mapping system and circumferential mapp-
ing catheter were used. Voltage mapping using NAVX ensite (ST. Jude) software
with coronary sinus pacing around left and right pulmonary veins recorded. CPVA
ablation was then performed in regions of highest voltage in the antral regions in a
segmental fashion. The procedural endpoint was bidirectional block in each PV.

Results: There were 33 patients, (mean age 59±16 years; 13 female; left atrium 63±21 mm; left ventricular ejection fraction 61±6%). A mean of 54±12 voltage points per PV antrum were recorded. The mean of maximum voltages areas per
antrum was 3±1.1 areas. Mean voltages for RVPs and LVPs were 1.7±0.1 and
1.9±0.2 respectively, while RF was (40.9±17.4 vs. 48.1±15.5), Fluoro (29.2±0.4
vs. 33.6±17.7) and procedure times (233.8±36.1 vs. 248.8±53.6) for the voltage
ablation were not different between control group (p=0.05). Voltage guided ablation
showed no superiority on widely used WACA in both isolation time and delay in
PV potentials during the procedure (p=0.05).

Full 24-hour holters were performed at 12 weeks in all pts. Recurrent AF >30sec
duration was identified in 1/13 in Voltage guided ablation group and 5/20 in the
control group (p=0.19).

Conclusion: A voltage guided CPVA strategy was highly efficacious in identifying
critical points for PV isolation and short term freedom from AF recurrence has
been promising. Further studies are required to validate this approach particularly if
coupled with catheter contact sensing technology.

P3406 | BEDSIDE
Relationship of lungs to left atrium in patients undergoing atrial
fibrillation ablation
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Background: The anatomic relationship between left atrium (LA) and lung tissue
(LT) has not been characterised. This may be of relevance to patients undergoing
radiofrequency ablation (RFA) for Atrial Fibrillation (AF).

Purpose: To describe the relationship of LT to LA in a cohort of patients under-
going RFA for AF.

Methods: We analyzed clinical data and CT Coronary Angiograms (CTCA) of
100 patients who underwent CTCA prior to RFA for AF. We measured distances
between LT and bronchi to LA regions commonly targeted during RFA of AF using
Osiris DICOM viewer.

Results: 100 patients (71 male, age 60±8 yrs, 46% paroxysmal, mean LA axial
area 25±5.5 cm²): 23% with LA enlargement, 33% with hypertension, 24% with
structural heart disease, 15% with obstructive coronary disease and 0% with ob-
structive lung disease. The right PVs (RPVs) but not the left PVs (LVPs) were
closer to LA compared to LT. The endocardial of posterior RPV antrum was 5.5 mm
from LT in 94%, minimum distance from LA endocardium to LT was 1.2±0.7 mm.
The right inferior PV ostium was <5 mm from LT in 94% (mean distance 2.4±0.8
mm). The right superior PV ostium was <5 mm from RLL in 29% (mean distance
3.7±0.9 mm). LT was <5 mm from the carina between RPVs in 83% (mean dis-
tance 3±1.1 mm). The mitral isthmus was <5 mm from LT in 5%. The LPV antrum
was <5 mm from LT in just 3% as the constant presence of the descending tho-
racic aorta close to the posterior LPV antrum prevented close contact with LT in
most patients. The bronchi were <5 mm from LA in 5 patients.

Conclusion: The lungs are intimately related to the LA in patients undergoing
RFA for AF. Whether LA RFA causes pulmonary complications merits further
study.

P3405 | BEDSIDE
Ablation of atrial fibrillation II / Ablation of atrial fibrillation III

The anticoagulant effect of heparin during radiofrequency ablation
(RFA) in patients taking apixaban and rivaroxaban
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Background: Measuring the anticoagulant effect of heparin during radiofre-
quency ablation (RFA) in patients taking apixaban and rivaroxaban is challeng-
ing, since the activated coagulation time (ACT) does not seem to reflect the true
anticoagulant activity of these drugs. We therefore evaluated various coagula-
tion assays and compared the values with anti-factor Xa activity in order to better
guide intraprocedural heparin administration.

Methods: The study included 96 patients (mean age 61±12 years) who under-
went left atrial RFA procedures. All patients received 20 mg rivaroxaban once or 5
mg apixaban twice daily four weeks prior to the procedure. Dosage was modified on
the day of the procedure to 10 mg rivaroxaban or 2.5 mg apixaban twice daily.
During RFA, heparin i.v. was given to maintain an activated clotting time (ACT) of
270–300 seconds. Blood samples were before heparin administration, after 10,
60 and 360 minutes. Thromboplastin time (TPT), activated partial thromboplastin
time (aPTT), ACT and anti-factor Xa were measured.

Results: The anticoagulant effect of rivaroxaban was associated with an increase in
aPTT and ACT already before application of heparin. In contrast the effect of
apixaban was associated with an increase in TPT as compared to rivaroxaban.

As heparin dosage was led by the values of the ACT, patients with apixaban
received more heparin (IU/kg). This resulted in elevated anti-FXa levels in the
patients receiving apixaban as compared to rivaroxaban. However this was not
associated with an increase in bleeding complications.

Conclusion: We found variable responses of different FXa inhibitors rivaroxaban
and apixaban on global coagulation assays. This has to be taken into account when performing ACT guided RFA.

P3407 | BEDSIDE
Loss of pace capture on the ablation line for pulmonary vein isolation
can improve the clinical outcome of catheter ablation for atrial fibrillation
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Background: Reconnections of isolated pulmonary vein (PV) are the major
cause of recurrence after ablation for atrial fibrillation (AF). In this study, we inves-
tigated the possibility that additional ablation on the ablation lines for PV isolation
(PVI) to obtain unexcitability can reduce the reconnections of isolated PVRs (PVRs)
and improve clinical outcome of AF ablation.

Methods: A total of 120 patients who received initial ablation for AF including
46 non-paroxysmal AF (38%) were participated in this study. Patient population
was divided into two group; pace-and-ablate group (n=60) and control group
(n=60). Patients in pace-and-ablate group received pace-and-ablate procedure with
radiofrequency ablation to obtain unexcitability by bipolar pacing at an output
10 mA and 2ms pulse on the ablation lines for PVI. In the both groups, we
routinely checked the presence or absence of time-dependent PVRs more than
20 minute after the last ablation for PVI or pace-and-ablate procedure, and ab-
lated to eliminate them. And then, we also checked that of ATP-dependent PVR
by injecting 0.4mcg/kg of adenosine triphosphate, and tried to eliminate all these
dormant conductions. We set a blanking period for 3-month, investigated the initial
clinical outcome 6 month after procedure, and compared it between the groups.

Results: PVRs were less frequent in pace-and-ablate group than in control group
significantly (30% vs. 57%, p=0.0057). All the PVRs except ATP-dependent one in
pace-and-ablate group were successfully eliminated. Initial clinical outcome was
significantly better in pace-and-ablate group than in control group (recurrence free
rate; pace-and-ablate group vs. control group, 86% vs. 72%, p=0.033).

Conclusion: The pace-and-ablate procedure after PVI could reduce the inci-
dence of PVR during procedure, and could improve the initial clinical outcome
even in AF patients who received ablation of time-dependent and ATP-dependent
PVRs after PVI.
Background: Some earlier reports have suggested pulmonary vein isolation (PVI) by catheter ablation can cure atrial fibrillation (AF) in patients on chronic hemodialysis (HD). However, because advanced renal failure is often linked with extensive systemic vascular diseases, patients on chronic HD may be more susceptible to serious periprocedural complications of AF ablation than others.

Methods and results: Japanese Heart Rhythm Society (JHS) and Japan Society for Electrophysiology (EP) centers registered the data of patients who underwent catheter ablation for AF in designated four months from 2011 to 2013. In this report, we assessed the incidence and predictors of ischemic stroke and bleeding complications during AF ablation.

Results: Two hundred and four EP centers reported the data of 4422 AF ablation cases (age: 62.5±10.6 years; male: 76.1%; paroxysmal AF: 64.6%). Bleeding complications and ischemic stroke occurred in 107 subjects (2.4%). These complications include 52 cases of peri-procedural, which needed drainage, 48 cases of massive bleeding at the puncture site, seven cases with ischemic stroke. These complications occurred in five of 59 patients on HD (8.5%), while they were seen in 102 of other 4363 patients (2.3%, P<0.005). Univariate analysis revealed that these complications were associated with higher age (complications>90; 62.4±10.7 years, P<0.005), chronic HD (4.7% vs. 1.3%, P<0.005), higher CHA2DS2-VASc score (2.1±1.5 vs. 1.7±1.4, P<0.02), structural heart disease (20.6% vs. 13.8%, P<0.05), and procedures performed without a three-dimensional (3-D) mapping system (82.2 vs. 79.7%, P<0.05), and deep sedation (58.1% vs. 45.8%, P<0.05). None of sex, type of AF, a previous ablation session, left ventricular ejection fraction, left atrial fraction, or CHADS2 score affected the incidence of complications. Additional ablation other than PVI and use of a percutaneous catheter was associated with a decreased rate of complications. Multivariate regression analysis showed that HD (Odds ratio [OR] 3.93 [95%: 1.50–10.28], P<0.01), disuse of 3-D mapping system (OR 0.34 [0.20–0.50], P<0.0001), and deep sedation (OR 1.48 [1.00–2.18], P<0.05) were independent predictors of adverse events.

Conclusions: Thus, bleeding complications and stroke occurred more frequently when AF ablation is performed without the aid of 3-D mapping system, under deep sedation, and in patients on chronic HD. We conclude that HD is one of predictive factors of complications related with AF ablation.

P3411 | BEDSIDE
Immediate and medium-term outcomes of cryoballoon in patients with paroxysmal and persistent atrial fibrillation: A large cohort of data derived from real world multicentric experience

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Background: Pulmonary vein (PV) isolation with cryoballoon (CB) has been recently proposed also for the treatment of persistent atrial fibrillation (PER).

Purpose: In a large cohort of patients treated in real world clinical settings, we aimed to evaluate demographics, procedural and outcomes data in patients suffering from PER versus Paroxysmal AF (PAX).

Methods: From April 2012 to January 2015, 532 pts without structural heart disease (71% male; 59±10 years), prospectively followed, underwent PV cryoballoon. Data were collected in ClinicalService® framework One Shot TO Pulmonary vein isolation (1STOP) project. Cohort was divided into 2 groups according to AF type as defined in the Consensus Statement document: 103 (19%) PER and 429 (81%) PAX.

Results: PER patients were significantly more compromised from cardiac predictors (advanced NYHA, history of heart failure, mitral valve disease) and procedures performed without a three-dimensional (3-D) mapping system were risk factors for a lower success rate and a higher rate of complications. Univariate analysis revealed that these complications were associated with: higher age (>90; 62.4±10.7 years, P<0.005), chronic HD (4.7% vs. 1.3%, P<0.005), higher CHA2DS2-VASc score (2.1±1.5 vs. 1.7±1.4, P<0.02), structural heart disease (20.6% vs. 13.8%, P<0.05), and procedures performed without a three-dimensional (3-D) mapping system (82.2 vs. 79.7%, P<0.05), and deep sedation (58.1% vs. 45.8%, P<0.05). None of sex, type of AF, a previous ablation session, left ventricular ejection fraction, left atrial fraction, or CHADS2 score affected the incidence of complications. Additional ablation other than PVI and use of a percutaneous catheter was associated with a decreased rate of complications. Multivariate regression analysis showed that HD (Odds ratio [OR] 3.93 [95%: 1.50–10.28], P<0.01), disuse of 3-D mapping system (OR 0.34 [0.20–0.50], P<0.0001), and deep sedation (OR 1.48 [1.00–2.18], P<0.05) were independent predictors of adverse events.

Conclusions: Thus, bleeding complications and stroke occurred more frequently when AF ablation is performed without the aid of 3-D mapping system, under deep sedation, and in patients on chronic HD. We conclude that HD is one of predictive factors of complications related with AF ablation.
for AF recurrence, while the annual rate of cardiovascular hospitalization was significantly lower in PAF vs PER (Rate*100pt/years respectively: 0.4 vs 5.6;IRR: 15.3 (95% CI 7.3–31.8) p<0.001

Conclusions: Cryoablation approach is acutely safe and efficient both in PER and PAF patients. However, a lower incidence of AF recurrence was documented in PAF at the mid-term follow up thus, suggesting that a more diffuse ablation strategy and the timing of cryoaablation have an impact on the clinical outcome.

### P3412 | BEDSIDE

Comparison between multi electrodes mapping with the flower catheter and point-by-point technique for multiple atrial tachycardias in the context of atrial fibrillation ablation

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**Introduction:** Activation mapping can be challenging and time-consuming in case of multiple atrial tachycardias (ATs). We report our experience with multi-electrodes mapping using the flower catheter PTY (Pentaray, Biosense) for ATs in the context of atrial fibrillation (AF) ablation.

**Methods:** All procedures using the PTY for AT, either as an initial approach or after or during persistent AF ablation were analyzed. A control group of patients (pts) with AT using the point-by-point technique (PBP) was used for comparison of mapping times. Procedure time indexed to the number of ATs per patient (IPT) and fluoroscopy time were also assessed.

**Results:** 16 pts (52.8±11 y) with a mean number of 2.1 ATs per patient, were included. 44±520 points within 26±14 min were acquired per AT in the PTY group and 42±18 points (p<0.0001) within 33±25 min (p<0.04) in the PBP group (n=16; 63,±14 y; 1.42 ATs per patient). Owing to far better mapping resolution, all AT's ishthums (n=25) were easily identified and ablated in the PTY (100%) versus in only 19/22 (86%) in the PBP group. IPT and fluoroscopy times were not significantly different between the two groups: respectively 170±84 min versus 188±68 min (p<0.14) in the PBP group and 13±18 min versus 15±10 min (p<0.56) in the PBP group. 2 patients had a recurrence in each group after a mean follow-up of 6 months.

**Conclusion:** Multi Electrodes Mapping is acutely faster and more accurate in multiple AT's ablation when compared to the PBP technique.

### P3413 | BEDSIDE

Remote magnetic catheter navigation versus conventional ablation in atrial fibrillation ablation: comparing efficacy, safety and fluoroscopy time


**Background:** Percutaneous transcatheter radiofrequency ablation with remote controlled magnetic navigation has been shown to be effective and safe in complex arrhythmia ablations and allows reduction in fluoroscopy time.

**Aims:** We compare the acute success rate, acute complication rate, fluoroscopy and procedural times between remote controlled magnetic navigation guided ablation versus conventional catheter ablation of atrial fibrillation.

**Methods and results:** Catheter ablation for atrial fibrillation was performed utilizing remote magnetic controlled navigation in 208 consecutive patients and manually in 259 patients. Acute procedural success was seen in 99.5% (207 of 208) of patients who underwent remote magnetic navigation ablation compared to 96.9% (251 of 259) of patients in the manual catheter ablation group (p=0.039). Comparing catheter related complications, there was a non-statistically significant trend towards lower catheter/ablation related complications in the remote navigation group over 6 months follow-up data (freedom from any atrial tachycardia or AF episodes). In more than 40% of procedural time, patients showed BIS levels defined as an index <45 which has been found to increase anesthesis related risk.

**Results:** 22/30 (73%) of patients had a recurrence in each group after a mean follow-up of 170±84 min versus 188±68 min (p<0.14) in the PBP group and 13±18 min versus 15±10 min (p<0.56) in the PBP group. 2 patients had a recurrence in each group after a mean follow-up of 6 months.

**Conclusions:** Multi Electrodes Mapping is acutely faster and more accurate in multiple AT’s ablation when compared to the PBP technique.

### P3414 | BEDSIDE

Monitoring of sedation depth with bispectral index during ablation of atrial fibrillation - are we sedating too deep?


**Introduction:** Procedural safety of propofol sedation administered for catheter ablation (CA) of atrial fibrillation (AF) has been demonstrated but remains challenging in some patients. Bispectral Index (BIS) monitoring allows measurement of sedation depth with a BIS index <45 which has been found to increase anesthesis related risk.

**Purpose:** We sought to determine the sedation levels with BIS monitoring in propofol sedation during AF ablation.

**Methods:** 50 consecutive patients (pts) (mean age 63±11 years, 42 male (69%), BMI 27.6±4.4 kg/m², mean CHA2DS2-VASc-Score 2.4±1.5) undergoing AF ablation were included. Deep sedation was performed with propofol (20 mg/ml). Fentanyl and midazolam boli were administered at operator’s decision during the procedure. Pts were monitored with pulse oximetry, noninvasive blood pressure, continuous ECG and BIS monitoring (BIS VISTATM, Covidien, Mansfield, MA, USA). BIS index was measured continuously every minute during the procedure from the beginning of sedation to extraction of sheaths and was blinded to the operator and staff. Low BIS levels were defined as an index <45 over a minimum of 3 consecutive minutes.

**Results:** Propofol was commenced in all patients at a mean infusion rate of 0.096±0.044 mg/kg/min. Additional fentanyl (mean 0.04±0.02 mg) and midazolam (mean 0.05±0.12 mg) bolus were administered. Mean procedural duration was 138.9±40.1 minutes. Mean BIS level was 48.4±7.7. Cumulative percentage of low BIS (<45) mean 36.8±7.0 was found in 44.0±28.8% of procedural time. No case of respiratory depression occurred requiring assisted ventilation occurred. Persistent hypotension resulted in propofol cessation and switch to midazolam/fentanyl in 1 patient (1%).

**Conclusions:** The use of BIS monitoring provides improved information on sedation depth during CA for AF. In more than 40% of procedural time, patients showed BIS levels <45 indicating a deep narcotic state and deeper sedation levels than recommended. Whether BIS guiding monitored during AF ablation procedures improves procedural outcome needs to be investigated.

### P3415 | BENCH

Randomized comparison of catheter ablation of atrial fibrillation with or without non-fluoroscopic sensor-based catheter navigation

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**Introduction:** Nonfluoroscopic sensor tracking (NFST) within precorded x-ray loops offers the potential to perform catheter ablation of atrial fibrillation (AF) almost free from fluoroscopy use.

**Purpose:** Randomized comparison of standard AF ablation with or without NFST application.

**Methods:** Patients with AF were randomized into two groups before scheduled radiofrequency ablation: (1) catheter navigation using NFST together with established mapping systems and fluoroscopy, (2) control group with standard electroanatomic mapping system and fluoroscopy alone. Procedures were performed in the same lab by 2 experienced operators altogether. Moreover, the same strategies (circuitual pulmonary vein isolation followed by voltage mapping + targeted substrate modification) and ablation catheters were applied.

**Results:** A total of 80 patients (48 men, mean age 60 years, 44 patients with paroxysmal AF) were equally randomized into both groups. Clinical parameters between both groups were similar. Procedural parameters and preliminary 6-months follow-up data (freedom from any atrial tachycardia or AF < 30 sec) can be derived from table.
Ablation of atrial fibrillation III / Ablation of atrial fibrillation IV

P3416 | BEDSIDE
Catheter ablation of persistent AF: anatomically-based circumferential PV ablation in combination with a potential-guided segmental approach to achieve PV isolation - long-term FU results (6 years)
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Background: Catheter ablation has become the first line of therapy in patients with symptomatic, recurrent, drug-refractory atrial fibrillation. However, catheter ablation of persistent AF is still a challenge. Various rather complex ablation strategies exist and their results are not very favourable.

Therefore, the aim of our study was to perform a well-defined reasonable approach to catheter ablation of persistent AF. The strategy consisted of a circumferential pulmonary vein ablation in combination with a potential-guided segmental approach to achieve complete PV isolation and a linear lesion at the roof of the left atrium.

Methods: A total of 260 patients (154 men, 106 women; mean age 60 years (SD ± 9 years)) with symptomatic persistent AF were enrolled in this study. All patients underwent catheter ablation of persistent AF using the above-mentioned approach (electro-anatomical mapping system). Additionally, catheter ablation of the mitral isthmus and the right atrial isthmus was performed in selected cases. In all patients, a 3-D TEE was performed before the procedure to evaluate the PV morphology.

After discharge, patients were scheduled for repeated visits at the arrhythmia clinic at 1, 3, 6, 12, 24, 36, 48, 60 and 66 months after the ablation procedure.

Results: The ablation procedure could be performed as planned in all 260 patients. Ninety patients had to undergo a repeat ablation procedure, so that a total of 350 procedures were evaluated.

An additional linear lesion was created at the mitral isthmus in 6 patients during the initial procedure and in 20 patients during the second procedure. Catheter ablation of the right atrial isthmus was performed in 20 patients during the first procedure and in 15 additional patients during the redo procedure.

Sixty-five out of 260 patients (25.0%) experienced an arrhythmia recurrence within the first 3 months after ablation requiring an electrical cardioversion. At 66-month follow-up, analysis of a 168-hour ECG recording revealed no evidence for an arrhythmia recurrence in 158/260 patients (60.8%). In 78/260 patients (30.0%), atrial fibrillation recurred within the first 3 months. In 32 patients, atrial fibrillation recurred between the 4th and 6th month. In 3 more patients, atrial fibrillation recurred between the 6th and 12th month. In 1 patient, atrial fibrillation recurred 19 months after the initial procedure.

Conclusions: Catheter ablation of persistent AF can be performed safely and effectively using this ablation strategy (especially in patients with short-lasting persistent AF (< 3 months)).

P3417 | BEDSIDE
Safety and feasibility of atrial fibrillation ablation in biological valve patients while on uninterrupted novel oral anticoagulant
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Introduction: Biological valve replacement (BVR) with warfarin therapy is associated with a higher risk of thromboembolic complications. In recent years, novel oral anticoagulants (NOACs) such as dabigatran, rivaroxaban and apixaban have been introduced in the market to replace warfarin. We sought to report the safety and feasibility of performing catheter ablation of AF in patients with BVR while on uninterrupted NOACs.

Methods: 105 consecutive patients with a biological valve undergoing AF ablation at different institutions have been enrolled in this study. All patients were anticoagulated for at least 4 weeks prior to ablation with one of the NOACs. All patients underwent the ablation with an uninterrupted anticoagulation strategy. All patients underwent a TEE prior to the procedure. When ablation included the mitral valve, a transesophageal echocardiography was performed during the procedure, and as per the ISKOP guideline, the International Shocking Point of Termination (ISPT) was utilized, and if needed, a trial of cardioversion was performed.

Results: The majority of patients underwent replacement (61, 58%), while mitral valve was replaced in 41 (39%) pts, which did not differ from control (59 [56%], 43 [41%]; mitral and tricuspid valve respectively). Baseline characteristics were similar between NOAC (age=63.3±11.4, male=68%) and control group (age=66.7±11.1, male=68%). Majority of the patients had non-paroxysmal AF (71 [68%] NOAC and 73 (69.5%) control=0.8). The CHADS2 Score was ≥2 in 74 (71.0%) NOAC and 71 (68%) control (p=0.7) patients. Predominantly pts underwent ablation with uninterrupted rivaroxaban (74 [70%], last dose taken the night prior the procedure), while the remaining 31 pts (30%) underwent the ablation while on apixaban (last does taken the morning of the procedure). Overall, 2 complications (both groin hematoma) were observed periprocedurally in both groups. No stroke/TIA was reported.

Conclusion: Catheter ablation of atrial fibrillation with uninterrupted NOACs in patients with biological valves is feasible and safe.

P3418 | BEDSIDE
Stepwise approach ablation versus pulmonary vein isolation in patients with paroxysmal atrial fibrillation: randomized controlled trial
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Background: Pulmonary vein isolation (PVI) is a central procedure for the treatment of paroxysmal atrial fibrillation (PAF). However, in patients with PAF and structural atrial disease, PVI ablation may fail and cause progressive atrial remodeling, often leading to persistent/permanent atrial fibrillation.

Objectives: We performed a prospective, single-blind, randomized controlled study to report the efficacy of the two strategies of PAF ablation in reducing the recurrence rate of atrial fibrillation (AF) or atrial tachycardia (AT).

Methods: Participants were randomized to perform either a first catheter ablation either through PVI or through PVI plus substrate modification based upon stepwise approach (CFAEs and linear ablation). Data were recorded at 3, 6 and 12 months after both ablations. The subjects who experienced AF/AT recurrence were assigned to repeat the same technique of the first ablation.

Results: 150 subjects were enrolled (mean age 62.8±8.7y; 61.3% males; 69.3% hypertensive; AF mean duration 10.7 months); 75 patients in each group.

The AF/AT recurrence rate significantly differed by ablation type at all time points and after both procedures. At the end of the target follow-up (12 months), the above rates were 46.7% (35/75) and 26.7% (20/75), respectively (p<0.001). AT occurred more frequently in patients treated with the stepwise procedure: 10/20 AT occurred in the stepwise group vs 4/35 in the PVI group. Adjusting for several potential confounders, the hazard ratio of 12-month AF/AT recurrence after the first ablation was 0.53 (95% Confidence Interval: 0.30-0.91) for those converted usingstepwiseablation. The overall rate of complication was 10.0% of the 150 patients after the first ablation and 5.8% of the 52 patients after the redo ablation. No significant differences in the rate of complications were observed across the 2 groups. The addition of CFAE and linear ablation significantly prolonged procedural time: in the first procedure, 105±13 minutes were required for PVI alone and 148±127 minutes for the stepwise ablation (p<0.001). Both fluoroscopy and radiofrequency times were significantly longer in the stepwise ablations group (p<0.001). Similar results were observed during the second ablation.

Conclusions: In conclusion, the stepwise ablation relevantly enhanced the clinical outcome of PAF control strategy. However, this approach had to add more overall procedure and/or fluoroscopy times and more episodes of AT as compared PVI approach.

P3419 | BEDSIDE
Mitrail isthmus ablation with a circular mapping catheter positioned in the left atrial appendage as a reference for complete conduction block

Purpose: In cases with perimetal flutter (PMFL), to create complete conduction block in the mitral isthmus (MI) is mandatory but still challenging. We investigated the feasibility of making linear lesions in the MI just beneath the neck of the left atrial appendage (LAA) under the guidance of the activation time in the LAA during pacing from the coronary sinus (CS). Methodology: This study consisted of 75 patients undergoing MI ablation (76 male, 61±8.1 years, Persistent AF: n=60). After a circular mapping catheter was positioned at the neck of the LAA, the MI ablation was performed aimed at the earliest activation site of the LAA during pacing from the CS. The ablation catheter was equipped with a 3.5mm irrigated tip and utilized through a sterable sheath with a radiofrequency (RF) power of 30W. When ablation during CS pacing was not successful, an RF delivery during LAA pacing was applied targeting the earliest activation site just below the mitral isthmus line. If the endocardial approach failed to create conduction block at the MI, an RF application inside the CS was attempted.

Results: With the endocardial approach, acute success was achieved in 54/82 patients (66%). Additional epicardial ablation from the CS was performed in 26/82 endocardially unsuccessful patients and conduction block in the MI was achieved in 20/26 patients (77%). Overall, complete MI conduction block was achieved in 52 patients (91%). In the 7 failed cases, 4 were suspected to have persistent conduction via the vein of Marshall. No complications were observed.

Conclusions: Creating linear lesions just beneath the neck of the LAA was highly successful.

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successful under the guidance of a circular mapping catheter in the LAA using a steerable sheath. An RF application from the CS was needed in less than half of the cases.

P3420 | BEDSIDE
Esophageal temperature monitoring during atrial fibrillation ablation: sensitivity of a conventional probe to detect significant temperature increases


Luminal esophageal temperature (LET) monitoring during radiofrequency (RF) delivery at the left atrium posterior wall has been advocated to detect and prevent esophageal damage and is regularly used in many centres. However, the esophagus is a wide anatomical structure and conventional temperature probes may be limited to detect distant temperature rise or may remain in the lumen with poor contact with the esophageal wall.

Methods: 32 (68 y, 21 male) consecutive patients (P) with atrial fibrillation (AF) who underwent pulmonary vein isolation (PVI) by RF application were prospectively enrolled in the study. A conventional esophageal probe (CEP, sensitherm, SJM) with 3 temperature sensors was used in all patients. In addition, a custom made steerable probe (SEP) with a distal temperature sensor was introduced in the esophagus. RF was delivered by point-by-point application all around the 4 pulmonary veins (PV) ostia from an irrigated tip ablation catheter (30W, 48°C, 17 ml/min). Both probes were frequently relocated during the ablation procedure trying to achieve the closest distance to the RF application site. The procedure was blinded and not guided by LET monitoring and RF was delivered at each target site for at least 30 seconds irrespectively of the detected LET.

Results: No differences in LET were detected at baseline by the SEP (36.2±0.7°C) and the CEP (35.9±0.5°C). ETS > 37°, > 40° and > 45°C were detected in 100%, 100% and 56.7% respectively of P with the CEP but only in 93.1%, 37.9% and 0% of P with the CEP (χ², P<0.05, P<0.001 and P<0.001). The number of PVs showing LET > 37°, > 40° and > 45°C by the CEP vs the SEP during RF application were 2.7±1 vs 1.6±0.8 (P<0.001), 1.8±0.8 vs 0.8±0.01 (P<0.001) and 0.9±0.8 vs 0 (P<0.001) respectively. Maximum LET was significantly higher when detected by the SEP than by the CEP: 45.5±2.7°C (rank 40.1-49.0) vs 39.7±2.1°C (rank 36.8-44.0) respectively (P<0.001). The maximum LET was detected in a left PV in 70% of P by the SEP and in 56.7% of P by the CEP. After excluding from the analysis common pulmonary trunks, the maximum LET was detected in an inferior PV in 81.8% of P and 77.3% of P by the SEP and the CEP respectively.

Conclusion: LET during RF delivery for PVI is underestimated by CEP. Rises in LET respectively.

P3421 | BEDSIDE
Echocardiographic assessment of atrial and ventricular remodelling after hybrid epicardial transdiaphragmatic and percutaneous endocardial radiofrequency ablation of persistent atrial fibrillation

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Aims: An endoscopic transdiaphragmatic epicardial ablation procedure with combined percutaneous endocardial radiofrequency ablation - hybrid procedure is potentially curative treatment option for patients with persistent atrial fibrillation (AF). Long-term effects of ablation lesions and/or arrhythmia elimination on atrial and ventricular remodelling are not completely understood. Therefore, the aim of our study was to quantify echocardiographic structural and functional changes of left atrium (LA) and left ventricle (LV) after combined ablation.

Methods and results: Thirty-seven consecutive patients with symptomatic drug refractory persistent AF were included in analysis. All underwent hybrid procedure to achieve complete pulmonary vein and LA posterior wall electrical isolation. The insertable cardiac monitor measured AF burden. At 12 months, follow-up mean AF burden was 17.1% (±31.0%) for all patients. In patients with low AF burden (<0.5%, 19/37 pts), we observed significant decrease of LA diameter (4.6 cm vs. 4.0 cm, p<0.05), LA volume (96 ml vs. 81 ml, p<0.05), improvement of LA emptying fraction (21% vs. 45%, p<0.05) and LA global longitudinal strain (11.2% vs. 18.8%, p<0.05). In addition, LV ejection fraction (60% vs. 70%, p<0.05) improved in comparison to patients with mean AF burden > 0.5.

Conclusion: Hybrid ablation procedure of persistent AF achieved stable sinus rhythm in significant proportion of patients resulting in positive LA and LV remodelling after 12 months of follow-up.

P3422 | BEDSIDE
The impact of CT image integration using CartoSound™ image directly acquired from the left atrium in atrial fibrillation ablation

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Introduction: CartoSound™ (CS) might be useful for integrating CT for catheter navigation during atrial fibrillation (AF) ablation. However, the optimal method of CT integration has not been established.

Methods: Fifty-two AF patients who underwent successful circumferential pulmonary vein isolation (CPVI) using CS were analyzed. CT integration was performed with two methods: (1) using the left atrial (LA) model created by CS probe located in the right atrium and right ventricular outflow tract (RA/RVOT-merge) and (2) using the LA model directly derived by CS probe in the LA added to images derived from the RA/RVOT (LA/RA/RVOT-merge). The accuracy of these methods was assessed by measuring the distances between integrated CT and the actual ablation point for CPVI.

Results: The average integration error between the LA model and integrated CT was comparable between the 2 methods (LA/RA/RVOT-merge = 1.7±0.4 mm, RA/RVOT-merge = 1.6±0.5 mm; p=0.34). However, the distance between the ablation point and integrated CT was significantly shorter in LA/RA/RVOT-merge (2.1±0.6 mm vs. 2.5±0.8 mm; p<0.01). The LA, especially the left-sided pulmonary veins and LA roof, were more sharply delineated by CS probe located in the LA than in the RA/RVOT, and they may have improved the accuracy of CT integration.

Conclusions: Direct LA imaging by CS results in improved LA visualization and CT integration.

P3423 | BEDSIDE
Atrial rhythm and atrial electrogram amplitude

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Purpose: The magnitude of fibrillatory replacement of atrial myocardium can be estimated by electroanatomic voltage mapping. The amplitude of atrial electrograms (EGMs), however, depends on atrial rhythm or dominant cycle length in case of atrial fibrillation. The relationship between EGM characteristics in atrial fibrillation/tachycardia and in sinus rhythm is generally unknown. We investigated left atrial EGMs while pacing at different rates in the high right atrium.

Methods: The study was completed in 18 patients (63±6 yrs, 13 males) with paroxysmal atrial fibrillation undergoing pulmonary vein isolation. Atrial EGMs were recorded in interposterior (IP) region close to the right inferior pulmonary vein and in anterosetal (AS) region close to the right superior pulmonary vein. The stimulation protocol consisted of series of pacing trains delivered from right atrial appendage with basic cycle length of 600ms followed by single extrastimuli with coupling interval gradually shortened in 20-ms steps until the atrial effective refractory period (ERP).

Results: The atrial ERP was 219±33 ms. In comparison to reference (in-train voltage), significant (P<0.05) reduction of EGM amplitude proportional to coupling interval of extrastimulus was observed in both IP and AS regions (maximum reduction is shown in Table). There was weak correlation between reference and short-coupled-EGM amplitudes (R=0.35, P=0.05).

Conclusions: Left atrial EGM voltage is rate-dependent. Relative reduction of voltage (up to 50% of reference value) was observed for short-coupled extrastimuli. Further reduction could be expected at shorter atrial cycle length in the setting of atrial fibrillation. Magnitude of rate-dependent voltage reduction of atrial EGMs is widely variable. It implies that voltages in sinus rhythm cannot be predicted by voltages in atrial tachycardia/fibrillation.

Abstract P3423 – Maximum change in atrial EGM amplitude

Unipolar voltage (mV) Bipolar voltage (mV)

Reference voltage Reference voltage

Voltage close to ERP Voltage close to ERP

Relative reduction Relative reduction

Inferoposterior LA 2.64±1.04 1.72±0.71 64±22% 1.72±1.18 0.97±0.32 54±25%

Anterosetal LA 3.03±1.43 1.81±0.66 62±28% 1.90±1.43 0.82±0.30 51±27%

Legend: EGM, electrogram; ERP, effective refractory period; LA, left atrium. All P<0.05.
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® Smarttouch™ (ST) catheter was better than the Thermocool ® Surround Flow catheter ablation as standard therapy. However ablation, which generally involves point circumferential radiofrequency ablation around the veins, without any extra prolongation of PR interval seems to be protective from delayed LAA activation after completing of LAL.

Methods: We utilized the electronatomic data from left atrial (LA) mapping in 68 patients (46 men, 59±10 years) who underwent catheter ablation for paroxysmal (75%) or persistent (25%) atrial fibrillation. The LA activation maps in SR were carefully edited to localize the lateral perimetric collision zone. The electrical distance between the base of LAA and this collision zone was used to estimate the relative delay in LAA activation if virtual ablation at the LAL is achieved.

Results: In SR, the activation time of LAA base was -7±4±4 ms before the onset of QRS complex. The activation time at the collision zone was -52±4±1 ms. In the setting of hypothetical LAL block, LA activation time would be delayed by 64±5±6 ms and 4±4±4 ms in the reduction of LAA activation time relatively to the QRS onset (-21±32; range -97→68 ms) in 14 (21%) patients, LAA LA activation would start after the QRS onset. Only 10 (15%) patients would have LAA activated earlier than 50 ms prior to the QRS offset. Out of those 10 patients, 6 (60%) have PR interval longer than 200 ms, which is significantly higher proportion than in rest of cohort (21%), P<0.01.

Conclusions: The experimental model helped to demonstrate that the block at the LAL is associated with significant delay of LAA activation. Consequently, the anterior mitral block may adversely influence the benefit from SR restoration because of worsening of LAA function. Prolonged PR interval seems to be protective from delayed LAA activation after completing of LAL.

P3427  |  BEDSIDE 
Early redo procedure of atrial fibrillation ablation: the energy source did have a role? 


Purpose: Recurrences of atrial fibrillation (AF) after the first ablation procedure are frequent. In addition of radiofrequency (RF), cryo energy has acquired high availability in the last years. The aim of this study was to identify if the energy source plays a role on early AF recurrence and if it is related to a site-specific reconnection in pulmonary veins.

Methods: From 1460 AF ablation procedures performed in our centre from 2010 to 2014, 164 patients (11%, 72% male, mean age 58±6 years), undergoing redo procedure, were retrospectively evaluated. The mean time to redo procedure was 30±29 months. Redo procedure was realized for paroxysmal AF in 107 patients (65%), persistent AF in 55 (34%), permanent AF in 2 (1%). According to the ablation energy source 2 groups were identified: - Group 1: RF (143 patients, 87%), - Group 2: cryo (21 patients, 13%). Forty-five patients (27%), in whom the redo procedure was realized 6 months after the first ablation, were analyzed. The energy source of the first ablation was RF in 30 patients (87%) and cryo (first generation balloons) in 15 patients (33%).

Results: The use of cryo energy in the first procedure leaded to more frequent early redo procedure than the use of RF (respectively 15/21, 71% vs 30/143, 87%); - Group 2: cryo (21 patients, 13%). Forty-five patients (27%), in whom the redo procedure was realized after the first ablation, were analyzed. The energy source of the first ablation was RF in 30 patients (87%) and cryo (first generation balloons) in 15 patients (33%).

Conclusions: With cryo energy, early reconnection was statistically more frequent than RF in the carena (respectively 7 patients (47%) vs 4 patients (13%), P=0.014) and ridge of left superior pulmonary vein (LSPV) [respectively 8 patients (53%) vs 7 patients (23%), P=0.044], and showed a trend of greater early reconnection in left inferior pulmonary vein (LIPV) [respectively 12 patients (80%) vs 15 patients (50%) P=0.053] especially in the inferior wall [respectively 5 patients (33%) vs 3 patients (10%), P=0.054]. On the contrary, using RF, reconnection was more frequent than using cryo in right inferior pulmonary vein (RIPV) [respectively 26 patients (87%) vs 9 patients (60%), P=0.043].

Conclusion: Early redo procedures for AF recurrences were more frequent after the first ablation with cryo (first generation balloons) than with RF. Sites of greater reconnection were the carena and ridge of LSPV with cryo, while the RIPV using RF.

P3428  |  BEDSIDE 
Role of atrial fibrillation in patients with acute coronary syndrome and elevated high-sensitive troponin T levels 

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Background: Studies have shown that high sensitive Troponin (hs Troponin) is highly specific for myocardial damage and for the diagnosis of acute coronary syndrome (ACS).

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Objective: We investigated its Trop utility and predictive value in patients with atrial fibrillation (AF) in the acute setting.

Methods: We studied 2038 consecutive patients undergoing coronary angiography between July 2013 and October 2014. In patients with ACS cardiac biomarkers (hs Tropinin T and cardiac creatinin) were obtained on presentation and if needed again after 3–4 hours. In patients with Non ST-segment elevation myocardial infarct (NSTEMI) history of AF and heart rhythm documented by electrocardiogram were assessed and compared with coronary angiography result.

Results: Of the study population 351 (17%) patients had NSTEMI and 503 (25%) patients a history of AF. Ninety patients (26%) of NSTEMI patients showed AF on presentation. Mean patients’ age was 74 years ± 9 and 73% were men. Prior coronary artery disease was known in 75% of the 90 patients and paroxysmal AF was known in 53% of patients. Mean left ejection fraction was 50±16.

Conclusions: The female gender (AHF+ vs AHF−) (p=0.001), heart failure symptoms (AHF+ vs AHF−) (p<0.001), the presence of systolic hypertension (AHF+ vs AHF−) (p=0.001) and BNP levels (B=1162.86 pg/mL, DP=1118.03 pg/mL, p<0.001) were significantly higher in the AHF+ group in comparison with AHF−. Patients who developed AHF were longer hospitalized (9±6 vs 6±5 days) and died more frequently (21% vs 10%).

Conclusion: Prospective study of 289 consecutive patients (mean age: 68±11 years, 61% men) admitted with AMI between April and November 2012 to our Centre for Heart Diseases, Hospital, Poland. AMI was diagnosed based on the 3rd Universal Definition of Acute Myocardial Infarction. AHF was diagnosed based on 3 criteria: 1) dyspnoea at rest or during minimal physical effort; 2) pulmonary congestion demonstrated on chest X-ray; 3) applied specific treatment including loop diuretic i.v. and/or nitroglycerin i.v. within first 24 hours of hospitalization.

Results: 13% of patients experienced AHF at the time of admission. In a multivariable analysis, the female gender (AHF+ vs AHF−) (p=0.01), systolic hypertension (AHF+ vs AHF−) (p=0.01), heart failure symptoms (AHF+ vs AHF−) (p=0.001) were independently associated with an increased risk of developing AHF in the course of AMI. Surprisingly, neither history of systolic HF for diabetes mellitus were predisposing factors for AHF development. There were no differences for maximal cardiac troponins measured during hospitalization between these two groups whereas NT-proBNP was higher (4128 [2397–9261] vs 742 [259–2043], p<0.001) in AHF+ vs AHF− group.

Conclusion: Prospective study of 1051 consecutive patients, diagnosed with ACS attending the emergency department (CA) in 2072 successive patients scheduled for acute CA on clinical basis. Reperfuson strategies were aimed to achieve the clinical outcomes of patients with acute coronary syndromes attending the emergency department (CA) in 2072 patients, and no epicardial coronary lesion in 95 patients (ACS-like). Patients were followed on average 7 years for mortality.

Results: In the ACS patient group 474 (23%) patients died during follow up. Acutely measured TIMP-1 was significantly higher (p<0.001) in those patients, than those who survived the follow up-period, whereas MMP-8 was not (p=0.55) (Figure 1). In the ACS-like patient group 8 (8%) patients died during follow up. However, TIMP-1 and MMP-8 were not significantly different in ACS-like patients in terms of survival (p=0.145 and p=0.082, respectively).

Conclusion: Inflammatory mediator TIMP-1 is a prognostic marker of long term survival in patients with ACS, MMP-8 and TIMP-1 do not provide such value in noncoronary acute cardiac disease. TIMP-1 may thus be considered a marker of severe coronary inflammation with prognostic implication.
Emergency Department to facilitate early diagnosis of myocardial infarction. However, myocardial injury occurs in a range of conditions and there is concern that widespread use of these assays may lead to diagnostic uncertainty and unnecessary hospital admissions.

**Purpose:** To define the prevalence of myocardial injury in consecutive patients attending the Emergency Department without suspected acute coronary syndrome.

**Methods:** We identified all patients (n=1,054) who presented to the Emergency Department of a large teaching hospital in whom serum was received as part of routine clinical care over 10 consecutive days. Cardiac troponin was measured using the third-generation assay in all patients, but only reported where requested by the attending clinician. Clinical characteristics, diagnosis, and outcomes were obtained through the patients’ electronic patient records.

**Results:** Cardiac troponin was requested in 136 patients (11%) by the attending clinician. In the remaining 918 patients without suspected acute coronary syndrome (age 55±23 years, 48% men), 107 (10%) patients had myocardial injury with troponin concentrations greater than the upper reference limit (≥34 ng/L in men, ≥18 ng/L in women). Patients with myocardial injury were older, and were more likely to have cardiovascular risk factors and coronary heart disease (P<0.001). Cardiac troponin was associated with haemodynamic compromise based on physiological parameters in the National Early Warning Score (NEWS) (P<0.001), renal impairment (P<0.001), myocardial ischemia on the electrocardiogram (P<0.05) and was an independent predictor of death at 30 days (hazard ratio 1.35 [95% confidence interval 1.20–1.53] per doubling of troponin concentration). The majority of patients with myocardial injury (86%) were admitted to hospital for further investigation.

**Conclusion:** Myocardial injury with suspected acute coronary syndrome is common and detectable in 1 in 10 patients attending the Emergency Department. Myocardial injury is associated with cardiovascular risk, haemodynamic compromise and early death with the majority already admitted to hospital for further investigation.

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**P3434 | BEDSIDE**

**Impact of renal dysfunction at admission on survival in mechanically ventilated ST-elevation myocardial infarction patients after cardiopulmonary resuscitation**

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**Background:** Renal dysfunction (RD) is associated with an increased risk for a worse outcome after coronary intervention (PCI). Data about the impact of RD at admission on survival in ST-elevation myocardial infarction (STEMI) complicated with cardiopulmonary resuscitation (CPR) and mechanical ventilation are sparse.

**Purpose:** We tried to establish the possible influence of RD at admission in patients with STEMI, complicated with CPR and mechanical ventilation on inhospital mortality.

**Methods:** The present study was an analysis of 120 mechanically ventilated patients after CPR with STEMI. The group with RD (45 patients) was compared with the group without RD (75 patients). RD was defined as glomerular filtration rate less than 60 ml/min/1.73m². In-hospital and long-term all-cause mortality were observed. Median follow-up time was 363 days (25th, 75th percentile: 2, 958). Kaplan-Meier estimation was used for unadjusted survival. Cox proportional analysis was used to establish possible independent predictors for in-hospital and long-term mortality. We controlled for age, gender, TIMI flow before and after PCI, PCI of left main coronary artery, PCI of LAD, PCI of RCA, multivessel PCI, drug eluting stents, GPI use and RD at admission. Distributions of continuous variables in the 2 groups were compared with the 2-sample t test. Distributions of categorical variables were compared with the chi-square test. All p values were two-sided and values less than 0.05 were judged statistically significant.

**Results:** RD at admission in STEMI patients after CPR and mechanical ventilation was associated with higher in-hospital or long-term all-cause mortality. In the RD group 27 patients (60.0%) died in the hospital whereas 20 (26.7%) did so in the non-RD group; p<0.0001. Long-term mortality during observation period was also higher in RD group [31 patients (68.9%) with RD vs. 26 (34.7%) patients in the group without RD; p<0.0001]. In-hospital mortality was predicted with RD at admission (adjusted HR 2.44; 95 CI 1.31 to 4.56; p<0.0001), age (adjusted HR 1.05; 95 CI 1.02 to 1.08; p<0.0001) and TIMI flow <1 before PCI (adjusted HR 0.46; 95 CI 0.24 to 0.90; p=0.024). RD at admission (adjusted HR 2.92; 95 CI 1.67 to 5.13; p<0.0001), and age (adjusted HR 1.04; 95 CI 1.01 to 1.06; p=0.002) predicted long-term death.

**Conclusion:** STEMI patients with RD at admission who had undergone CPR and were mechanically ventilated had a worse outcome than patients without RD at admission. This is especially true for older patients. Special attention regarding renal function should be considered for these patients.

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**P3435 | BEDSIDE**

**Angiographic findings and survival in patients undergoing coronary angiography after sudden cardiac arrest in Western Sweden**


**Purpose:** The present study was an analysis of 120 mechanically ventilated patients after CPR with STEMI. The group with RD (45 patients) was compared with the group without RD (75 patients). RD was defined as glomerular filtration rate less than 60 ml/min/1.73m². In-hospital and long-term all-cause mortality were observed. Median follow-up time was 363 days (25th, 75th percentile: 2, 958). Kaplan-Meier estimation was used for unadjusted survival. Cox proportional analysis was used to establish possible independent predictors for in-hospital and long-term mortality. We controlled for age, gender, TIMI flow before and after PCI, PCI of left main coronary artery, PCI of LAD, PCI of RCA, multivessel PCI, drug eluting stents, GPI use and RD at admission. Distributions of continuous variables in the 2 groups were compared with the 2-sample t test. Distributions of categorical variables were compared with the chi-square test. All p values were two-sided and values less than 0.05 were judged statistically significant.

**Results:** RD at admission in STEMI patients after CPR and mechanical ventilation was associated with higher in-hospital or long-term all-cause mortality. In the RD group 27 patients (60.0%) died in the hospital whereas 20 (26.7%) did so in the non-RD group; p<0.0001. Long-term mortality during observation period was also higher in RD group [31 patients (68.9%) with RD vs. 26 (34.7%) patients in the group without RD; p<0.0001]. In-hospital mortality was predicted with RD at admission (adjusted HR 2.44; 95 CI 1.31 to 4.56; p<0.0001), age (adjusted HR 1.05; 95 CI 1.02 to 1.08; p<0.0001) and TIMI flow <1 before PCI (adjusted HR 0.46; 95 CI 0.24 to 0.90; p=0.024). RD at admission (adjusted HR 2.92; 95 CI 1.67 to 5.13; p<0.0001), and age (adjusted HR 1.04; 95 CI 1.01 to 1.06; p=0.002) predicted long-term death.

**Conclusion:** STEMI patients with RD at admission who had undergone CPR and were mechanically ventilated had a worse outcome than patients without RD at admission. This is especially true for older patients. Special attention regarding renal function should be considered for these patients.

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**P3434 | BEDSIDE**

**Patients with moderate cerebral perfusion deficit upon hospital arrival may be good candidates for therapeutic hypothermia following out-of-hospital cardiac arrest**

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**Background:** Therapeutic hypothermia at a target temperature of 33°C was recently reported to not confer a benefit compared with management at a target temperature of 36°C.

**Aim:** Our study aimed at evaluating the relationship between regional brain oxygen saturation (rSO2) upon hospital arrival and neurological prognosis in patients with or without therapeutic hypothermia after out-of-hospital cardiac arrest (OHCA).

**Methods:** We admitted 315 survivors to hospital after OHCA (presumed cardiac cause) from the Prediction of Neurological Outcomes in Patients Post-cardiac Arrest Registry, and measured their rSO2 immediately upon hospital arrival. Of these, 152 patients underwent therapeutic hypothermia, while 163 did not. We also assessed the percentage of patients with a good neurological outcome (defined as cerebral performance categories 1 or 2) 90 days post-cardiac arrest.

**Results:** After 90 days, 55 (36%) and 13 (8%) patients had good neurological outcomes in each respective group. The percentage of patients with a good 90-day neurological outcome increased significantly in proportion to rSO2 levels upon arrival at the hospital in each group (P<0.001). However, in patients with rSO2 upon hospital arrival between 41% and 60% (n=42; 13%), the percentage of patients with good neurological outcomes was significantly higher (P<0.01; Figure) in patients with therapeutic hypothermia (20/28, 71%) than in those without (1/14, 7%).

**Conclusion:** Our data indicate that patients with moderate cerebral perfusion deficit upon hospital arrival may be good candidates for therapeutic hypothermia after OHCA.

**Acknowledgement/Funding:** JSPS KAKENHI (grant numbers 24390400 and 26462753)
P3436 | BEDSIDE
Optimal blood pressure for favourable neurological outcome in adult patients following in-hospital cardiac arrest
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Background: Adequate cerebral blood flow maintained by optimal blood pressure is important in neurological recovery for patients sustaining transient brain ischemia.

Purpose: To investigate the relationship between blood pressure and neurological outcomes of patients resuscitated following cardiac arrest.

Methods: This was a retrospective observational study, from a single medical center, of adult patients between 2006 and 2012 who had in-hospital cardiac arrest and achieved sustained return of spontaneous circulation (ROSC). Multivariable logistic regression analysis was used to identify factors associated with a favourable neurological outcome at hospital discharge. Maximal mean blood pressure (MBP) during the initial 24 hours after sustained ROSC was used for analysis.

Results: Of the 319 study patients, 93 (29.2%) survived to hospital discharge and 56 (17.6%) achieved a favorable neurologic outcome. The mean MBP was 95 mm Hg. MBP above 85 mm Hg was found to be correlated with a favorable neurological outcome (odds ratio [OR] 2.30, 95% confidence interval [CI] 1.05–4.56, p=0.03). For patients without chronic hypertension, the optimal MBP was between 85 and 115 mm Hg (OR 8.80, 95% CI 3.13–28.55; p=0.001). For patients with chronic hypertension, the threshold MBP for achieving a favorable neurological outcome was above 88 mmHg (OR 4.04, 95% CI 1.41–13.03).

Conclusions: The blood pressure over the first 24 hours following resuscitation was correlated with neurological outcome. There may be a threshold blood pressure required to effect a favorable neurological outcome. The optimal blood pressure may be dependent on the presence or absence of chronic hypertension.

Acknowledgement/Funding: This study was funded by the academic research grant NTUHY103.N003 from the National Taiwan University Hospital Yurun Branch.

P3437 | BEDSIDE
Clinical profile, treatment, and outcomes of patients with type B acute aortic syndromes: findings from a large multicenter Italian registry
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Objective: To assess the epidemiological characteristics, clinical presentation, diagnostic strategies, treatment, and outcome of patients with type B Acute Aortic Syndrome (AAS).

Methods: "AESA" (Archivio Elettronico delle Sindromi Aortiche acute) multicenter registry includes consecutive patients with AAs (Aortic Dissection, AD; Intramural Hematoma, IH; Penetrating Ulcer, PU) referred to 2 Italian Hub hospitals. 502 patients (including both type A and type B) were enrolled from 2000 to 2014. In all cases the diagnosis was confirmed by a multidisciplinary team. For this study, only patients with type B AAS were considered.

Results: AESA registry enrolled 190 patients with Type B AAS: 122 (65%) with AD, 49 (25%) with IH and 19 (10%) with PU. The mean age of study population was 67±13 years, 72% were male. The “classic” risk factors for AAS were confirmed to be uncommon, with the exception of a history of hypertension (70% of patients). The clinical presentation included: back pain (70%), anterior chest pain (52%), abdominal pain (39%), migran pain (14%), pulse deficit (20%), syncope (3%), stroke/TIA (1%). Acute coronary syndrome (ACS)-like ECG abnormalities were found in 18% of cases, while cardiac troponin T (TntT) elevation was observed in 25 (20%) of the 126 patients who were tested with TntT assay during the initial management of chest pain. The combination of ACS-like ECG findings and TntT positivity was independently associated with late diagnosis and inappropriate therapy such as antithrombotic therapy/coronary angiography (OR 2.48, 95% CI 1.14–5.8, p=0.03). An initial diagnosis different from AAS was made in 23% (of which 35% ACS, 13% renal/biliary colic, 13% acute gastritis, 11% pulmonary embolism, 7% lower limb ischemia). The first “diagnostic” test which demonstrated an AAS was: CT scan (83% of cases), abdominal ultrasound (12%), TT (3%) and TE (1%) echocardiography. 90 of 190 patients (47%) underwent endovascular (n=76) or surgical intervention (n=14) during hospitalization. In-hospital mortality was 12.6%, without difference between patients treated with invasive approach and those managed with medical therapy alone (13% vs. 12% respectively, p=0.86).

Conclusions: The outcome of AAS Italian patients enrolled in AESA registry is in line with that reported by the current international literature. Of note, even in type B AAS, ACS-like ECG abnormalities and TntT elevation are frequent findings and they are associated with significant risk of late diagnosis and inappropriate therapy.

ISCHAEMIA, EXPERIMENTAL STUDIES

P3438 | BENCH
Efficacy and safety of intensive statin treatment in Chinese old patients with acute coronary syndrome undergoing percutaneous coronary intervention

Background: Previous study showed that loading or pre-loading with statin improved clinical outcomes in patients undergoing percutaneous coronary intervention (PCI), however the efficacy and safety of statin in Asian elderly acute coronary syndrome (CAD) patients who undergoing PCI were unknown.

Objectives: The objective of this study is to test whether Chinese old patients undergoing PCI can tolerate and benefit from intensive statin treatment.

Methods: Patients who were aged from 65–80 years undergoing PCI from 2012–2013 in 5 large volume PCI centers in China were included. Patients were randomly divided into two groups, regular statin treatment group: atorvastatin 20mg pre PCI, 10mg/d till 30 days, intensive statin treatment group: atorvastatin 80mg pre PCI, 20mg/d till 30 days, intensive statin treatment group: atorvastatin 80mg pre PCI, 10mg/d till 30 days. MACE which includes all cause of death, myocardial infarction, target vessel revascularization; Hepatotoxicity, muscle toxicity were also followed up at 1 month, 6 month.

Results: 225 and 250 patients were included in the intensive and regular statin treated group respectively. Compared with regular statin treatment group, intensive statin treatment group reduced per-procedure myocardial injury (23.6% vs 35.7%, p<0.05). At follow up of 6 month, intensive statin treatment also reduced MACE (6.8% vs. 12.2%, p=0.05). Both group had similar incidence of hepatotoxicity (3.2% vs 3.8% in regular statin group) and muscle toxicity (5.3% vs. 5.4% in regular statin group). Multivariable analysis showed that intensive statin as a predictor of decreased risk of 6 month MACE in elderly ACS patients (odds ratios, 0.63 95% confidence interval: 0.25 to 0.87 p=0.037).

Conclusions: Intensive statin treatment pre PCI in elderly Chinese patients can reduce periprocedural myocardial injury and MACE at no cost of safety.

P3439 | BEDSIDE
Two-year clinical outcome of bioilmus-eluting stent in coronary bifurcation lesions compared with everolimus-eluting stent

Background: Newer-generation drug-eluting stents (DES) have the improved safety and similar efficacy compared with first-generation DES. However, there is little data regarding the optimal newer-generation DES for bifurcation lesions. The aim of this study was to compare clinical outcome between the NOBORI biolimus-eluting stent (BES) and XIENCE/PROMUS everolimus-eluting stent (EES) in patients with bifurcation lesions.

Methods: Between February 2010 and August 2012, a total of 888 patients treated only with BES (508 patients with 560 lesions) or EES (390 patients with 411 lesions) in bifurcation lesions were retrospectively analyzed. The study endpoint was the cumulative 2-year incidence of major adverse cardiovascular event, defined as a composite of cardiac death, myocardial infarction (MI), clinically-driven target lesion revascularization (CDTLR), and definite stent thrombosis.

Results: Baseline patient characteristics were similar between the BES and EES groups except for the prevalence of dyslipidemia, previous MI and previous per-
cutaneous coronary intervention. At 2-year, the incidence of MACE was similar between the 2 groups (9.2% vs. 6.7%, P=0.16). Cumulative incidence of MI, CDTLR, and definite stent thrombosis were not significantly different between the 2 groups (1.8% vs. 1.4%, P=0.65; 5.9% vs. 4.4%, P=0.27; 0.8% vs. 0.6%, P=0.61, respectively).

Conclusions: Two-year clinical outcome of BES is similar to that of EES in patients with bifurcation lesions.

P3440 | BEDSIDE
Sex-based differences in 2-year clinical outcome after percutaneous coronary intervention with new generation drug eluting stent


Background: Sex-based differences in clinical outcome after percutaneous coronary intervention (PCI) with new generation drug eluting stent (DES) remains unclear. We sought to assess whether sex differences in clinical outcome exist in patients treated with new-generation DES.

Methods: We evaluated consecutive patients treated with new-generation DES between February 2010 and May 2012. This primary endpoint was the cumulative incidence of major adverse cardiovascular events (MACE), defined as a composite of cardiac death, myocardial infarction (MI), clinically-driven target lesion revascularization (CDSLTR), and definite stent thrombosis at 2-year. Cox proportional hazards models were used to assess independent predictors of MACE. Multivariate models were constructed by including all univariate predictors with a p-value <0.1.

Results: Among 2496 patients, 660 (26.4%) were women. Clinical follow-up information at 2 years was obtained 98.4%. Compared with men, women were older and had less current smokers, previous MI and previous PCI. The cumulative 2-year incidence of MACE and cardiac death in women were significantly higher than those in men (12.2% vs. 8.2%, P=0.003; 4.7% vs. 2.4%, P=0.005, respectively). The cumulative incidence of CDTLR and MI were not significantly different between the 2 groups (7.2% vs. 5.5%, P=0.13; 1.0% vs. 1.9%, P=0.13, respectively). In a multivariate analysis, women was associated with MACE (hazard ratio 1.41; 95% confidential interval 1.04–1.90; P=0.03).

Conclusion: Women had worse 2-year clinical outcome than men in the new-generation DES era. Women was an independent predictor of MACE.

P3441 | BENCH
Investigating the molecular signaling pathway of preconditioning: focused on STAT5 and eNOS inhibition


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Purpose: To determine the role of STAT5, eNOS and apoptosis in PerC.

Methods: Anesthetized rabbits were subjected to 30-min ischemia (isc) and 180-min reperfusion (rep) for STAT5, eNOS and caspase-3 assessment. To determine the role of STAT5, eNOS and apoptosis in PerC, rats were treated with respective groups, tissue samples were taken at the 10th min of rep for STAT5, eNOS and caspase-3 assessment. Blood samples were drawn at baseline and at rep for malondialdehyde (MDA) and nitrotyrosine (NT) assessment.

Results: The inhibition of JAK-2, Src and AT1 did not abrogate the infarct size limiting effects of PerC (29.3±3.7% in PerC, 26.2±2.2% in PerC-AG, 13.2±0.6% in PerC-PP1, 10.7±0.5% in PerC-Val vs 47.7±1.0% in Control, 39.7±3.8% in AG and 35.2±1.8% in PP1, p<0.05). Val reduced infarct size limiting effects of PerC (38.2±1.6% and 37.2±1.6% in L-NAME and Perc-L-NAME groups respectively, p<NS vs Control and p<0.05 vs Perc). STAT5 was activated in PerC groups independently of the presence of AG, whereas no STAT5 phosphorylation was observed in PP1 and Val groups (with or without PerC). eNOS was phosphorylated in all Perc groups compared to the Control group and to the groups treated with AG or PP1. The cumulative incidence of CDTLR and MI were not significantly different than those in men (12.2% vs. 8.2%, P=0.003; 4.7% vs. 2.4%, P=0.005, respectively). The cumulative incidence of CDTLR and MI were not significantly different between the 2 groups (7.2% vs. 5.5%, P=0.13; 1.0% vs. 1.9%, P=0.13, respectively). In a multivariate analysis, women was associated with MACE (hazard ratio 1.41; 95% confidential interval 1.04–1.90; P=0.03).

Conclusion: Women had worse 2-year clinical outcome than men in the new-generation DES era. Women was an independent predictor of MACE.

P3442 | BENCH
Sex-based differences in 2-year clinical outcome after percutaneous coronary intervention with an alginate-scaffold


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Purpose: Investigating the molecular signaling pathway of perconditioning:

Methods: Intramyocardial injection of GH via an alginate-scaffold attenuates post-MI LV remodeling and improves LV function, displaying higher efficacy compared to alginate alone or biventricular restraint. These favorable effects can be attributed to enhanced neovascularization and myofibroblast-proliferation.

Results: LV dimensions were smaller and ejection fraction (EF) was higher after alginate+GH compared to alginate alone. Increased neo-vascular density and myofibroblast-count were found in the infarct and peri-infarct areas after alginate+GH (Table). Data are mean ± SEM. EDD, end diastolic dimension; EDS, end systolic dimension; EF, ejection fraction. ***p<0.001 vs control, **p<0.01 vs control, *p<0.05 vs control, **p<0.01 vs alginate, *p<0.05 vs alginate.

Conclusions: Intramyocardial injection of GH via an alginate-scaffold attenuates post-MI LV remodeling and improves LV function, displaying higher efficacy compared to alginate alone or biventricular restraint. These favorable effects can be attributed to enhanced neovascularization and myofibroblast-density in the peri-infarct area.

Acknowledgement/Funding: ADV, EB, MK were supported by a scholarship from the Experimental Research Center ELPEN (Greece)

P3443 | BENCH
Natriuretic peptide inhibits endoplasmic reticulum stress and enhances myocellular ischemia/perfusion injury in diabetic rats

H. Zhang, W. Wang, Z. Shi, F. Fu, X. Liang. The Fourth Military Medical University, Experimental Teaching Center, Xi’an, China, People’s Republic of Background: Diabetes mellitus (DM) increases morbidity/mortality of ischemic heart disease. Although the ability of the natriuretic peptides to modulate cardiac function and cell proliferation has already been recognized, their effects on myocardial ischemia/reperfusion (MI/R) injury, especially in diabetic state, is still uncertain.

Purpose: This study was designed to investigate the effects of the artificial synthetic natriuretic peptide – vasonatrin peptide (VNP) on MI/R injury in diabetic rats, and to further elucidate its mechanisms.
Acknowledgement/Funding: Supported by the NSFC (81270330 and 81300190) and the Shaanxi Province S & T Program (2013KZXX-89).

P3444 | BENCH
Hyperglycaemic exacerbation of myocardial ischaemia/reperfusion injury is mitigated by SGLT inhibition
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Background: Epidemiological data reveal that hyperglycaemia in the context of acute myocardial infarction (AMI) is associated with higher morbidity and mortality when compared to normoglycaemia. Both diabetics and non-diabetics are affected, but non-diabetics suffer a greater augmentation of risk compared to diabetics with equivalent plasma glucose. The mechanism underlying the adverse relationship between glucose and outcome is unclear.

Purpose: To determine whether hyperreperfusion hyperglycaemia dose-dependently enlarges myocardial infarct size. Moreover, we hypothesised that injury would be more marked in non-diabetics than in diabetics, and that this excess injury would be mitigated by reduction in myocardial glucose uptake by administration of a sodium/glucose transporter (SGLT) inhibitor.

Methods: Male Sprague Dawley rats (SDR) and weight-matched diabetic Goto Kakizaki rats (GKR) underwent Pentobarbitone euthanasia and heart harvest. Cardiac function was maintained on a Langendorff perfusion rig supplying modified Krebs-Henseleit buffer (KHB) with 11 mmol Glucose at 70mMhg. Anterior ischaemia was induced left coronary artery ligation for 35 mins, followed by 60 mins reperfusion with KHB containing 5, 11, 16.5 or 22mmol Glucose, using D-Mannitol to maintain osmolality, with or without the non-selective SGLT inhibitor Phlozin. Infarct sizes (IS) as a proportion of the area at risk (AAR) was quantified by tetrazolium chloride-based planimetry.

Results: IS with 11mmol Glucose was 45±2.6% of AAR in SDR and 31±4.6% in GKR (p<0.05). SDR hearts reperfused with 5mmol and 22mmol Glucose had significantly increased IS (53±1.8% and 65±4.2% respectively, p<0.05) compared to normoglycaemic SDR hearts reperfused with 11mmol Glucose (37±5.8%). In GKR, IS increased to 57±5.8% in 5mmol Glucose, and to 68±5.9% in 22mmol Glucose.

Conclusion: Glucose regulates myocardial IR injury, with a greater effect observed in GKR. Increasing glucose from 11 to 22mmol in non-diabetic SDR hearts reduced IR injury, while only moderately increasing IS in GKR. The magnitude of the increase in myocardial IS with 22mmol Glucose is comparable to that observed in diabetic heart, reflecting established epidemiological outcome data in AMI.

P3446 | BEDSIDE
Oxidative DNA damage in acute myocardial infarction
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Background: Oxidative damage of DNA in acute myocardial infarction is caused by free oxygen radicals excessively released at reperfusion. We evaluated possibility of using comet assay method for measurement of oxidative DNA damage in patients with acute myocardial infarction.

Methods: Comet assay measure DNA damage and repair in peripheral leucocytes, oxidized pyrimidines with endonuclease III (ENDO III) and oxidized purines with foramidopyrimidine-DNA glycosylase (FPG).

Results: Blood samples were obtained from 23 patients with STEMI, before and after primary PCI from aorta and coronary sinus, with follow up 6, 12 and 30 months after PCI. Controls group were 23 elective patients. DNA damage (SSB; END0 III & FPG) was significantly higher in STEMI patients, before primary PCI (30.26±15.19; 37.25±26.68 & 32.92±20.04 resp.) compared to the elective group (16.65±16.58; 11.59±7.94 & 12.99±14.31 resp., p<0.001). Level of damage did not change immediately after reperfusion (29.55±17.05; 59.58±33.78 & 52.61±20.55 resp., p>0.05). DNA was repaired and after 6 hours reparation became significant (21,00±14.95; 20.55±13.25 & 18.21±11.06 resp, p<0.05) with full recovery after 24 hours (10,32±9.91; 13.02±13.58 & 12.68±11.66, p<0.001) when damage become like in elective group (p=ns). Neither severity of myocardial infarction (troponin T and creatinkinase) nor extension of coronary heart disease or tissue hypoperfusion did correlate with level of DNA damage.

Conclusion: A single RIPC manoeuvre induces the release of (a) dialyzable, humoral factor(s) which reduce(s) infarct size no later than after 30 min and remain(s) operative for up to 6 days after RIPC. These results imply that cardioprotection is at least in part effected by a factor which is quickly released/activated and present for quite some time after the RIPC manoeuvre.

P3444 | BENCH
Kinetics of cardioprotection by plasma dialysate from healthy volunteers undergoing remote ischemic preconditioning
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Objective: Remote ischemic preconditioning (RIPC) by transient limb ischemia/reperfusion protects against myocardial injury in animals and humans. Humoral and neuronal factors contribute to the signal transfer from the remote organ to the heart. We have now analyzed the temporal kinetics of cardioprotection by humoral factor(s) in healthy volunteers undergoing RIPC, using infarct size in a Langendorff mouse bioassay heart as read out.

Methods: Ten healthy volunteers underwent a RIPC-manoeuvre of 3 cycles of 5 min upper-limb blood pressure cuff inflation and 5 min deflation. Venous blood samples were obtained at baseline before RIPC and after 5 and 30 min, 1, 6 and 24 hours and daily up to 7 days. Isolated mouse hearts were mounted on a Langendorff apparatus and perfused at a pressure of 100 mmHg with modified Krebs-Henseleit-buffer (37°C) before undergoing 20 min global ischemia and 120 min reperfusion. Before ischemia, the hearts were perfused for 15 min with dialyzed plasma (cut off 12–14 kDa, 1:20 dilution). Infarct size was assessed by TTC-staining. Infarct size over time was analyzed using one-way repeated measures ANOVA.

Results: Dialyates from healthy volunteers undergoing RIPC reduced infarct size in isolated Krebs-Henseleit buffer by 64% no later than 30 min after the completion of the manoeuvre. The cardioprotective effect lasted for at least 6 days and vanished thereafter.

Conclusion: We demonstrated measurement of oxidative DNA damage in and myocardial infarction in patients after reperfusion. We did not find correlation with severity of myocardial infarction. DNA damage is fully repaired in 24 hours; in future we will try to find relation with the clinical status.

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Endothelial progenitor cell-conditioned medium delivery by polymer nanoparticles in an ischemic hindlimb model

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Background: Endothelial progenitor cells (EPCs) contribute to ischemic repair by paracrine factor secretion, with hypoxic stress up-regulating factors related to their migration, proliferation and tissue repair. In this study, EPC-conditioned medium (CM) has been demonstrated effective for ischemic tissue revascularization. Nanoparticles (NPs) were tested for controlled release in ischemia, with a further improvement.

Purpose: To characterize the in vivo effect of hypoxic EPC-CM-loaded NPs, comparing it to hypoxic EPC-CM.

Methods: EPCs were obtained from peripheral blood of healthy donors and cultured for 24 h at 1%O2 in growth factor- and serum-free medium to obtain CM. 36 rats were divided into 3 groups: control (vehicle); EPC-CM; EPC-CM NPs. For each animal, 500 μl injections were performed at 3 sites into the ischemic hindlimb, immediately after ischemia and after 1 week. The effect of ischemia was evaluated both using Laser Doppler Blood Flow imaging (ratio between ischemic and contralateral limb), histology (hematoxylin/eosin, H&E, staining) to evaluate the inflammatory reaction and immunohistochemistry to evaluate capillary (CD31+) and artery (alpha-smooth muscle actin, alpha-SMA+) number per mm².

Results: A significant increase of perfusion was observed at 2 weeks in CM-NP vs. control (p < 0.005 vs. control) and 2 weeks (p < 0.0005 vs. control and p < 0.005 vs. control) and while CM and CM-NPs. Treatment with CM-NP significantly increased capillary number at both 1 (p < 0.05 vs. control) and 2 weeks (p < 0.005 vs. control and p < 0.005 vs. control) while CM treatment had a significantly higher effect than control only at 2 weeks (p < 0.005). No significant difference in the numbers of arteries among different groups was observed, suggesting a more pronounced effect on angiogenesis rather than arteriogenesis.

Conclusions: Novel therapeutic strategies that target on EPC paracrine factors may replace cell transplantation, as “cell-free” therapy could overcome the risk of adverse immunological reactions and the problem of heterologous rejection. Release of EPC-CM from loaded NPs was effective for blood flow and capillary enhancement in an in vivo model of hindlimb ischemia, underlining the advantages of using controlled release in regenerative medicine.

Circulating microRNAs as potential novel biomarkers for clinical outcome in patients with acute coronary syndrome

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Background: MicroRNAs (miRNAs), small RNAs, which interfere with gene expression at the post-transcriptional level, have been identified as critical mediators of cardiovascular homeostasis. miRNAs relevant for cardiovascular biology are dysregulated in patients with coronary artery disease and heart failure. Release of miRNAs into the circulation in pathophysiological cardiovascular processes, such as in patients with acute myocardial infarction, has been observed and selected circulating miRNAs (c-miRNAs) have been tested for their potential as biomarkers. However, the role of miRNAs as a diagnostic biomarker in a multi-center prospective cohort with patients presenting with an acute coronary syndrome (ACS) has not been performed.

Purpose: Analysis of prognostic impact of c-miRNAs related to major adverse cardiovascular events (MACE) and c-miRNAs detectable in all samples. Importantly, 13 c-miRNAs were significantly altered (p < 0.05) in patients presenting with STEMI and experiencing a MACE as compared with patients without MACE at 1 year FUP. c-miRNAs significantly associated included c-miR-18, c-miR-15 and c-miR-19. They were identified to be predictive of a worse outcome in left ventricular hype trophy and c-miR-20, which inhibits cardiomyocyte apoptosis.

Conclusions: The present study reveals c-miRNAs significantly associated with MACE at 1 year FUP in patients with STEMI derived from a multi-center prospective ACS-cohort. The identified c-miRNAs need to be further validated for the ability to predict MACE.

A prospective multi-center Swiss-ACS cohort study. The identified c-miRNAs need to be further validated for the ability to predict MACE.

Early atherosclerosis predictors in healthy population:

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Background: The aging suppressor gene klotho encodes a single-pass transmembrane protein, which is considered a “chronological clock” and responsible for the aging process. Klotho protein has been found to increase nitric oxide (NO) availability and to protect against endothelial dysfunction. In some recent trials it was shown that higher klotho levels is associated with lower cardiovascular disease prevalence. Epocardial fat thickness (EFT) and carotid intima-media thickness (c-IMT) are clinically related to subclinical atherosclerosis. Flow-mediated dilatation (FMD) is an easy and non-invasive method of detecting endothelial dysfunction and is associated with serum klotho levels. EFT measurements were done with echocardiography, c-IMT and FMD were measured by ultrasonography.

Methods: Total of 50 healthy volunteers (21men and 29 women, aged 32 (27–38)) were enrolled in this study. Study population was divided into two subgroups according to serum klotho levels. EFT measurements were done with echocardiography, c-IMT and FMD were measured by ultrasonography.

Results: The ages, body mass indexes and all biochemical assessments of the subgroups were similar. The EFT (0.75 (0.70–0.80) vs. 0.55 (0.30–0.50), p = 0.03) and c-IMT (0.80 (0.60–
Background: Acute chest pains without troponin rise are particularly challenging in patients with past medical history of coronary artery disease (CAD).

Methods: We analysed retrospectively 1149 STEMI pts admitted, consecutively, in primary percutaneous coronary intervention era.

Conclusion: This monocentric prospective study included 91 consecutive patients with acute chest pain and borderline hs-cTnT admitted in the intensive care unit for chest pain lasting for less than ten hours. Acute coronary syndrome (ACS) was excluded with ECG and hs-cTnT values <14ng/L at baseline and with dynamic changes ≤50% three hours later and <20% if baseline hs-cTnT between 14 and 50ng/L (Roche Diagnostics). Copeptin was measured at admission and the cut-off was validated as previously reported, with the upper reference limit (99th percentile) of 14ng/L and limit of detection at 5ng/L. Blood samples for determination of copeptin (Thermofisher, Kryptor Compact) were collected at presentation and results of dosages were blinded. Copeptin value was considered as positive when >10pmol/L (detection limit at 2pmol/L). Prognosis evaluation concerned absence of severe stenosis (>90%) or fractional flow reserve >0.80 at coronary angiography, or absence of ischemia induced with nuclear stress imaging. Results: Mean age of patients was 58±8 years and 72 (79.3%) were male. The mean time between chest pain onset and blood samples of copeptin was 4±2 hours. According to clinical decision, coronary angiography was performed in 63 patients (69.2%), with 12 severe stenosis diagnosed (19%). No ischemia was detected with the stress tests (26 patients). Among the 52 patients with a negative kinetic of hs-cTnT and a negative copeptin at baseline, only 2 (3.8%) had a critical stenosis (NPV 95%) both related to in stent restenosis (table 1). There was no MACACE at one month follow-up.

Conclusion: In patients with pre-existing CAD, acute chest pain and once ACS is excluded, copeptin provides a useful additional triage strategy to exclude severe coronary stenosis or stenosis inducing myocardial ischemia.

Table 1. Predictive values of hs-cTnT and copeptin

<table>
<thead>
<tr>
<th>Test Value</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive predictive value</th>
<th>Negative predictive value</th>
</tr>
</thead>
<tbody>
<tr>
<td>hs-cTnT &gt;14 ng/L</td>
<td>0.22, CI (0.028–0.6)</td>
<td>0.73, CI (0.604–0.830)</td>
<td>0.10, CI (0.02–0.317)</td>
<td>0.87, CI (0.755–0.947)</td>
</tr>
<tr>
<td>Copeptin &gt;10 pmol/L + hs-cTnT &gt;14 ng/L</td>
<td>0.75, CI (0.428–0.945)</td>
<td>0.6, CI (0.476–0.715)</td>
<td>0.24, CI (0.118–0.412)</td>
<td>0.93, CI (0.817–0.986)</td>
</tr>
<tr>
<td>Copeptin &gt;10 pmol/L + negative kinetic of hs-cTnT at 3 hours</td>
<td>0.79, CI (0.4–0.972)</td>
<td>0.39, CI (0.14–0.669)</td>
<td>0.19, CI (0.068–0.352)</td>
<td>0.95, CI (0.823–0.994)</td>
</tr>
</tbody>
</table>

Acute Intensive Cardiovascular Care I

P3451 | BEDSIDE

Incremental value of copeptin with high sensitivity troponin T for exclusion of severe coronary stenosis in patients with preexisting coronary artery disease

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Background: Acute chest pain without troponin rise are particularly challenging in patients with past medical history of coronary artery disease (CAD).

Methods: We analysed retrospectively 1149 STEMI pts admitted, consecutively, in primary percutaneous coronary intervention era.

Conclusion: The factors related to acute CT are related to coagulopathy or surgical anticoagulation, while the associated variables for subacute or late CT (sICCT) have not been well defined.

Purpose: The primary objective of this study is to identify the factors associated with the development of sICCT.

Methods: A case-control study of a historic cohort made up of all the adult patients who underwent cardiac surgery between 2006 and 2013 in a Level III cardio-vascular institution. The data base review showed a global incidence of CT of 2.1%, equal to 78 patients (cases) with sICCT. For the adjusted analysis, a logistic model was constructed with 55 variables including pre-, intra-, and post-operative data. A step-wise technique was employed, starting from a complete model. The model’s calibration was evaluated using the Hosmer-Lemeshow test.

Results: Seventy-eight cases were compared to 158 controls. Of these 78 patients, 23 were CABG (29%), 24 were aortic valve replacement (30%), and 18 were mitral valve replacement (23%). sICCT presented on the third POP day in 8 cases (10%), between 7 and 14 days POP in 48 cases (61%), and the remaining cases were distributed between the third and fourth week. Mortality of patients with sICCT was 11% vs. 0% in the controls. Among the 55 evaluated variables, 5 were identified as independently and significantly associated with the outcome: pre- or post-operative anticoagulation, re-intervention in the first 48 hours, surgery other than CABG, and red blood cell transfusion. The goodness of fit tests shows that the proposed model fits the observations well.

Conclusions: Our study identifies five variables associated with sICCT, and establishes that this is a complication with a high mortality rate. These findings may allow the implementation of standardized, intensive, follow-up measures for patients identified as higher-risk, in order to detect this complication early or prevent it.

Acknowledgement/Funding: Instituto de Cardiologia-Fundacion Cardioinfantil.

P3454 | BEDSIDE

Nonnocclusive mesenteric ischemia (ONMI) after out of hospital cardiac arrest: incidence and outcome of an underappreciated phenomenon

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Background: Non-occlusive mesenteric ischemia (OMI) is characterised by hypoperfusion of the intestines without evidence of mechanical obstruction, potentially leading to extensive necrosis. More often than not, the patients present with cardiogenic shock or respiratory failure with no clear cause. In such cases, there is a need to consider the possibility of mesenteric ischemia as the etiology of the hypotension. OMI is a complication that is often misdiagnosed or underdiagnosed.

Purpose: To conduct the first systematic investigation on the incidence of ONMI in out of hospital cardiac arrest survivors.

Table 1. Predictive values of hs-cTnT and copeptin

<table>
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<td>0.19, CI (0.068–0.352)</td>
<td>0.95, CI (0.823–0.994)</td>
</tr>
</tbody>
</table>
Methods: A prospectively maintained database of out of hospital cardiac arrest survivors, that had successful resuscitation of spontaneous circulation (ROSC), was retrospectively screened for clinical, radiological or pathological evidence of NOMI.

Results: 2469 patients treated between 1991 and 2014 were included into the analysis. Thirteen patients (0.5%) suffered from NOMI and 7 of those died (54%). Patients with NOMI tended to have a longer duration of time until ROSC (27 vs 20 min, p<0.108) and had significantly higher lactate (15 mmol/l vs 8 mmol/l, p=0.010) and base excess levels at admission (−18 vs −10, p=0.002) (Table 1).

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>No. of patients</th>
<th>NOMI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>2469</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Time from cardiac arrest to – median in minutes (IQR)</td>
<td>80 (50–110)</td>
<td>50 (50–100)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Complete ROSC</td>
<td>2040</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Ventricular fibrillation</td>
<td>1343 (55)</td>
<td>21</td>
<td>n.s.</td>
</tr>
<tr>
<td>Asystole</td>
<td>362 (16)</td>
<td>48</td>
<td>(52.6)</td>
</tr>
<tr>
<td>PE A</td>
<td>498 (20)</td>
<td>49</td>
<td>(52.6)</td>
</tr>
<tr>
<td>Clinical measurements at admission – median (IQR)</td>
<td>8.5 (5–12)</td>
<td>15 (10.5–18.3)</td>
<td>0.010</td>
</tr>
<tr>
<td>Lactate (mmol/l)</td>
<td>5.2</td>
<td>17</td>
<td>0.212</td>
</tr>
<tr>
<td>Base excess</td>
<td>−10</td>
<td>−18</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

CPR, cardiopulmonary resuscitation; ROSC, return of spontaneous circulation; PE, pulsatile electric activity.

Discussion: NOMI is a rare but dangerous complication following successful CPR. Lactate and base excess at admission could help to identify patients at risk for developing NOMI who might benefit from increased clinical watchfulness.

P3457 | BEDSIDE

Acute coronary syndromes without chest pain: a high risk group?

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Introduction: Many patients (pts) with acute coronary syndromes (ACS) have atypical symptoms and don't complain of chest pain. Some studies point to a worse prognosis of these pts because of misdiagnosis and undertreatment. The aim of this study was to compare the prognosis of the patient with ACS that presents without chest pain (WOPCP) to the one with typical clinical presentation (WCP).

Methods: We retrospectively analyzed the registries of ACS's included in the Portuguese National Registry of ACS, between October of 2010 and October 2014. We compared pts WOPCP and WCP at presentation regarding demographic data, cardiovascular risk factors and previous history, admission data, coronary angiography results, treatment and complications during hospitalization. Then we analyzed the prognostic implications of presentation WOCP when considering the patients who survive in-hospital mortality (IH). Pts presenting in cardiac arrest were excluded.

Results: A total of 11058 ACS were considered, 999 (9.0%) WOCP at presenta-
tion. The most common type of ACS was without ST-segment elevation (61.8%). Pts WOPCP were mostly males (57.2%) and significantly older, more frequently diabetic and hypertensive and with a higher prevalence of previous heart failure (HF), valvular heart disease, previous stroke, peripheral artery disease, renal failure, neoplasia, chronic obstructive lung disease and dementia. The main com-
plain was dyspnea (49.4%) followed by non-cardiovascular symptoms (22.2%) and syncope (21.3%). Time to first medical contact was similar between groups but time from symptoms onset to admission (TSAO) and time from first med-
cal contact to admission were significantly higher in pts WOCP (median 289 vs 201 min; p<0.001) and 194 vs 110 min; p<0.001 respectively. 2–3 vessel dis-
aease was more frequent in this group (60.7% vs 45.9%; p<0.001) and they were less likely to undergo reperfusion therapy (41.0% vs 67.4%; p<0.001). During hospitalization pts WOCP had more frequently HF (42.3% vs 14.1%; p<0.001), atrial fibrillation (10.7% vs 4.8%; p<0.001), stroke (2.4% vs 0.7%; p<0.001), major bleeding (3.1% vs 1.4%; p<0.001) and higher IHM (11.2% vs 7.2%; p<0.001).

Discussion: It is important to distinguish between WOCP and WCP. The main differences between the two groups were the time from symptoms onset and the delay between the patient arriving at the hospital and starting specific treatment. These differences may influence the outcomes of these patients. A possible explanation is that the WOCP group was more likely to present at a later stage of the disease, leading to an increased risk for adverse outcomes. More studies are needed to confirm these findings and to better understand the mechanisms behind these differences.
Complications during hospitalization including higher IHM. This higher risk didn’t seem to be explained by delayed start of treatment or the type of ACS.

**ISCHAEMIA, EXPERIMENTAL STUDIES II**

**P3458 | BEDSIDE**

Circulating endothelial progenitor cells are actively involved in the reparative mechanisms of stable ischemic myocardium

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1 University of Pisa, Department of Surgical, Medical and Molecular Pathology and Critic Area, Pisa, Italy; 2 University of Pisa, Dipartimento di Ricerca Traslazionale e delle Nuove Tecnologie in Medicina e Chirurgia, Pisa, Italy; 3 University of Pisa, Dipartimento di Patologia Chirurgica, Medica, Molocelare e delle Area Critic Cura, Surgery Section, Pisa, Italy

**Background and aim:** Mobilization of endothelial progenitor cells (EPCs) into circulation from bone marrow in patients with acute myocardial infarction has strong scientific evidence however less is known about EPC mobilization in patients with stable ischemic heart disease. The aim of this study was investigate the impact of stable ischemic heart disease on EPC level both in tissue and blood.

Methods: Consecutive patients admitted at our hospital for valve or CAGS surgeries were included in the study. Exclusion criteria were emergencies and redo surgeries. Blood samples were collected in the morning before surgery and analyzed by flow-cytometry in order to evaluate peripheral EPC levels (EPClini). Tissue sections (CD34+VEGF-R2+) levels were monitored on a right atrial appendage segment collected during cardiopuligia induction. Tissues were fixed in formalin and embedded in paraffin. Three μm sections were quantified immunohistochemically by counting double positive cells. Continuous data are expressed as mean ± SD, categorical data are expressed as frequency or percentage. T test was used in paired data. The interaction between the number of CD34+VEGF-R2+ cells and coronary artery disease was examined by multivariate analysis using the logistic regression model. Differences of p < 0.05 were considered statistically significant.

Results: 55 patients were included in the study. 46% were male with a mean age of 76±5. 53% of patients had coronary artery disease (CAD). 21% of patients had positive family history, 80% had hypertension, 22% of patients were smoker and 23% of patients were obese. The number of CD34+VEGF-R2+ cells in the tissue of patients with CAD was significantly higher when compared with control subjects (30/mm² vs 20/mm² p < 0.005) and circulating EPC showed a tendency to be reduced by approximately 20% in peripheral blood of patients with CAD when compared with healthy patients.

Conclusion: Patients with ischemic heart disease have higher EPC density value (EPC/mm²) and are more likely to have lower EPC blood levels when compare with controls. These results show that chronic ischemic heart disease, same as acute myocardial infarction, can be a stimulus to increase bone marrow mobilization and homing in myocardium. However more studies needed to confirm these evidences in larger population.

**P3459 | BENCH**

Inhibition of Rap1 enhances mesenchymal stem-cells-mediated heart protection following myocardial infarction

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1 The University of Hong Kong, Medicine, Hong Kong, Hong Kong SAR, People’s Republic of China; 2 The University of Hong Kong, Ophthalmology, Hong Kong, Hong Kong SAR, People’s Republic of China

**Background:** Mesenchymal stem cells (MSCs)-based therapy for myocardial infarction (MI) is mainly through paracrine effects responsive to different stimuli. However, the molecular mechanism regulating paracrine polarization of MSCs remains elusive.

**Purpose:** This study was to investigate the role of Rap1 in regulation of cytokine profiling of bone marrow-MSCs (BM-MSCs) treatment for myocardial infarction (MI).

**Methods and results:** Rap1−/− BM-MSCs and BM-MSCs were isolated from Rap1−/− and wild type mice respectively. Neutal cardiomyocytes (NCMcs) were isolated from neonatal rat. The conditioned mediums (CDM) of Rap1−/− BM-MSCs and BM-MSCs under normoxia or hypoxia were collected and concentrated. The secreted cytokines and the inflammatory cytokines were measured. MSCs apoptosis under normoxia or hypoxia were determined by TUNEL staining. The expression of phosphorylated p38-NF-κB, p65-NF-κB, Bcl-2 and Bax were detected by western blot. The cardioprotective effects of CDM of Rap1−/− BM-MSCs and BM-MSCs were examined when co-cultured with NCMcs under hypoxia. Rap1−/− BM-MSCs and BM-MSCs were transplanted into the peri-infarct region following MI model of mice. Heart function was evaluated by PV-Loop study and infarction size was assessed at 4 weeks post cell transplantation. Our results showed that compared with BM-MSCs, the apoptosis was greatly reduced in Rap1−/− BM-MSCs when exposed to hypoxic condition. TUNEL staining also demonstrated that the apoptosis of MSCs induced by hypoxia was significantly reduced when treated with Rap1−/− BM-MSCs hypoxic CDM compared with BM-MSCs hypoxic CDM. Analysis of cytokines revealed that the pro-inflammatory cytokines in Rap1−/− BM-MSCs hypoxic CDM were greatly reduced compared with BM-MSCs hypoxic CDM. These effects were associated with inhibition of NF-κB signal pathway. Furthermore, in vivo study showed trans-plantation of Rap1−/− BM-MSCs significantly improved heart function, decreased infarction size, prevented CMCs apoptosis and inhibited inflammation compared with MI and BM-MSCs group (P < 0.01).

**Conclusion:** Transplantation of Rap1−/− BM-MSCs effectively improved heart function following MI. Compared to BM-MSCs, superior therapeutic efficacy of Rap1−/− MSCs against MI may be attributed to their enhanced cell survival and paracrine actions.

**P3460 | BEDSIDE**

Inhibition of receptor activator of NFkB ligand (RANKL) in hematopoietic progenitor cells improves outcome after experimental myocardial infarction in mice

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1 University of Veterinary Medicine Vienna, Unit of Physiological Pathology and Experimental Endocrinology, Vienna, Austria; 2 University of Veterinary Medicine Vienna, Department for Small Animals and Horses, Vienna, Austria; 3 University of Veterinary Medicine Vienna, VetCore, Vienna, Austria; 4 Phyllon Pharma Services, Newbury Park, United States of America

**Background:** The RANK/RANKL/Osteoprotegerin signalling axis is activated after myocardial infarction (MI) but its role in the pathophysiology of cardiac dys-function is not yet known.

**Methods:** MI was induced by permanent ligation of the left descending coronary artery. To establish a model of selective inhibition of RANKL from hematopoietic and mesenchymal cellular sources, we exploited the specificity of the monoclonal anti-human RANK antibody AMG161 to inhibit human but not murine RANKL, together with human RANKL knock-in (huRANKL-KI) mice that express a chimeric RANK protein wherein most of the RANK binding domain is human. Lethal irradiation and reconstitution with unfractionated bone marrow leads to engraftment of hematopoietic, but not mesenchymal precursors. Thus, AMG161 treatment selectively inhibits RANKL derived from hematopoietic or mesenchymal cellular sources based on cross-genotype bone marrow transplantation between wild-type (WT) and huRANKL-KI mice. Global RANKL protein inhibition was achieved by treatment of non-irradiated huRANKL-KI mice with AMG161. AMG161 or an isotype control antibody was s.c. injected over 4 weeks post MI. Cardiac function was assessed by echocardiography and intra-cardiac catheter. Infarct size was assessed using Masson’s trichrome staining. Transcription of cytokine genes was measured by quantitative PCR analysis.

**Results:** MI increased RANKL expression mainly in cardiomyocytes and infiltrating cells adjacent to the infarct region. MI significantly decreased fractional shortening (FS) and contractility. Global RANKL inhibition by AMG161 in huRANKL-KI mice did not affect survival, cardiac function or infarct size after MI. Similarly, AMG161 treatment did not influence cardiac function in huRANKL-KI mice reconstituted with WT bone marrow. However, AMG161 administration to WT mice reconstituted with huRANKL-KI bone marrow significantly improved FS for about 5%. Infarct size did not differ between the groups. Interestingly, inhibition of RANKL derived from hematopoietic sources, but not inhibition of mesenchymal RANKL, reduced the expression of pro-inflammatory genes such as IL-1α, TNFα, IL-1β and NFκB in the left ventricle and also in bone marrow post-mi.

**Conclusion(s):** Inhibition of RANKL derived from hematopoietic cellular sources has beneficial effects on post-ischemic cardiac function by reduction of inflammation and cytokine production.

**Acknowledgement/Funding:** The Austrian Science Fund (FWF) grant to Erben G

**P3461 | BEDSIDE**

Intracoronary adenosine: dose-response relationship with hyperemia

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1 Oiv Hospital Aalst, Cardiology, Aalst, Belgium; 2 Weatherhead PET Center for Preventing and Reversing Atherosclerosis, Division of Cardiology, Department of Medicine, Cleveland Clinic, University of Texas Southwestern Medical Center, Houston Texas, United States of America; 3 University Hospital Centre Vaudois (CHUV), Department of Cardiology, Lausanne, Switzerland

**Background:** Despite the widespread adoption of intracoronary (IC) adenosine in clinical practice, no wide-ranging, dose-response study has been conducted.

**Purpose:** The present study sought to establish the dosage of IC adenosine as close to minimal side-effects and above which no further increase in flow can be expected.

**Methods:** In 30 patients, Doppler-derived flow velocity measurements were obtained in 10 right coronary arteries (RCA) and 20 left coronary arteries (LCA) free and at 4 different fixed IC bolus doses of adenosine at baseline and after 8 mL bolus administrations of 9 escalating doses of adenosine (4 to 500 μg). The hyperemic value was expressed in percent of the maximum flow velocity reached in a given artery (Q/Qmax, %).

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Results: Qmax did not increase significantly beyond dosages of 60 μg for the RCA and 160 μg for LCA. Heart rate did not change, while mean arterial blood pressure decreased by a maximum of 7% (p < 0.05) after bolus injections of IC adenosine. The incidence of transient atrioventricular blocks was 40% after injection of 100 μg, in the RCA, and was 15% after injection of 200 μg in the LCA. The incidence of transient ventricular arrhythmia was 40% after injection of 100 μg in the RCA and 21±6 seconds after the injection of 200 μg in the left LCA. A progressive prolongation of the time needed to return to baseline was observed.

Conclusions: This wide-ranging dose-response study indicates that an IC adenosine bolus injection of 100 μg in the RCA and 200 μg in the LCA induces maximum hyperemia while being associated with minimal side effects.

Acknowledgement/Funding: Financial support: Research grant from Fedecardio

P3462 | BENCH Early detection of low-grade myocardial ischemia by miniaturized 3-axis accelerometer S. Hyler1, S. Pischke2, O.J. Grymyr1, A. Espinoza2, H. Skulstad3, J. Bergsland1, 3-axis accelerometer Early detection of low-grade myocardial ischemia by miniaturized 3-axis accelerometer. A linear relationship among coronary blood flow, myocardial ischemia / reperfusion injury and tissue lactate in CX area during the reductions in coronary artery flow. A loglinear correlation between coronary flow reductions and the decreases in velocity correlated closely throughout and LDH release was measured during reperfusion. Both H9c2 cells and isolated hearts underwent 20 min ischemia / reperfusion (I/R). Cells were treated with 1 μg/ml Exo, 3-MA or rapamycin (Rapa), a known anti- or pro-autophagic agent. Cell viability WST assay, cell injury-induced LDH release, a flow-based apoptosis assay and GFP-LC3 labeled autophagosomes were measured. Isolated hearts underwent 20 min ischemia / 60 min reperfusion (I/R), with or without Exo. Cardiac function was monitored throughout and LDH release was measured during reperfusion. Both H9c2 cells and isolated hearts were collected for WB analysis.

Results: Exo reduced I/R injury as indicated by higher cell viability, WST activity and reduced LDH and apoptosis (Exo vs. H-R, p < 0.05). 3-MA showed similar protective effects. Rapa-induced injury was partially blocked by Exo. Exo increased cardiac functional recovery by ~2-fold (vs. I/R) and reduced LDH release. WB from both H9c2 and tissue demonstrated that Exo increased the LC3-II/I ratio and p62, indicators of reduced autophagy. Exo also inhibited autophagosome formation (Fig). Bcl-2 was significantly upregulated by Exo but not by 3-MA. Exo down regulated Tr1R and upregulated mTORC1/p-s6E1.

Conclusions: The epicardially attached miniaturized 3D accelerometer enabled quantifying different levels of myocardial ischemia during stepwise reductions in coronary artery flow. A linear relationship among coronary blood flow, myocardial ischemia and function was found. These results demonstrate that 3D accelerometers can be used to detect graft failure during and after heart surgery.

Acknowledgement/Funding: The study was funded by The Norwegian Health Authorities

P3463 | BEDSIDE Low molecular weight dextran usage in intracoronary imaging guided percutaneous coronary intervention was associated with high incidence of filter no re-flow phenomenon M. Nozoe, Y. Yamamoto. Department of Cardiology, Saiseikai Fukuoka General Hospital, Fukuoka, Japan Background: Intravascular frequency-domain optical coherence tomography (OCT) image acquisition with low molecular weight dextran L (LMD-L) could reduce the total amount of contrast media without loss of image quality. LMD-L is a highly viscous solution, however, there were no data about the influence of LMD-L on the PCI with filter distal protection device.

Purpose: The purpose of this study was to evaluate whether LMD-L has negative effect on PCI with a filter distal protection device or not.

Methods: We retrospectively reviewed consecutive 110 patients who underwent PCI with a filter distal protection device. They included 43 cases of acute myocardial infarction with ST elevation (39.1%), 34 cases of non-ST elevation acute coronary syndrome (30.9%), and 33 cases of stable angina (30%). We performed the PCI using a filter distal protection device with OCT in 66 cases, with IVUS in 35 cases, and without imaging modality in 9 cases. We performed OCT-guided PCI using LMD-L in 44 cases (LMD-L group) and using only contrast media in 22 cases (Contrast group). We compared an incidence of filter slow flow phenomenon and filter no-reflow with ST re-elevation between LMD-L group (n=44), Contrast group (n=22), and IVUS group (n=35).

Results: Patients characteristics were not different between three groups. The incidence of filter slow flow phenomenon and filter no-reflow with ST re-elevation in LMD-L group (65.9%, 43.2%) were significantly higher than those in Contrast group (36.3%, 13.8% P < 0.05) and in IVUS group (40%, 22.9%, P < 0.05). When we analyzed only among ACS cases, the same tendency was demonstrated (P < 0.05). TIMI flow ≤ 2 at final angiogram was not different between three groups. Myocardial Blush Grade ≤ 2 at final angiogram was more frequently observed in LMD-L group, but did not reach significance.

Conclusions: LMD-L usage might facilitate a filter no-reflow phenomenon in OCT-guided PCI. When we use LMD-L in conjunction with a distal protection device, we should pay attention for the possibility of filter no-reflow phenomenon.
Acknowledgement/Funding: The authors thank all the participants of the study for their contribution. This study was supported by the National Natural Science Foundation of China (81330006, 81170192, 81470389, 81270282), and National Science Foundation of China (7-11-BS-93).

Methods: In the current study, the oxidative stress level was determined by measuring the protein expression and activity of p53, p62, and Mtor. The levels of protein expression were measured by Western blot analysis and the activity of p53 and p62 was measured using the luciferase reporter assay. The oxidative stress was determined using the 2-thiobarbituric acid (TBARS) test.

Conclusion: The results of the current study suggest that high dose atorvastatin (80 mg) is more effective in reducing oxidative stress and improving myocardial function compared to the control group. The use of high dose atorvastatin may be a potential therapeutic strategy for the treatment of acute coronary syndrome.
patients with the use of Holistic Coronary Care software, a program developed by our study group.

**Results:** Among a total of 290 patients 45 received IABP as a rescue therapy. Among baseline clinical parameters the left ventricular ejection fraction (LVEF) and the glomerular filtration rate (GFR) was significantly higher in the rescue IABP group (LVEF 39% SD:8 vs. 34% SD:9, p=0.005; GFR [ml/min/1.73 m^2]: 69 SD:22 vs. 60 SD:23 p=0.01). There was no significant difference in the calculated AMR between patients with rescue IABP therapy and those in whom IABP was inserted earlier, during the PCI (62.3% SD 25.8 vs. 58.6% SD 25.5; p=0.098). The in-hospital mortality rate did not differ significantly in the two groups, while duration of hospitalization was significantly longer (22 vs. 17 days p=0.05) and the mortality rate was significantly higher at both 30 and 365 days in the rescue IABP therapy group as compared to those with earlier initiation of IABP therapy (16% vs. 3.8% p=0.018; 29% vs. 6% p=0.001 for 30 days and 1 year, respectively).

**Conclusion:** Patients with ACS who receive IABP therapy during the PCI due to an early development of cardiogenic shock have better survival at 30 and 365 days as compared to patients with the need of rescue IABP therapy.
Acute coronary syndrome and atrial fibrillation a world of many questions


Introduction: Atrial fibrillation (AF) is a very common arrhythmia in patients (P) with cardiovascular disease. Acute coronary syndromes (ACS) remains an important risk factor for the onset of AF.

Purpose: To evaluate the differences between patients with ACS and AF on admission or during in-hospital stay regarding the cardiovascular risk profile, therapeutic approach, in-hospital mortality (IHM) and major cardiac events (MACE) follow-up of 17±9 months.

Methods: We reviewed 1039 P admitted with ACS, 38.9% STEMI; 41.2% NSTEMI; 15.6% unstable angina; 4.3% unspecified myocardial infarction. P were unselected STEMI population. This study highlights the importance of an optimal selection of patients during PPCI in order to do or not to do TA.

Results: There were not differences between patients with and without TA regarding mortality (4.7% vs. 6.7%, p=0.063); reinfection (2.7% vs. 2.9%, p=0.056) or heart failure (8.3% vs. 8.5%, p=0.293). After propensity score matching, results were similar between the two groups for these events (7.5% vs. 6.9%, p=0.004). After propensity score matching, we have not find differences between the two groups for mortality (HR 0.87, 95% CI 0.53–1.43, p=0.589), reinfection (HR 1.78, 95% CI 1.04–3.77, p=0.129) or HF (HR 0.94; 95% CI 0.53–1.67; p=0.945). Figure shows the Kaplan Meier curves after propensity score matching for the composite endpoint after PPCI (HR 1.18; 95% CI 0.89–1.58, p=0.242).

Conclusion: We have not find benefit on clinical outcomes of TA in a real-world unselected STEMI population. This study highlights the importance of an optimal selection of patients during PPCI in order to do or not to do TA.

Tissue Doppler estimation of hemodynamic status of cardiogenic shock due to acute coronary syndrome or acute degradation of chronic heart failure

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Background: The ratio of early mitral inflow velocity to tissue Doppler mitral annular early diastolic velocity (E/e') and isovolumic relaxation time (IVRT) are simple, well known parameters and have been well correlated with pulmonary capillary wedge pressure (PCWP) in a wide variety of cardiac conditions. However, the usefulness of non-invasive estimation of PCWP among patients with acute de-compensated chronic heart failure (ADCHF) or in cardiogenic shock (CS) is still unclear. The aim of this study was to determine the reliability of tissue Doppler velocities for PCWP estimation in patients with ADCHF and in CS complicating acute coronary syndrome (ACS).

Methods: Two groups of prospective consecutive patients admitted to Intensive Cardiac Care Unit presenting with cardiogenic shock complicating ACS and candidates for heart transplantation with acute decompensation of severe chronic lower revascularization rate (73% vs 83%, p=0.027). Bare metal stents were most used, but with no t difference (50% vs 46%, p=0.364). Medical therapy was similar in both groups, with the exception of dual antiplatelet therapy at the time of release (p=0.199).

IHM was overlapping in both groups (6.1% vs 5.9%, p=0.942). At follow-up, there was no significant difference in the incidence of MACE (30.4% vs 27.7%, p=0.06) but a higher mortality was found (27% vs 17%, p=0.007).

Conclusions: In ACS P there is a high prevalence of AF. These P have a more severe clinical profile, the presence of AF being associated with adverse events including increased mortality at follow-up. Revascularization therapy should be individualized taking into account the overall risk of the patient.
systolic heart failure. A total of 61 patients were included. Clinical data are outlined in Tab. 1. Both groups underwent simultaneous echocardiographic and hemodynamic evaluation. For the purpose of the study, according to the published data PCWP >18 mmHg was a cut-point for E/e' value estimation. **Results:** There was statistically significant difference in mitral E/e' ratio between ADCHF patients and in CS (27±11 vs. 13±5, p=0.0001). The correlation between PCWP and E/e' ratio was statistically significant (r=0.51, p=0.05) in CS patients. In addition there were significant correlation between IVRT and PCWP (r=0.50, p=0.047) in ADCHF patients. We observed statistically significant difference of E/e' ratio in patients subgroups defined on PCWP value >18 mmHg or in ADCHF group; 19±6 vs. 30±5±11; p=0.00831 respectively and in CS group 11,4±2 vs. 17±7 p=0.0492 respectively.

**Conclusion:** In patients with cardiogenic shock complicating ACS and in the patient with ADCHF tissue Doppler-derived mitral E/e' ratio may be a reliable and simple tool in predicting elevated PCWP.

**P3476 | BEDSIDE**

Mini-invasive circulatory support systems and extracorporeal membrane oxygenation in the management of cardiogenic shock and refractory cardiac arrest: results from a prospective registry

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**Purpose:** Mini-invasive circulatory support systems and particularly vena-arterial extracorporeal membrane oxygenation (ECMO) has been recently introduced for circulatory support in the management of critical conditions caused by severe cardiac failure.

**Methods:** We analyzed a prospective registry of 110 primarily non-surgical patients (mean age 61 (30–82) years, 83% were males), treated in our institution by Impella 2.5 (N=2), PulseCath (N=16), TandemHeart (N=17), and ECMO (N=75). The major indicator for circulatory support therapy was cardiogenic shock, followed by refractory cardiac arrest, arrhythmic storm, and support of high-risk interventions.

**Results:** Median duration of circulatory support was 2 days, maximum 66 days. The all-cause 30-day mortality was 30.0%; in the subgroup of 51 patients with severe cardiogenic shock as the reason for circulatory support the 30-day mortality was 44.4%. In patients with refractory cardiac arrest, where ECMO was introduced during continuous chest compressions (extracorporeal cardiopulmonary resuscitation, ECPR), 4 individuals from 18 treated survived with good neurological outcome. We found significant survival differences between subgroup with urgent circulatory support placement and patients with semi-urgent or planned support (30-day mortality 46% vs. 11.6%, P<0.001). We did not find differences between survivors and non-survivors in the major characteristics including age or left-ventricle ejection fraction. Multiple logistic regression analysis revealed that urgent device placement and cardiac arrest before implantation were independent predictors of death.

**Conclusions:** Mini-invasive circulatory support systems and particularly vena-arterial ECMO are promising tools in the management of severely compromised patients with rapidly progressing cardiogenic shock or refractory cardiac arrest. Frequently the mechanical circulatory support in these high-risk patients represents the last chance to survive.

**Acknowledgement/Funding:** Grant from the Czech Ministry of Health, Nr. 121530 and Institutional grant MH ČZ - DRO (Nemocnice Na Homolce - NNH, 00023884)

**P3477 | BEDSIDE**

Impact of acute heart failure in patients with non-ST elevation acute coronary syndrome by their functional classification and the application of early invasive strategy

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**Background:** Little is known about the outcomes of non-ST-elevation acute coronary patients and their outcomes (NSTE-ACS) complicated with acute heart failure (AHF). Further, early invasive strategy (EIS) is recommended in the clinical guidelines but difficulty on its real-world application is noted.

**Purpose:** We aimed to quantify the short-term impact of 1) AHF condition on the in-hospital outcome by their functional classification and also 2) the “real-world” application.

**Methods:** Between 2009 and 2014, 3287 patients with NSTE-ACS were enrolled in our interhospital Cardiovascular Studies, an ongoing prospective multicenter registry. EIS was defined as PCI performed within 48 hours after presentation. The individual and composite outcome of in-hospital death, cardiogenic shock after the procedure, stroke, major bleeding, and new requirement for hemodialysis were analyzed.

**Results:** In total, 441 (13.4%) patients had AHF on presentation. Patients with AHF had a substantially higher in-hospital mortality rate than those without (3.9% vs. 0.6%, P<0.001); the frequency of mortality and major complication rate cumulatively increased with severity of the functional class (Figure). EIS was less frequently applied in AHF patients (75.3% vs. 57.2% in HF, P<0.001). After adjustment, AHF severity remained significantly associated with clinical outcomes in patients with NSTE-ACS (OR 2.79; 95% CI 1.78–4.37). However, EIS had no observed impact on clinical outcomes in AHF patients after adjustment (OR 1.13; 95% CI 0.64–2.01).

**Conclusion:** Patients with NSTE-ACS complicated with AHF had a significantly higher event rates, increasing with severity of functional class at presentation. In contrast, EIS was paradoxically less frequently applied in these patients, despite strong recommendation in the clinical guidelines.

**Acknowledgement/Funding:** Grant-in-Aid for Scientific Research (C)

**P3478 | BEDSIDE**

Tissue inhibitor of matrix metalloproteinase 1 (TIMP-1) as a novel marker to distinguish acute coronary syndrome (ACS) from other acute cardiac conditions

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**Introduction:** Electrocardiogram and cardiac enzymes identify acute cardiac pathology of various aetiologies, irrespective of coronary status. In ACS, to prevent worsening of the patients' condition, coronary angiography (CA) should not be delayed. In other settings postponing, or even omitting, CA could be beneficial.

**Purpose:** We hypothesised that systemic inflammatory mediators matrix metalloproteinase 8 (MMP-8) and tissue inhibitor of matrix metalloproteinase 1 (TIMP-1) could identify acute cardiac injury and distinguish ACS from other acute cardiac conditions.

**Methods:** Serum samples were obtained in conjunction with CA in 3794 successes. Patients were scheduled for CA on clinical elective and acute basis. Concentrations of MMP-8 and TIMP-1 were measured using enzyme-linked immunosorbent assay (ELISA). Of the elective (N=1627) patients 653 had no coronary artery disease (no-CAD), and 974 had stable CAD. Of the acute patients 2072 had ACS, and 95 did not (ACS-like).

**Results:** Both MMP-8 and TIMP-1 concentrations were significantly higher in the acute patients (ACS and ACS-like, p<0.001) relative to the stable patients (stable CAD and no-CAD). The concentrations of MMP-8 and TIMP-1 did not differ within stable patients (no-CAD vs CAD, p=0.411 and p=0.599, respectively). In acute patients MMP-8 concentrations did not differ significantly, but TIMP-1 concentrations were significantly higher in ACS patients than in ACS-like patients (p=0.174 and p=0.001, respectively).

**Conclusions:** As novel markers of cardiac injury MMP-8 and TIMP-1 identify acute cardiac pathology. Elevated TIMP-1 concentration can further distinguish ACS patients from those without target coronary lesion. Inflammatory mediators MMP-8 and TIMP-1 can be used in acute setting to select patient in need of immediate CA.

**Acknowledgement/Funding:** The Finnish-Norwegian Medical Foundation

**ACUTE CARDIAC CARE IN THE EMERGENCY DEPARTMENT II**
Copeptin 38 84 83 29 0.007

Background: Male gender is a consolidated cardiovascular risk factor in medical literature. However, studies show most often unfavorable outcomes in women as well as underutilization of established therapeutic strategies. The time between the onset of chest pain (CP) and hospital admission (delta T) can affect therapeutic efficacy in acute coronary syndromes (ACS). This paradigm is controversial and its impact on the stratification of the probability of ACS in the emergency room is not clear.

Purpose: To compare the delta T between genders in patients with clinical suspicion of ACS and different clinical presentations.

Methods: This prospective study included 878 patients admitted to the chest pain unit (CPU) with clinical suspicion of ACS. The delta T was estimated by the interval between the onset of symptoms and admission at the CPU. Clinical presentation was classified as typical CP (definitely angina and probably angina) and atypical CP (probably not angina and definitely not angina). Patients underwent serial assessment of EKG and troponin I on admission and 6 hours later. The diagnosis of ACS was performed by ischemia detection in stress tests or in the presence of significant obstruction in coronary angiography. Statistical analysis was performed using student t-test and chi square.

Results: Mean age was higher among women (64.4±16.4y vs 62±16.1y;p<0.04), the ACS occurrence was higher in males (29.0% vs. 12.5%; p<0.001). Atypical presentations were more common in women (62.3% vs. 47.8%; p<0.003). There was no difference between the median delta T of both genders for the total population (men vs women:120 min vs 115 min; p=0.16), with typical DT (men vs women:120 min vs 91 min; p<0.03), or SGA (men vs women:80 min vs 96 min; p=0.36).

Conclusion: Women were admitted to CPU with more atypical symptoms and an older age. The higher incidence of ACS in men reinforces the risk in this group. There was no difference in delta T between genders, even in individuals with ACS.

PPV, positive predictive value; NPV, negative predictive value.

Conclusions: In patients admitted to emergency department with chest pain and non-conclusive ECG, copeptin tends to improve sensitivity and NPV of hs-TnT early after symptom onset. Therefore copeptin can be regarded as a co-efficient marker in the rapid diagnosis of patients with non-STE ACS and non-conclusive ECG.

Purpose: The aim of this study was to evaluate the impact of neurologic status on the outcome of patients with cardiogenic shock.

Results: In the cohort of 154 patients, 105 (68%) met the criteria for NSTEMI, 49 (32%) for STEMI. Mean age was higher among women (64.4±16.4y vs 62±16.1y;p=0.04). The ACS occurrence was higher in males (29.0% vs. 12.5%; p<0.001). Atypical presentations were more common in women (62.3% vs. 47.8%; p<0.003). There was no difference between the median delta T of both genders for the total population (men vs women:120 min vs 115 min; p=0.16), with typical DT (men vs women:120 min vs 91 min; p<0.03), or SGA (men vs women:80 min vs 96 min; p=0.36).

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Background: The ongoing evolution of troponin assays has enabled the more accurate determination of very low troponin concentrations which assist the clinician to rule out Acute Myocardial Infarction (AMI). The recent launch of a commercially available assay for heart fatty acid binding protein (hFABP) has enabled this biomarker to now be measured more accurately and reliably in a clinical setting, hence overcoming previous issues with rapid tests and ELISA-based assays. We tested the hypothesis to combine both hs-cTnI (hstNI), hFABP and electrocardiography to rule out AMI within two hours of patients presenting with chest pain to emergency departments. We validated the derived cutpoint in a separate cohort.

Methods: hstNI and hFABP were measured on presentation and two hours later in patients presenting to an emergency department with possible ACS with or without ST-elevation on electrocardiograph (ECG). AMI was adjudicated by cardiologists using the ECGs, local TnI results, and clinical information. hstNI cutpoints were >16 ng/L for females and >34 ng/L males. A positive index test was an ECG positive for new or incipient ST and an hstNI above the cutpoint. In the development cohort we calculated the hFABP cutpoint at which on addition of hFABP to the index test the sensitivity exceeded 99% and determined the proportion of low risk patients who could potentially be discharged from ED into the care of their general practitioner. We validated the hFABP cutpoint in a separate cohort.

Results: In the development cohort AMI was diagnosed in 227 (23.1%) of 981 presentations. The index test identified 638 patients (65.0%) as negative of whom 12 were false negatives (Sensitivity 94.7% [95% CI 91.0% to 97.0%]. A sensitivity of >99% (98.8% to 99.9%) was achieved with the addition of hFABP at a cutpoint of 4.35 ng/ml. 415 (42.3%) presentations were negative (low risk) of whom 2 were falsely negative. In the validation cohort AMI was diagnosed in 50 (14.0%) of 356 presentations. The index test identified 295 patients (82.5%) as negative of whom 5 were false negatives (Sensitivity 90.0% [78.6% to 95.7%]). The addition of hFABP at a cutpoint of 4.35 ng/ml reduced the number of false negatives to 3 (Sensitivity 93.8% [83.2% to 97.9%]) all of which had an hFABP >3.9 ng/ml. 39.0% remained low risk.

Conclusion: The addition of hFABP with a cutpoint of 4.3 ng/mL to the index test comprising hstNI and ECG reduced the rate of false negatives whilst maintaining a clinically useful proportion of low risk patients at around 40%.

Acknowledgement/Funding: hFABP assay kits were provided free of charge by Random Cardiology, Funding by the Health Research Council of NZ & the Christchurch Heart Institute.

P3484 | BESIDIDE

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


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

Methods: In a prospective international multicentre diagnosis study enrolling 2213 patients presenting with suspected AMI to the emergency department, the final diagnosis of AMI was adjudicated by two independent cardiologists using all available clinical information including serial hs-cTnT concentrations. Safety was quantified as the negative predictive value for AMI in the rule-out zone of the respective rule-out strategy. Efficacy was quantified as the percentage of the overall patient group assigned to the rule-out zone by the respective strategy. Both strategies were applied using the two best-validated hs-cTn assays (hs-cTn Roche: LOD <5ng/L; 1h-algorithm 0h<12ng/L and >0.1<1h<3ng/L; and hs-cTn Abbott: LOD <2ng/L; 1h-algorithm 0h<5ng/L and >0.1<1h<2ng/L) to ensure that findings are independent from the hs-cTn assay used. As both strategies should only be applied in combination with an hs-cTn assay at ED admission. Further, using follow-up: 0% false negative rate [CI 0.0–0.9], sensitivity 100% [94.1–100], negative predictive value 100% [98.2–100], positive predictive value 25.7% [CI 20.6–31.7].

The HEART score (without troponin) was <1 in 200 patients (31.2%) and none of them had MACE: false negative rate 0% [CI 0.0–1.9], sensitivity 100% [94.1–100], negative predictive value 100% [98.2–100]. Among them, a sensitive troponin 1 assay was performed for 119 patients: all tests were under reference range.

Discussion: In patients with a HEART score <3 or a HEART score <1, the 6-week MACE rate was very low. HEART score appears safe to rule out ACS and to allow discharge after a single troponin test. In addition, ‘HEART’ score might be useful on anamnesis and ECG data without any biological test in a significant proportion of patients.

Conclusion: In patients admitted to ED for non-traumatic chest pain, HEART and ‘HEART’ scores seem accurate to rule out ACS and may lead to significant decrease in troponin test requirement and ED length of stay. A larger multicentric study is needed to confirm these results.

P3484 | BESIDIDE

High sensitivity troponin T in the rule-out of acute coronary syndrome at the emergency department: the age matters


The best use of high sensitivity troponin T (hs-tnt) in the rule-out of myocardial infarction (MI) is still unknown. Values >14 ng/L should be regarded as the cutoff for a MI. However, multiples cardiac and no cardiac causes can elevate hs-tnt levels in absence of MI.

Methods: We retrospectively analyzed all measurements of hs-tnt at the emergency department (ED) during one year.

Results: We reviewed 17251 hs-tnt measurements in the ED, in 6495 patients (62% male), age 69±21 years. 9099 (52.7%) determinations were <14 ng/L. Selecting only concentrations >14ng/L, the diagnosis at discharge was "MI" in 28%, 41% was attributed to other cardiac disease other than MI and 31% were diagnosed with non-cardiac disease. MI classified patients into two groups: ≤65 yo (n=1112) and >65 yo (n=2108). In younger patients group, diagnosis was MI in 48% (vs 18%, p<0.02). No cardiac condition was the diagnosis in 28% of <65 yo vs 38% in elderly population (p=0.03). No differences were found between groups in cardiac but non MI elevation.

Discussion: To identify patients at lower risk of MI, a new cutoff of ≤50 ng/L should be considered. The cutoff of 14 ng/L is not suitable to rule-out MI in all age groups.
Underlying cause for pre hospital cardiac arrest - incidence of culprit lesions after successful resuscitation and their predictability by ECG recordings

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Purpose: An acute coronary syndrome is suspected to be the leading cause of out of hospital cardiac arrest (OHCA). In our present study we examined the reliability of the ECG in predicting an acute coronary syndrome (culprit lesion at angiography) as the underlying mechanism for OHCA.

Methods: We retrospectively analysed all successful resuscitation attempts from our mobile ICU from 2007 to 2012. Patient charts and electronic databases were reviewed including ECG's and coronary angiograms from patients admitted to our hospital.

Results: We found 767 out of hospital resuscitation attempts. 220 (28.7%) where successful, 166 (21. 6%) were admitted to our hospital. In 83 out of the 166 patients coronary angiography was performed. Pre-hospital or hospital ECG recording where diagnostic for STEMI in 39 cases (group A) and not diagnostic for STEMI in 44 cases (group B). Culprit lesions were found in 77% in group A and in 48% in group B. Overall, acute coronary syndrome confirmed through angiography was found as the underlying mechanism in 38.4%, chronic coronary artery disease and reduced ejection fraction in 15%.

Conclusion: Acute coronary syndrome was found in 38% of cases as underlying mechanism in survivors from out-of-hospital cardiac arrest. ECG recording was a reliable predictor of culprit lesions (correctly in 77%), but culprit lesions were also found in 48% of cases with non-diagnostic ECG’s. Our data support an early invasive strategy after successful resuscitation from OHCA even in the absence of ECG recordings for STEMI.

ACUTE INTENSIVE CARDIOVASCULAR CARE III

P3487 | BEDSIDE
Therapeutic hypothermia in patients resuscitated from out-of-hospital cardiac arrest: a meta-analysis of randomized controlled trials

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Background: Therapeutic hypothermia (TH) is recommended by current guidelines for survivors of out-of-hospital cardiac arrest (CA). The supportive evidence showing beneficial outcomes is limited.

Purpose: We performed a meta-analysis of randomized controlled trials (RCT) to assess the efficacy and safety of TH in patients successfully resuscitated from CA.

Methods: We conducted electronic search of RCT. The primary endpoint was all cause mortality. Secondary endpoints included favorable neurological recovery and new onset arrhythmias or re-arrest. Odds ratios (OR) and 95% confidence intervals (CI) were computed using the Mantel-Haenszel (MH) method. Fixed-effect model was used; if heterogeneity (I²) >40, effects were analyzed using a random model.

Results: Five RCT (n=1,358 patients) were included. Overall survival was 51.7% and full neurological recovery was 45.7%. Pooled data demonstrated no significant difference from TH for the primary outcome of all-cause mortality (OR 1.26 [95% CI 0.91–1.40], p=0.73). Also, no significant difference was seen for the secondary outcomes of favorable neurological recovery (OR 1.45 [95% CI 0.86–2.44], p=0.16) and new onset arrhythmias or re-arrest (OR 0.95 [95% CI 0.71–1.31], p=0.73). Exclusion of a single study from the analysis did not alter the overall result.

Conclusion: Our meta-analysis showed that TH in patients resuscitated from out-of-hospital CA does not improve mortality, favorable neurological outcomes, new onset arrhythmias or re-arrest. Overall survival rate and odds of neurological re-covery are low in these patients, indicating that alternative therapeutic strategies need to be developed.

P3488 | BEDSIDE
Peak systolic velocity by tissue Doppler detects changes in myocardial contraction related to inotropic effects of levosimendan in patients with acute heart failure complicating myocardial infarction

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Purpose: Peak systolic velocity (PSV) by tissue Doppler imaging (TDI) has been proposed for serial non-invasive assessment of myocardial contraction in patients receiving inotropic therapy due to its relative load- and heart rate-independent properties. However, this hypothesis has so far not been tested in a clinical setting. We therefore examined the ability of PSV by TDI to detect changes in contraction in a subset of the LEVosimendan in Acute heart Failure following myo-cardial infarction (LEAF) trial (NCT00324766).

Methods: A total of 61 patients developing clinical signs of heart failure within 48 hours after a percutaneous coronary intervention-treated ST-elevation myocardial infarction (including cardiogenic shock), were randomized double-blind to a 25 hours infusion of levosimendan or placebo. Levosimendan is an inotrope where the effects, due to active metabolites with very long half-lives, last for several days after end of the infusion. Echocardiography was performed before infusion (baseline), on day 1, on day 5 and after 6 weeks. PSV (mean of septal, lateral, anterior and posterior mitral annular peak systolic velocity) measured by tissue velocity imaging, and global longitudinal strain (GLS) of the left ventricle measured by speckle tracking were analyzed at all time-points.

Results: There was significantly larger improvement in PSV from baseline to day 1 (P<0.007) and day 5 (P<0.001) in the levosimendan group compared to placebo (levosimendan: 4.70 cm/s ± 1.34 to 5.74 cm/s ± 1.47 (day 1) and 6.07 cm/s ± 1.47 (day 5) vs.placebo: 4.77 cm/s ± 1.02 to 5.08 cm/s ± 1.35 (day 1) and 4.90 cm/s ± 1.26 (day 5)). No significant differences were found in PSV after 6 weeks or in GLS at any time-point between the treatment groups. We have previously shown that levosimendan improved left ventricular function measured as changes in wall motion score index (WMSI) from baseline to day 5 compared to placebo (p=0.031, primary endpoint of the LEAF trial), however no significant changes in WMSI were found on day 1 or after 6 weeks between the treatment groups.

Conclusion: PSV by TDI seems to be a more sensitive echocardiographic method to detect changes in myocardial contraction during inotropic stimulation with levosimendan than WMSI and GLS. These results suggest that PSV by TDI can be used for assessment of changes in contraction in patients hospitalized for acute heart failure receiving inotropic therapy.

P3489 | BEDSIDE
Role of copeptin in the postoperative management of patients after on-pump cardiac surgery

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Background: Copeptin is rapidly emerging as a fast and reliable tool in detecting myocardial ischemia. However, to date, predictive power of Copeptin has only been tested in the settings of acute coronary syndromes and heart failure.

Purpose: To investigate the predictive power of Copeptin among patients who underwent cardiac surgery.

Methods: A total of 166 patients (mean age 71±6 years, 66% male) scheduled for first-time, elective, on-pump cardiac operations between September and December 2014 were enrolled, with recent myocardial infarction being an exclusion criteria. Blood samples were collected at the time of surgery (T0), at the end of...
Further studies are warranted to confirm these findings. Copeptin dosage following CABG early and reliably identifies the total left ventricular (LV) function in healthy pigs and compared to dobutamine infusion across pressure-volume anaesthesia. Method: 9 anaesthetised, closed-chest pigs (67.2 kg) were acutely instrumented for invasive pressure-volume analysis. Temperature was controlled by an intravascular device. Baseline measurements at HT, intravenous dobutamine infusion was titrated to double LV dp/dtmax. Pigs were then cooled to NT and further down to MH and, at each temperature step, titrated dobutamine infusion was repeated. LV function was assessed by pressure-volume relationships derived from short aortic occlusions. Results: The cardiac output at end-systolic LV pressure of 100 mmHg (LVV-Pes100) was taken as a parameter of LV contractility. Lower values indicate increased contractility.

Results: Heart rate and cardiac output decreased with cooling from HT to MH, while LV contractility increased (graph). The effect of cooling on LVV-Pes100 was of comparable effect size as dobutamine at a given temperature.

Conclusion: Cooling from HT to NT and from NT to MH increases LV contractility to a similar degree as a clinically relevant dose of dobutamine in the normal porcine heart. These data indicate that cooling can reduce the need for catecholamines during acute cardiac dysfunction and cardiogenic shock.

Background: Conduction abnormalities are common and affect survival in acute heart failure and myocardial infarction, but their role in cardiogenic shock (CS) is not clear. Purpose: The aim was to investigate the prevalence of conduction abnormalities and evaluate their association with survival in patients with CS.

Methods: We analyzed the baseline ECG of 197 patients included in a multi-national prospective cohort study of CS (n=219) conducted in 2010–2012 with 1-year all-cause mortality follow-up. The multivariate models were calculated using logistic regression adjusting for age, gender, and comorbidities.

Results: The CS was caused by acute coronary syndrome (ACS) in 175 (81%) patients. The overall mortality within one year was 40%, most of the deaths occurring during the hospital stay. Mortality was higher in ACS (42%) than in non-ACS patients (24%). More than half (n=102, 53%) of the patients had ventricular conduction defects: the most common were IVCD (QRS >110ms without specific partial or complete block) 19.1%, LAD 18.6%, and RBBB 12.4%. LBBB (4.6%) and LPHF (6.7%) were less common. One-year mortality was higher in all patients with a conduction defect (Figure). In the multivariate model, isolated hemiblock (LAD or LPHF) independently predicted mortality (adjusted OR 2.6, Cl 1.1–6.4, p=0.03), and IVCD had a similar trend (adjusted OR 2.2 Cl 0.91–5.2, p=0.08) compared to those with normal ventricular conduction. Both findings were pronounced in ACS: for isolated hemiblock the adjusted OR was 4.5 (CI 1.6–12.7, p=0.004), and for IVCD the adjusted OR was 2.8 (Cl 1.1–7.4; p=0.04).

Conclusions: Ventricular conduction defects are common in patients with CS and are associated with increased mortality. In particular in CS caused by ACS, hemiblocks and IVCD predict death.
Despite its growing use, data on long-term prognosis in patients treated with extracorporeal membrane oxygenation (ECMO) may be the only option to achieve hemodynamic stability. In patients with cardiogenic shock refractory to standard treatment, immediate percutaneous intervention after bypass surgery complicated by periprocedural myocardial infarction may improve clinical outcomes. This observational study was performed prospectively in patients above 70 years of age with no need for coronary artery revascularization. Purpose: To compare left ventricular (LV) remodelling in patients with AS after treatment with TAVR vs. SAVR.

Methods: Transthoracic echocardiographic studies were performed before and 12 months after TAVR and SAVR. The study was stopped due to insufficient enrollment of TAVR patients. LV remodelling after TAVR was compared with pooled data from patients treated with SAVR.

Results: 232 patients were included in the study at our institution, 120 were randomized to TAVR and 112 to SAVR. From baseline to 12 months after the procedure, the aortic valve area (AVA) changed from 0.77±0.04 to 1.32±0.08 cm² (p=0.0001) in the TAVR group compared to 0.74±0.04 to 1.65±0.09 cm² (p=0.0001) in the TAVR group. The increase in AVA was significantly larger in the TAVR group. At 12 months, LV mass decreased by 0.25±0.14 g (p=0.0001) in the TAVR group and from 50.2±10.9 to 42.4±5.6 g (p=0.0001) in the SAVR group. The reduction in LV mass was largest in the SAVR group (p=0.0002). The difference in LV mass regression between groups was correlated with differences in end-diastolic volume (EDV). In the TAVR group at 12 months, EDV increased by 57±21 ml (p<0.0001) and in the SAVR group, EDV decreased by 87±21 to 71±15 ml (p<0.0001) with a significant difference between the two groups (p<0.0001). At 12 months, 27% of the TAVR patients had no or trace paravalvular leak (PVL), 59% had mild PVL and 14% had moderate PVL. Among the SAVR patients 82% had no or trace PVL and 18% had mild PVL. Changes in EDV were correlated with the degree of PVL. In TAVR patients, EDV was unchanged in patients with no or trace PVL, but EDV increased by 13±6 ml (p=0.02) in those with mild or moderate PVL. In SAVR patients with no or trace PVL, EDV decreased by −17±6 ml (p=0.01), and in those with mild PVL by −9±9 ml (p=0.04).

Conclusion: Patients treated with TAVR have a larger AVA compared to those treated with SAVR. However, patients undergoing SAVR had larger LV mass regression, which correlated to a more pronounced reduction in EDV. Even mild to moderate PVL were associated with diminished LV mass reduction after TAVR.

Current development in transcatheter valve technology to minimize paravalvular leak may be important to optimize long-term results after TAVR.

P3496 | BEDSIDE

Differences in left ventricle mass regression in patients with aortic valve stenosis treated with transcatheter or surgical aortic valve replacement: an echocardiographic study

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Introduction: Certain high-risk patients with severe aortic valve stenosis (AS) can be considered for treatment with either transcatheter (TAVR) or surgical aortic valve replacement (SAVR). Little is known about the effect on left ventricle mass regression after TAVR vs. SAVR. This study was an echocardiographic substudy of the NOTION trial, a randomized controlled trial comparing TAVR and SAVR in patients above 70 years of age with no need for coronary artery revascularization.

Purpose: To compare left ventricular (LV) remodelling in patients with AS after treatment with TAVR vs. SAVR.

Methods: Transthoracic echocardiographic studies were performed before and 12 months after TAVR and SAVR. The study was stopped due to insufficient enrollment of TAVR patients. LV remodelling after TAVR was compared with pooled data from patients treated with SAVR.

Results: 232 patients were included in the study at our institution, 120 were randomized to TAVR and 112 to SAVR. From baseline to 12 months after the procedure, the aortic valve area (AVA) changed from 0.77±0.04 to 1.32±0.08 cm² (p=0.0001) in the TAVR group compared to 0.74±0.04 to 1.65±0.09 cm² (p=0.0001) in the TAVR group. The increase in AVA was significantly larger in the TAVR group. At 12 months, LV mass decreased by 0.25±0.14 g (p=0.0001) in the TAVR group and from 50.2±10.9 to 42.4±5.6 g (p=0.0001) in the SAVR group. The reduction in LV mass was largest in the SAVR group (p=0.0002). The difference in LV mass regression between groups was correlated with differences in end-diastolic volume (EDV). In the TAVR group at 12 months, EDV increased by 57±21 ml (p<0.0001) and in the SAVR group, EDV decreased by 87±21 to 71±15 ml (p<0.0001) with a significant difference between the two groups (p<0.0001). At 12 months, 27% of the TAVR patients had no or trace paravalvular leak (PVL), 59% had mild PVL and 14% had moderate PVL. Among the SAVR patients 82% had no or trace PVL and 18% had mild PVL. Changes in EDV were correlated with the degree of PVL. In TAVR patients, EDV was unchanged in patients with no or trace PVL, but EDV increased by 13±6 ml (p=0.02) in those with mild or moderate PVL. In SAVR patients with no or trace PVL, EDV decreased by −17±6 ml (p=0.01), and in those with mild PVL by −9±9 ml (p=0.04).

Conclusion: Patients treated with TAVR have a larger AVA compared to those treated with SAVR. However, patients undergoing SAVR had larger LV mass regression, which correlated to a more pronounced reduction in EDV. Even mild to moderate PVL were associated with diminished LV mass reduction after TAVR.

Current development in transcatheter valve technology to minimize paravalvular leak may be important to optimize long-term results after TAVR.

P3497 | BEDSIDE

Left ventricular mechanical dispersion predicts clinical outcome in patients with moderate to severe aortic stenosis

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Background: New parameters to improve risk stratification and predict outcome in patients with aortic stenosis (AS) are needed. Left ventricular (LV) mechanical dispersion by strain echocardiography reflects heterogeneous myocardial contractility and is a novel marker of sudden cardiac death.

Purpose: We aimed to explore the prognostic value of mechanical dispersion in AS patients, and hypothesized that mechanical dispersion can be an additional cardiovascular risk assessment tool.

Methods: We included 55 patients (56 women, 75±9 years) with moderate to severe AS. Global longitudinal strain (GLS) was assessed by speckle tracking echocardiography from a 16 LV segments model. Mechanical dispersion was calculated as standard deviation of time from Q/R to ECG peak to strain in 16 LV segments.

Results: Average aortic stenosis area was 0.7±0.2 cm². Most patients had LV septal hypertrophy (12±2 mm) and preserved LV ejection fraction (EF) (57±10%). Aortic valve replacement (AVR) was performed in 37 (67%). During 38±14 months follow-up, 15 (27%) patients died (no 30-day mortality after AVR). LVEF and GLS did not differ between survivors and non-survivors (58±9 vs 54±13, p=0.16, and −17.0±3.4% vs. −16.7±4.0%, p=0.78, respectively). Mechanical dispersion was the only echocardiographic parameter that differed between survivors and non-survivors (35±2 vs 54±16 ms, p<0.001). C-statistics for mechanical dispersion showed an AUC of 0.70 (0.55–0.86) and a value of >76 ms indicated worse survival (log rank <0.01) (Fig.1)

Conclusion: LV mechanical dispersion was significantly higher in the AS non-
Dynamic 3-dimensional echocardiographic assessment of mitral valve in patients with functional mitral regurgitation caused by lone atrial fibrillation

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Background: The functional mitral regurgitation (FMR) in lone atrial fibrillation (AF) is caused by morphological changes of mitral valve (MV) associated with the atrial remodeling; however, little is known about the precise mechanism of that.

Purpose: We aimed to clarify what morphological features of MV contributing to aggravation of FMR in patients with lone AF.

Methods: The lone AF patients who underwent three-dimensional transesophageal echocardiography with appropriate image quality (n=1124) were retrospectively screened. Of these, we picked up 25 patients showing moderate or greater FMR despite normal left ventricular function (significant-MR group). Twenty-five patients without MR (controls) and 25 patients with mild FMR (mild-MR group) were randomly selected as references from the left cohort. The following parameters were measured during systole: (1) MA area and its fraction, (2) nonplanarity angle (NPA), representing the degree of saddle shape; (3) the ratio of total leaflet area to MA area, representing the degree of mitral leaflet adaptation; and (4) tethering angle of both leaflets.

Results: As shown in Table, MA area, NPA, and tethering angle of posterior mitral leaflet (PML) were the largest and MA area fraction was the smallest in significant-MR group compared to others. In multivariate models, Left atrial volume index, leaflet (PML) were the largest and MA area fraction was the smallest in significant-MR group, representing the degree of mitral leaflet adaptation; and (4) tethering angle of both leaflets.

Conclusion: FMR related to AF might be caused by multiple factors including reduced sphincterlike contraction, flatter annulus and PML tethering.

Predictive factors of left ventricular outflow tract obstruction after aortic surgery in patients with severe aortic stenosis


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Background: Asymmetric septal hypertrophy frequently coexists with severe aortic stenosis and can be unmasked after successful aortic valve surgery, jeopardizing the clinical and echocardiographic results. Left ventricular outflow tract obstruction (LVOTO) appears to be a marker for increased postoperative morbidity and mortality. The purpose of this study is to evaluate the predictive factors associated with LVOTO after surgical treatment for aortic stenosis.

Methods: Sixty seven patients with severe aortic stenosis were studies retrospectively before and after surgery by transhoracic and transesophageal echocardiography. We measured interventricular septum wall thickness in diastole (IVSd), the minimum diameter of the left ventricular outflow tract (MDOT), aortic annulus diameter, aorto-septal angle (ASA), including conventional echocardiographic parameters. Patients were divided into two groups based on the presence of LVOTO or absence of LVOTO. Sixteen patients had significant LVOTO and 51 patients did not have LVOTO. We analyzed the IVSd, MDOT, aortic annulus diameter and ASA with the receiver operating characteristic (ROC) curve.

Results: IVSd was significantly larger in obstruction group (p=0.0039), MDOT was significantly smaller in obstruction group (p=0.0025). Aortic annulus diameter was significantly smaller in obstruction group (p=0.047). There was no significant difference in ASA between two groups. The optimal cut-off value of the MDOT in predicting presence of LVOTO was 15.2 mm as calculated using ROC curve analysis. Patients with MDOT >15.2 mm were associated with sensitivity of 87.6% and specificity of 90.8% for LVOTO. Patients with IVSd ≥17.5 mm were associated with sensitivity of 43.8% and specificity of 94.1% for LVOTO.

Conclusion: Our study suggested that MDOT and IVSd were useful predictive factors of left ventricular outflow tract obstruction after aortic valve surgery for severe aortic stenosis. Concomitant myectomy may be considered treatment of choice for aortic stenosis.
mers of patients undergoing TAVI with or without BAV with a self-expanding bioprosthesis. Methods: A total of 210 patients (120 patients for non-direct TAVI and 90 patients for direct TAVI) with severe aortic valve stenosis were analysed. All patients underwent transesophageal echocardiogram prior to the procedure and before discharge. Results: The direct group had less moderate/severe paravalvular leakage (PVL) post TAVI compared to the non-direct group (8% vs 27%, p < 0.01). Both groups had similar 1-year mortality rates (15% in non-direct versus 11% in direct, p = 0.5). The Table depicts the echocardiographic differences between the 2 groups before and after the procedure.

Abstract P3504 | Table 1. Mitral valve parameters

<table>
<thead>
<tr>
<th>Mitral valve parameters</th>
<th>Before AV repair (n=14)</th>
<th>After AV repair (n=14)</th>
<th>p-value before vs. AV repair**</th>
<th>p-value before vs. AV repair***</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterolateral-posteromedial diameter (mm)</td>
<td>41.6±6.0</td>
<td>39.0±8.4</td>
<td>0.10</td>
<td>39.6±5.5</td>
</tr>
<tr>
<td>Anteroseptal diameter (mm)</td>
<td>38.6±5.5</td>
<td>35.1±5.8</td>
<td>0.19</td>
<td>35.6±4.5</td>
</tr>
<tr>
<td>Annular height (mm)</td>
<td>10.3±2.2</td>
<td>6.0±2.2</td>
<td>&lt;0.001</td>
<td>10.3±1.7</td>
</tr>
<tr>
<td>Annular height to commissural width ratio</td>
<td>0.24±0.05</td>
<td>0.16±0.05</td>
<td>&lt;0.001</td>
<td>0.26±0.04</td>
</tr>
<tr>
<td>Coaptation height (mm)</td>
<td>56.1±15.4</td>
<td>45.4±15.4</td>
<td>0.002</td>
<td>55.5±11.3</td>
</tr>
<tr>
<td>Tenting area (mm²)</td>
<td>108.1±43.4</td>
<td>53.5±30.3</td>
<td>0.005</td>
<td>102.4±25.6</td>
</tr>
<tr>
<td>Aorto-mitral angle (°)</td>
<td>112.8±9.6</td>
<td>121.1±8.3</td>
<td>0.018</td>
<td>108.7±8.6</td>
</tr>
</tbody>
</table>

*Paired t-test, **Independent samples t-test.

Conclusions: When compared to TEE performed days after TAVI, periprocedure TEE under-diagnosed the presence of AR. This might be explained by a lower BP immediately after TAVI, compared to follow-up, as well as mild short-term progression of AR. Acknowledgement/Funding: Portuguese Foundation for Science and Technology Grant HMSP-ICS/007/2012

P3504 | BEDSIDE Impact of aortic valve repair and valve-sparing procedures on the mitral annular geometry assessed by 3-dimensional transesophageal echocardiography

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Background: Annular non-planarity, referred as the “saddle-shape” of the mitral valve (MV) annulus, minimizes leaflet stress and plays a role in preserving adequate valve function. Aortic valve (AV) repair is an attractive approach increasingly used to treat young patients with severe aortic regurgitation (AR). However, the
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impact of AV repair and sparing procedures on MV annular geometry and function is unknown.

Purpose: We aimed at assessing the impact of AV repair on the MV annular geometry.

Methods: 2D and 3D transesophageal echocardiography (TEE) of the MV appara-
tus was acquired pre-operatively and immediately after surgery in 14 patients with severe AR (13 bicuspid, 1 tricuspid;12 males; age 45±4.1±14), and in 16 patients with normal TEE (9 males; age 60.4±13.3). MV annular morphology was retrospectively assessed by dedicated quantification software.

Results: No significant differences of valve-sparing root replacement with AV reimplanta-
tion and cusp repair in 12 patients, and external ring annuloplasty and cusp repair in 2. MV parameters are summarized in Table 1. Pre-operative MV parameters did not differ from those of the normal subjects. The annular height and annular length were on average lower than the normal values by 11% and 9% respectively after AV repair, as were the coaptation height and tenting area. The aorto-mitrall angle was increased after AV repair/sparing procedure.

Conclusions: AV repair procedures decrease the non-planarity of the MV annu-
lar and the height of coaptation of the MV leaflets. These alterations could have
term implications on MV function.

P350 | BEDSIDE
Mitra/altric flow velocity integral ratio as a simple and useful index to evaluate residual mitral regurgitation after MitraClip implantation

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Background: Percutaneous mitral valve repair using MitraClip (MC) has emerged as a therapeutic option for pts with functional mitral regurgitation (MR) at prohibitive surgical risk. The echocardiographic assessment of MR after MC implantation is challenging because the traditional semiquantitative and quanti-
tative echocardiographic methods, commonly used to assess MR severity, have important limitations in this setting.

Purpose: The aim of this study was to assess the accuracy and reliability of a simple Doppler index, the mitral/aortic flow velocity integral ratio (MAVIR), to evaluate residual MR severity after MC implantation.

Methods: From June 2012 to December 2014, 85 heart failure patients (age mean 64±11.5 yrs; 69 M, 16 F) with functional MR and LV dysfunction (LVEF ≤30%) were included. Pts were selected on the basis of two quantitative param-
eters of MR severity: the vena contracta width (VC) and the effective regurgitant orifice area (EROA). VC width was measured on a magnified parasternal long-

axis view. EROA was measured using the PISA method. MAVIR was expressed
as the ratio of mitral and aortic time velocity-integral (TVI) values. MAVIR was obtained with pulsed wave Doppler (PW) at mitral annulus level in four-chamber view whereas the aortic TVI was obtained at level of LVOT in the apical long-axis view. On the basis of VC, used as reference standard, 27 pts had mild MR (VC < 3 mm), 33 pts had moderate MR (VC 3–6 mm) and 25 pts had severe MR (VC > 7 mm). According to MR severity (VC ≥ 7 mm), 25 patients underwent MC implan-
tation and at 6 months a complete echocardiographic follow-up was performed.

Results: A significant linear relationship was found between MAVIR and both VC (r=0.74) and EROA (r=0.64). A MAVIR ≥ 7 mm identified pts with severe MR with a sensitivity of 86.7% and a specificity of 90.9%. At 6 months echocardiographic follow-up, after MitraClip implantation, we observed a significant reduction of LAVI (77.2±14.8 ml vs. 68.5±3.0 ml; P <0.03), LVED (254±92 ml vs. 242±89 ml; P <0.03), and LVEF increased from 39±13% to 49±13% (P<0.001). MAVIR significantly decreased at follow-up after MC implantation (1.2±0.2 vs. 1.0±0.1; P <0.003) and its decrease showed a significant linear relationship with LAVI reduction (r=0.79).

Conclusions: Our data show a closer relationship between MAVIR and tradi-
tional indexes of MR severity in patients with functional MR. This Doppler index, easy to obtain, seems applicable after MC implantation where traditional echocardiographic index of MR severity show significant limitations.

THE GREAT DIAGNOSTIC POWER OF STRESS EOCCHOCARDIOGRAPHY

P3505 | BEDSIDE
Diagnostic and prognostic features in patients with a positive exercise ECG testing but normal exercise echocardiography

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Although patients with a normal exercise echocardiography (ExE) are deemed to have good prognosis there is not much information about those who have pos-
itive exercise ECG findings in the context of a normal ExE study. We sought to assess subclinical ischemia in these patients with either: normal 27%, and 45 patients (27 with ischemia on ExE) were recruited. No differences were found between the two groups.

Methods: Retrospective analysis of prospectively collected data on 1,481 pa-
tients with LPP of CAD (<15%) that underwent a first treadmill ExE in our insti-
tution from March1995 to January 2015. Data were extracted from a database of 18,031 cases. Outcome (overall mortality, myocardial infarction [MI] before any revascularization, cardiac death, and revascularizations) during follow-up (FU) was assessed.

Results: Mean age was 50±12 years and 1,349 patients were women (91.1%). A fixed WMA was seen in 23 patients (1.7%) and ischemia in 115 (7.8%). During FU of 6.7±5.2 years 42 patients died (annualized death rate 0.42%), 27 patients had non-fatal MI (annualized MI rate 0.39%), and 167 underwent revascularization (annualized revascularization rate 0.47%). Independent pre-
dictors of combined overall mortality and MI in 62 patients were the presence of atrial fibrillation at the time of the ExE (Hazard ratio [HR]= 4.81, 95% Confidence Interval [CI]=1.99–11.65, P=0.001), fixed heart rate (HR-rate) by blood pres-
sure at rest (HR=1.13, 95% CI: 1.02–1.25, P=0.02), maximal achieved workload in Metabolic Equivalents (HR=0.86, 95% CI: 0.78–0.95, p=0.003), % achieved of the maximal age-predicted HR rate (HR=0.97, 95% CI: 0.94–0.99, p=0.009) and Δ in wall motion score index with exercise (HR=6.98, 95% CI: 1.63–29.88, p=0.009; incremental prognostic value of ExE, p=0.03). Clinical or ECG testing positivity was not predictive. The number of ExE required to detect an ischemic case was 12.9.

In conclusion, ExE still offer prognostic information in patients with LPP of CAD although the number of studies needed to detect a patient at risk is very high.
In patients referred for exercise testing. We hypothesized that a negative peak supine bicycle exercise stress echocardiography (ESE) might be able to identify a selected relatively healthy subpopulation among potential kidney transplant recipients with favourable cardiac prognostic course. However, there are currently no data to support this strategy in clinical practice.

Objectives: To assess the value of a comprehensive risk stratification prognostic strategy based on negative ESE in patients with end-stage renal disease (ESRD) awaiting renal transplantation (RT).

Methods: Retrospective analysis of a series of ESRD (with no active cardiac conditions and sufficient predicted functional status to perform exercise) awaiting RT undergoing normal ESE as part of a preoperative cardiac screening strategy regardless of the presence of coronary artery disease risk factors.

Results: Of 64 patients undergoing ESE, 59 had a normal exam (43 men, mean age 55±8.7 years). After a mean follow-up period of 3.8±2.4 years, one patient had cardiac death. Thirteen patients (22%) had hospitalizations for non-fatal acute coronary syndrome (5.7% per person-year of follow-up). Predictors of future cardiac fatal and non-fatal events included diastasis duration, smoking, previous PCI, peripheral vessel disease, low HDL level, and worsening diastolic dysfunction. Eighteen patients (30.5%) underwent renal transplantation at a median of 21.5 (25th-75th percentile 4.7–36.0) months after negative ESE and only one developed peripheric myocardial infarction.

Conclusions: In potential kidney transplant ESRD recipients a negative ESE may effectively predict a low incidence of cardiac death during follow-up and one of those who eventually underwent RT had peripheric myocardial infarction. However, the incidence of future non-fatal acute coronary syndrome continues to be a major limitation despite negative ESE both in patients in waiting list and after the transplant.

P3509 | BEDSIDE
Blunted stress upregulation of stroke volume index is related to impaired end-diastolic volume recruitment
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Background: In the normal heart, when exercise is performed, left-ventricular (LV) end-diastolic volume (EDV) increases slightly, whereas end-systolic volume (LVESV) decreases significantly. Little is known of end-diastolic volume (EDV) reserve. We analyzed interpretable data obtained in 891 patients: 593 men; age 63±12 years, ejection fraction 47±12%, with negative (exercise 172, dipyridamole 481, and dobutamine 237) SE result. Cardiac index (CI) was evaluated at rest and peak stress from raw measurement of heart rate by EKG, LVEDV and LVEFS by biplane Simpson rule from 2D-echo. Changes from rest to peak stress (reserve) were tested as predictors of combined death and heart failure hospitalization.

Results: For the overall population, CI increased from 2.05 to 3.33 L/min/m². At peak stress, 181 patients decreased the LVEFS and increased the LVEDV (Group I with a higher CI increase (+ 1.89 L/min/m² vs. rest); 573 patients decreased the LVEFS and the LVEDV (group II, increased systolic function and decreased relaxation; CI + 1.71 L/min/m² vs. rest); 136 patients increased the LVEVS during stress (Group III, decreased systolic function and decreased relaxation; CI +0.90 L/min/m² vs. rest); p<0.05 between Groups (Figure). During a median follow-up of 19 months (interquartile range 8–36), 50 deaths and 84 hospitalization occurred. The overall event-free survival for the Group I subjects was 89%, compared with 86% (Group II) and 76% (Group III) patients, p=0.02.

Conclusions: Patients with negative stress echocardiography may experience an adverse outcome, which can be identified by assessment of systolic function reserve and diastolic relaxation reserve during SE.

P3511 | BEDSIDE
Impact of pre-operative dobutamine stress echocardiography on outcomes in patients undergoing orthotopic liver transplantation
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Background: Coronary artery disease (CAD) increases mortality in patients undergoing orthotropic liver transplantation (OLT). Due to chronic vasodilatory state and poor exercise tolerance, dobutamine stress echocardiography (DSE) is preferred for preoperative evaluation of CAD prior to OLT.

Purpose: We sought to a) study the incidence of positive DSE results and b) assess the role of preoperative DSE in outcomes in patients undergoing OLT.

Methods: We studied 460 patients that underwent DSE within 1 year prior to OLT between 2004–2011. Clinical and DSE data was recorded. Primary outcome included death, stroke and myocardial infarction at 30 days post-OLT. We also recorded long-term deaths.

Results: Clinical and DSE data are shown in Table 1. 30-day events occurred in 14 (3%) patients, while there were 108 (24%) deaths at 4.6±2 years of follow-up. No patient with an abnormal DSE had an adverse 30-day event. On Cox survival analysis, only baseline left ventricular ejection fraction (HR 0.90 [0.85–0.96], p<0.001) and not ischemia on DSE (HR 1.05 [0.83–1.33], p=0.7) was associated with long-term deaths.

Table 1. Data of study population

<table>
<thead>
<tr>
<th>Variable</th>
<th>(N=460)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>58±7 years</td>
</tr>
<tr>
<td>Men</td>
<td>324 (70%)</td>
</tr>
<tr>
<td>MELD score 7</td>
<td>21±6.4</td>
</tr>
<tr>
<td>Etiology for OLT</td>
<td>Hepatitis C 187 (41%)</td>
</tr>
<tr>
<td></td>
<td>Alcohol 122 (27%)</td>
</tr>
<tr>
<td></td>
<td>NASH 85 (18%)</td>
</tr>
<tr>
<td></td>
<td>Other 66 (14%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>161 (35%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>114 (25%)</td>
</tr>
<tr>
<td>Medications</td>
<td>Aspirin 70 (15%)</td>
</tr>
<tr>
<td></td>
<td>Beta blockers 281 (61%)</td>
</tr>
<tr>
<td></td>
<td>Statins 29 (6%)</td>
</tr>
<tr>
<td>LV ejection fraction</td>
<td>58±4%</td>
</tr>
<tr>
<td>PAP (mm Hg)</td>
<td>30±8 Hg</td>
</tr>
<tr>
<td>% MPHR on DSE</td>
<td>84±9%</td>
</tr>
<tr>
<td>Max rate pressure product</td>
<td>1848±4407</td>
</tr>
<tr>
<td>Response to DSE</td>
<td>Ischemic 4 (9%)</td>
</tr>
<tr>
<td></td>
<td>Nondiagnostic 96 (21%)</td>
</tr>
<tr>
<td></td>
<td>Normal 360 (78%)</td>
</tr>
</tbody>
</table>

Conclusion: In patients undergoing preoperative DSE prior to OLT, there is a low incidence of ischemia on DSE; and it has no association with 30-day events. Ischemic response on DSE does not predict long-term outcomes following OLT.
P3512 | BENCH
Is ischemic cascade reproduced during dipyridamole-induced myocardial ischemia?

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Background: Transmural myocardial ischemia is known to derive a typical sequence of events characterized by left ventricular wall motion abnormalities (WMAs), ST-segment depression, and finally, angina. We hypothesized that ischemic cascade is also reproducible during subendocardial ischemia induced by dipyridamole stress test (DST).

Methods: We studied 87 consecutive patients (age 64±10 years, 53 M), admitted to our hospital to undergo coronary angiography for episodes of exercise-induced angina and evidence of myocardial ischemia during electrocardiographic (ECG) exercise stress test. No patient had previous evidence of coronary artery disease.

Results: DST (dipyridamole, 0.84 mg/kg iv in 6 minutes) was performed the day before coronary angiography under continuous echocardiographic and 12-lead ECG monitoring, and patients were invited to immediately report chest pain if it occurred. The times of appearance of myocardial left ventricular WMAs, ST-segment depression ≥1 mm (STD) in any lead and onset of chest pain sensation were carefully checked and recorded.

Conclusions: In patients with exercise-induced angina, the classical ischemic cascade does not seem to be consistently reproduced during DST-induced myocardial ischemia, which can variably be manifested initially by WMA, ECG changes or angina.

P3513 | BEDSIDE
Dobutamine-induced changes of longitudinal strain predict longterm mortality in severe heart failure

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Background: We investigated the dobutamine-induced changes of left ventricular (LV) multidimensional deformation and their relation with prognosis in patients with severe chronic systolic heart failure.

Methods: In 100 patients with advanced heart failure, we performed a low dose dobutamine echo stress study, including speckle tracking imaging. The patients' mortality was during 5 year follow-up. Brain Natriuretic Peptide (BNP) was also measured.

Results: Dobutamine infusion increased LV ejection fraction (EF), LV outflow tract peak velocity time integral (LVVTI), global longitudinal, circumferential, radial strain and strain rate (p<0.05). Patients with cardiac death at f/u (N=32) had lower longitudinal strain and strain rate at rest (−7.9±1.4 vs. −9.8±2.5% and −0.47±0.15 vs. −0.63±0.22 L/sec; P<0.001) and low dose dobutamine (−7.05±2.7 vs. −14.9±4.3 and −0.37±0.18 vs. −0.95±0.37 L/sec; P<0.001). Smaller differences were observed for circumferential and radial strain and strain rate (p<0.05).

Among all indices, the dobutamine-induced changes (Δ) in longitudinal strain and strain rate were the best predictors of cardiac death (HR: 2.4 (95% CI: 1.5–3.7) p<0.001, and HR: 2.3 (95% CI: 1.4–4.3) p<0.001, areas under the ROC curve of 91% (95% CI: 85–98%) and 88% (95% CI: 81–95%) respectively, with an independent and additive predictive value in a model including age, sex, resting LVFE, LVVTI, longitudinal strain (or rate), ΔEF, ΔLVVTI (as measures of contractile response), and type of cardiomyopathy (model x2=84.06 increased to x2=86.15 and x2=84.06 to x2=87.3 after inclusion of Δ longitudinal strain and strain rate, respectively, p for change <0.001)

Conclusion: In severe chronic systolic heart failure, the longitudinal, circumferential, and radial deformation are related with cardiac death. The dobutamine-induced changes of longitudinal myocardial deformation indices of LV function are the best predictors to stratify the risk for cardiac death.
NOVEL IMAGING TECHNIQUES IN CARDIAC DIAGNOSIS AND THERAPY

P3516 | BENCH
Contribution of ultrasound contrast in predicting conduction disturbances during percutaneous alcohol septal ablation
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Background: Alcohol diffusion has been incriminated in the risk of permanent atrioventricular (AV) block during alcohol septal ablation (ASA). We sought to evaluate the association between the risk of AV block and alcohol diffusion assessed by echocardiography ultrasound contrast.
Methods: Patients with symptomatic left ventricular obstruction referred for ASA were included in the study (n=42). Patients with previous pacemaker implantation were excluded. Measures to prevent permanent AV block were a slow alcohol injection and the use of ultrasound contrast agent to avoid multiple septal injections. Myocardial contrast-enhancement volume was quantified from full volume 3D apical views with contrast replenishment graded as severe when right and left ventricle were filled by contrast during the 3 cardiac cycles after contrast delivery.
Results: Despite the use of a limited alcohol dose (2.3±0.7 mL) and only one patient with ≤1 septal ablation, 10 (24%) patients experienced permanent AV block after ASA. Alcohol dose, CK level and contrast-enhancement volume were not associated to AV block. Patients with severe replenishment (n=20) had greater alcohol diffusion has been incriminated in the risk of permanent AV block during ASA and might be a marker of alcohol diffusion.
Conclusions: Severe alcohol diffusion contrast replenishment increased the risk of AV block during ASA and might be a marker of alcohol diffusion.

P3517 | BEDSIDE
The early impact of breast cancer radiotherapy on myocardial tissue properties in 2D echocardiography with increased echodensity of the myocardial walls, an ultrasound tissue characterization study
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Background: Radiotherapy (RT) in the thoracic region is associated with increased risk for heart failure morbidity and mortality. The aim of this prospective single-center study was to assess whether ultrasound tissue characterization (UCD) can indentify early RT related myocardial lesions.
Methods: Seventy-eight eligible patients with early stage breast cancer were evaluated retrospectively in patients with RT. Twenty patients had right-sided, and fifty-eight left-sided breast cancer. None received chemotherapy. A comprehensive echocardiographic examination included 3D measurements and UTC analysis for the right ventricular (RV) free wall, left ventricular (LV) septum and posterior wall. Calibration was done both for pericardium (cpIBS) and LV cavity (ccIBS). The following UTC parameters were evaluated with speckle tracking registering two waveforms: a peak negative strain wave corresponding to RV systole (RASa) and a peak positive strain wave representing RV reservoir phase, occurring during ventricular systole (RASs). Time from the beginning of QRS to RASs peak wave was measured as a surrogate of RV compliance. Wilcoxon test was used.
Results: We included 20 patients (18 female). Age was 44±7.8 years. Shows baseline and post iloprost variables.

P3518 | BEDSIDE
Myocardial scar evaluation by 2D contrast echocardiography
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Background: Scar identification and extension in ischemic cardiomyopathy is of paramount relevance. At present, cMR is the gold standard technique, but it has limited availability or may be in a subset of patients contra-indicated. Thus, alternative noninvasive methods would be desirable.
Purpose: In this study we evaluate whether 2D contrast echocardiography (2D-CE-Echo) could be used to identify myocardial scar and its trans-mural extent. We used cardiac magnetic resonance (cMR) as a reference standard technique.
Methods: We retrospectedively enrolled 38 subjects (76% affected by ischemic cardiomyopathy) who underwent cMR and 2D-CE-Echo for clinical indications. Two-dimensional echocardiography images were acquired with a low mechanical index (MI=0,1) so that normal myocardium appears hypo-echoic, whereas region with scar brighter. We used transpulmonary contrast agent to improve border definition and evaluate the trans-mural extent of scar. Results: A total of 687 segments (25% with scar) were evaluated. On a per-segment analysis, 2D-CE-Echo allowed the identification of cMR scars with a sensitivity of 60% and a specificity of 99%. When the presence of a scar is detected, 2D-CE-Echo discriminates with accuracy transmural (sensitivity=88%, specificity=71%) and subendocardial (sensitivity=74%, specificity=84%) infarct. Disagreement between 2D-CE-echo and cMR was principally due to false negative (60 segments) than false positive segments (6 segments). At univariate analysis, thin segments (-6 mm) and scar localization in anterior, anterolateral wall and apical segments, were predictors of disagreement.
Conclusions: This study shows that 2D-CE-Echo could be used to evaluate the presence and trans-mural extent of scar in patients with ischemic cardiomyopathy. In clinical practice, this technique can be used as alternative method when cMR is contra-indicated or not immediately available.

P3520 | BEDSIDE
Assessment of an echocardiographic model to predict significant perivalvular regurgitation after TAVI
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Aim: Paravalvular regurgitation is a major concern when performing transcatheter aortic valve implantation (TAVI), as it has been associated with adverse outcomes. Our aim was to develop a simple calculator to predict the risk of significant paravalvular regurgitation after TAVI.
Methods: We analyzed 217 consecutive patients with severe symptomatic aortic stenosis who underwent TAVI in a single center from 2009 to 2014. Prior to the procedure and immediately after valve deployment all patients underwent transesophageal echocardiographic assessment of the aortic valve.
Results: Thickness of the aortic leaflets, mobility and calcium distribution was assessed at 45° and 120–140° views in end diastole. Valve calcification were classified as either mild (1) [mean leaflet thickness <3mm, absence of nodules at the cusps and
annulus calcification), moderate (2) [mean thickness ≥ 3–5 mm with small calcium nodules at the cusps and localized calcification at the aortic annulus], or severe (3) [leaflet thickness > 5 mm, large nodules and diffuse calcification of the aortic annulus]. Mobility of aortic cusps was classified as slightly restricted (1) [all commissures seemed to be open], moderately restricted (2) [one fused commissure], or severely restricted (3) [two or more fused commissures]. Prosthetic nominal loss was calculated with the following formula: (nominal prosthesis diameter – maximal unfolding)/nominal prosthesis diameter.

Results: Mean age was 82.7±5.6 years, and 65% were female. Significant paravalvular regurgitation ≥ grade 2, mobility> 1 and percentage of prosthetic nominal loss divided into quartiles. The prediction accuracy was excellent, with an area under the ROC curve of 0.90 (95% CI: 0.78–1.00) and a Hosmer-Lemeshow goodness-of-fit of 0.920.

Conclusions: We found that echocardiographic factors (mobility, calcification of the native valve, and prosthetic nominal loss) were independently associated with paravalvular regurgitation. The risk for significant paravalvular regurgitation after TAVI can be predicted using a simple and accurate calculator.

Aortic stenosis in patients with bicuspid aortic valve

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Background: Bicuspid aortic valve (BAV) is one of the most common congenital heart diseases, frequently associated with diffuse alterations of aortic wall. The aim of this study is to detect whether increased aortic stiffness, very often found in these patients, and traditionally evaluated through echocardiography, has a correlation with aortic strain, evaluated by speckle tracking imaging (STI) technique.

Methods: We explored 20 patients (mean age 36.5±16.2 years) with BAV and 13 normal subjects (mean age 30.9±10.6 years), with comparable age and body surface area (BSA). We obtained all the measurements of aortic diameters (anulus, sinus of Valsalva (SV), sinu-tubular junction (STJ) and ascending aorta) by a parasternal long-axis view and indexed them for BSA. Aortic stiffness was calculated using the formula [ln(SBP/DBP)]/[Sn – Aod]/Aod, according to what already shown in literature, where AoS and AoD were systolic and diastolic diameters respectively, and SBP and DBP, systolic and diastolic blood pressure, respectively. Longitudinal strain (LS) of ascending aorta has been estimated as the average between anterior and posterior walls strain values; these measurements were obtained off-line by a software for STI analysis (EchoPac, GE Healthcare, Horten, Norway). The same software allows the calculation of ascending aorta circumferential strain (CS), obtained by the parasternal short-axis view at the level of aortic root, just above the valve level.

Results: Ascending aorta was larger in BAV patients than in controls (17±7.7 mm/m² vs. 10.5±6.2 mm/m²; p=0.002). Aortic stiffness was increased in BAV patients compared to controls (8.6±7.39 vs. 3.7±1.75; p=0.003), whereas LS by speckle tracking was reduced (22±9.77 vs. 38±11.3; p=0.001). In overall population, aortic stiffness was inversely related with left ventricle ejection fraction (r=-0.40, p=0.007) and aortic LS, estimated by STI (r=-0.46, p=0.014), whereas it was directly related with age (r=0.55, p=0.001) and aortic diameters (r=0.36, p=0.01; r=0.50, p=0.001; r=0.42, p=0.005 for SV, STJ and ascending aorta, respectively). An inverse relation has been found also between CS, estimated by STI, and aortic diameters (r=-0.35, p=0.019; r=-0.41, p=0.004; r=0.38, p=0.009, for SV, STJ and ascending aorta, respectively).

Conclusions: BAV is often associated with aortic elasticity impairment. Aortic LS and CS by STI well correlate with aortic dimensions and stiffness. STI allows a new evaluation of atheropathy that could be applied in different BAV types which probably cause a different aortic walls strain.

Stress speckle tracking; an underestimated tool in detecting myocardial viability

A.M. Saleh1, K. Zintl1, A. Elemin2, M. Elbaz2, H. Nembr1, B. Bluem1, H. Pless1, J. Brachmann1, C. Zito, L. Longobardo, M. Meschisi, R. Manganaro, M.C. Todaro, S. Carerj, University of Messina, Department of Cardiology, Messina, Italy

Introduction: Stress echocardiography (SE) with vasodilators or Dobutamine is a valuable tool for noninvasive investigation of coronary artery disease (CAD). Adenosine is easy to administrate, well tolerated and induces little increase in heart rate. Semiautomatic techniques allow quantification of the myocardial deformation and aid in the identification of an abnormal stress response. Global longitudinal strain (GLS) obtained with speckle tracking is recognised as a robust and useful marker of left ventricular function in various pathological conditions.

Objective: To determine if endocardial GLS (eGLS) in Adenosine SE could identify significant coronary stenoses in patients with chest pain.

Methods: 155 patients with chest pain, suspected for CAD and scheduled for invasive coronary arteriography (CA), were consecutively included. One week before CA, the patients underwent SE with Adenosine 140 μg/kg/min on a Vivid 7 scanner, GE. The CAs were analysed quantitatively in QAngio XA version 7.1, (Medis Medical Imaging Systems) by an experienced reader and the rest and stress echocardiograms were analysed offline with in EchoPac, ver. 113 blinded to the results of the CA. Seven (4%) patients dropped out and 16 (10%) were excluded due to poor acoustic signals yielding 122 patients (mean age (SD) 62.6 (9) years, 70% male)/2376 segments for analysis. Speckle tracking was successfully performed in 98.1% of the segments at rest and 97.7% during stress (p=0.12). Significant CAD - defined as one or more stenoses above 70% - was present in 44 (33%) of the patients: 48% had 1- vessel disease (1VSD); 36% 2V and 16% 3V.

Results: No difference in mean eGLS (sd) in patients with/without significant CAD was found at rest (−22.6 (4.1%−23.3 (3.3%)), p=0.27), but a highly significant difference was detected during Adenosine infusion (−23.7% (5.5%)−28.3% (4.1%), p<0.00001). ROC curves were produced and the area under the curve (AUC) for changes in eGLS (eGLS at rest − eGLS during stress) was 0.79. The best accuracy (78%) was achieved if the cut off value was +2.3% indicating that patients with less than 2.3% increase in i.e. more negative) eGLS during Adenosine infusion had significant CAD. This cut off value yielded a sensitivity of 64% and a specificity of 85%.

Conclusion: Endocardial GLS during Adenosine SE may be used as a noninvasive tool to stratify patients suspected of CAD. However, there seems to be a wide overlap in the increase in strain induced by Adenosine in patients with and without significant stenoses.

Stress echocardiography with vasodilators or Dobutamine is an underestimated tool in detecting myocardial viability

A.M. Saleh1, K. Zintl1, A. Elemin2, M. Elbaz2, H. Nembr1, B. Bluem1, H. Pless1, J. Brachmann1, C. Zito, L. Longobardo, M. Meschisi, R. Manganaro, M.C. Todaro, S. Carerj, University of Messina, Department of Cardiology, Messina, Italy

Introduction: The local deformation properties of viable and nonviable myocardium in response to dobutamine challenge have been well established but there are limited data on the feasibility of strain and strain rate in exercise stress echocardiography.

Methods: 54 patients were enrolled in our study. Dobutamine stress echocardiography was performed 4 days post-infarction accompanied with automated functional imaging (Speckle tracking) analysis of left ventricle during rest and during low dose stress. All patients underwent a follow up stress echocardiography at 6 weeks with concomitant speckle tracking analysis. Cardiac MRI took place at 4 days and 6 weeks post-infarction as well. We carried out an assessment of re-admission with ACS in a period of 12 months.

Results: The usual cardiac risk factors including hypertension, DM and smoking had no impact on the global and regional longitudinal strain rate obtained with speckle tracking. Global stress strain rate value of −10.35 at 6 weeks was able to differentiate viable myocardium with 85% sensitivity and 75% specificity in comparison to cardiac MRI. Accordingly regional stress strain rate of 3.5 at 6 weeks had 90% sensitivity and 80% specificity in viability assessment. Mean global and regional stress strain rate values of −9.5 and 4 were significant to predict re-infarction at 12 months, p-value <0.05.
Conclusion: Stress strain rate values obtained from speckle tracking are highly sensitive and specific in detecting myocardial viability in comparison with cardiac MRI. It can play a great role in eliminating the inter and intraobserver variability of analyzing stress echocardiography results.

P3524 | BESIDES
The quantitative assessment of the rotation and twist of the left ventricle during dobutamine stress echocardiography—comparison between patients with and without significant coronary artery stenosis

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Background: Rotation (R) and twist (T) of the left ventricle (LV) can be assessed quantitatively by speckle tracking echocardiography (STE). Although evaluated in various clinical settings at rest it is poorly validated during stress echocardiography. Aim: Our aim was to calculate and compare rotation at basal and apical levels of LV and twist of LV at rest (0), at peak stage (1) and recovery (2) of dobutamine stress echocardiography (DSE) in patients without (non-CAD) and in patients with coronary artery disease (CAD).

Methods: We analyzed 44 patients with angiographically excluded significant coronary stenosis (27 female, mean age 62±10 years) in whom DSE was performed and 50 patients with significant lesions in coronary arteries confirmed in coronaryography (18 female, mean age 62±9 years). Rotation was measured at basal and apical levels of LV. We compared rotation measured at aortic valve closure (R AVC) and twist (T)—calculated as a difference of basal and apical R AVC. Heart rate at all stages of DSE was similar in compared groups.

Results: Neither endystolic rotation nor twist changed significantly during DSE in both groups. Nevertheless, apical rotation at the peak stage of DSE and at recovery were higher in CAD patients whereas absolute value of basal rotation at peak stage was higher in non-CAD group, see Table

Rotation and twist parameters during DSE

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Non-CAD</th>
<th>CAD</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAVC basal segments (0)</td>
<td>-2.91±3.33</td>
<td>-2.47±2.20</td>
<td>ns</td>
</tr>
<tr>
<td>RAVC apical segments (0)</td>
<td>3.62±3.33</td>
<td>4.83±3.16</td>
<td>ns</td>
</tr>
<tr>
<td>Twist (0)</td>
<td>6.39±4.48</td>
<td>7.3±3.87</td>
<td>ns</td>
</tr>
<tr>
<td>RAVC basal segments (1)</td>
<td>-3.17±3.94</td>
<td>-2.79±3.35</td>
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</tr>
<tr>
<td>RAVC apical segments (1)</td>
<td>3.71±5.52</td>
<td>5.49±4.35</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>Twist (1)</td>
<td>6.71±5.3</td>
<td>8.22±5.13</td>
<td>ns</td>
</tr>
<tr>
<td>RAVC basal segments (2)</td>
<td>-3.87±3.37</td>
<td>-2.62±2.42</td>
<td>p=0.03</td>
</tr>
<tr>
<td>RAVC apical segments (2)</td>
<td>2.87±2.73</td>
<td>5.05±3.65</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>Twist (2)</td>
<td>6.27±4.61</td>
<td>7.68±4.72</td>
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</tr>
</tbody>
</table>

Conclusions: Endystolic rotation as well as twist of the LV are intrinsic features of LV mechanics, constant despite changing isotropic and chronotropic challenge. Contrary, the significant differences between groups with CAD and without CAD, indicate that ischemia impacts on rotational parameters.

P3525 | BESIDES
Value of peak cardiac power output-to-left ventricular mass to risk stratify patients with chronic systolic heart failure

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Background: Cardiac power output (CPO), which is the product of mean arterial pressure (MAP) and cardiac output (CO), is a measure of cardiac energy delivery. Echo-derived peak cardiac power output-to-mass (CPO/M) is a variable that couples CPO with LV mass at peak ejection or during maximal isotropic stimulation. Since it is a measure of the rate at which cardiac work is delivered with respect to the potential energy stored in LV mass, it provides indirect information about the efficiency of such transformation.

Aim: This study was designed to assess the value of CPO in the prognostication of patients with chronic stable heart failure (HF) submitted to exercise echocardiography (ECE).

Methods: A symptom-limited graded bicycle semi-supine ECE was performed in 125 patients (age: 61±11 years, 20% female) with LV systolic dysfunction (LV ejection fraction [EF]<30%). A complete echocardiographic study, including the assessment of ratio of mitral to myocardial early velocities (E/e’) as a surrogate marker of LV filling pressure, was performed at baseline. CPO was calculated as the product of a constant (K=2.2×1011) with CO and MAP divided by LV mass (M) to convert the units to watts/100 g; CPO = K × CO (l/min) × MAP (mmHg) × M (g). Patients were followed-up for the end point of all-cause mortality or ventricular assist device (VAD) implantation.

Results: There were 20 deaths and 3 VAD implantation during a mean follow-up of 819 days. In a multivariate proportional hazards survival model, COPM (HR 0.17, 95% CI 0.02-0.86, p=0.0004) was selected as the most powerful independent predictor of all-cause mortality or ventricular assist device (VAD) implantation.

Conclusions: STA offers sensitive measures of both global and regional LV function. However, in our population with severe LV dysfunction and sMR it seems that MR reduction by MVR did not lead to significant LV size reduction.

P3527 | BESIDES
Back to the future: head to head comparison of hemodynamically re-validated Doppler end-diastolic pulmonary regurgitant gradient and ASE-EACVI algorithm for the estimation of pulmonary wedge pressure

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Purpose: The echocardiographic continuous-wave Doppler end-diastolic pulmonic regurgitant gradient (PRG) has long been validated to calculate pulmonary artery wedge pressure (PAWP) when vascular resistances are normal. We re-validated PRG in patients undergoing diagnostic catheterization and used it as reference for the ASE-EACVI algorithm (ALGO) to predict increased PAWP in a large non-selected population.

Methods: We examined 183 patients (age 68±11 y.; NYHA: 2.4±.6; n=63, coronary artery disease; n=52, dilated cardiomyopathy; n=68, aortic stenosis) in a validation (VALI) and then 1019 patients (age: 10–93 y.; normal EF%, n=827; reduced <50%, n=192) in a prospective study (PROS) using GE Vivid7 or 9 systems. We both measured invasively PAWP and calculated PWPecho= PRG/Inverse (VALI) or noninvasive (PROS, using IVC collapse) right atrial pressure. The ALGO combined E/e’ (average), left atrial volume index (LAVi), transmural gradient and LA systolic function to obtain 3 groups (normal, increased and unclassified) which were compared to re-validated PAWPecho.

Results: In the VALI study, PWPecho correlated closely with PWP (r=0.73, p=0.001, independent of EF%) and predicted accurately increased PAWP (>12 mmHg) (AUC: 0.86, CI: 0.79–0.92) with excellent positive (PPV 91%) albeit low
negative predictive values (NPV 55%). In the PROS study, feasibility was high (PWPe 75%, E/e' 80%, LAVI 93%, EF 95%, E/e' 95%, SF 91%, PSPE 92%). Using the ALGO, 16% of patients were unclassified, prevalently secondary to combined E/e'≥9–13 range and LAVI ≥34ml/m². In the remaining (84%) patients, utility of ALGO to predict high PWPe was impaired by low PPV (EF 50%–60%, EF 50%–80%), whereas NPV was good (EF 50%–98%, EF 50%–80%). Furthermore, when E/e' alone was tested in the same patients at ROC analysis (cutoff = 15; AUC=0.72, CI: 0.6–0.8), accuracy was still impaired by a low PPV (53%), albeit a fair negative predictive value (NPV 79%). Correlation of E/e' with PWPe was poor when EF >50% (r=0.4, p=0.001) at regression analysis. E/e' was independently determined by age and mitral regurgitation in all patients, and by LV end-diastolic volume in EF <50% (r=0.7, p<0.001), and LV mass index in EF <50% (r=0.64, p<0.001).

Conclusions: PWPe performs better than ALGO in estimation of PWPe in unselected patients. The ALGO is limited by a low PPV irrespective of EF%, and utility of E/e' is limited by influence of patient age, preload and LV mass.

P3529 | BEDSIDE
Determination of the compensatory mechanism in HCM and severe aortic stenosis patients with preserved LV ejection fraction by 2D myocardial multi-layer speckle tracking strain echocardiography
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Background: Multi-layer speckle tracking strain echocardiography (STTE) can quantitatively measure strain in the endocardial and epicardial layers of the left ventricle (LV).

Purpose: To evaluate compensatory mechanisms in hypertrophic cardiomyopathy (HCM) and severe aortic stenosis (AS) subjects with a preserved LV ejection fraction (EF%), and to determine 2D LV global longitudinal strain (GLS) and circumferential strain (GCS) (absolute values) using STTE, and compared with controls.

Methods: A total of 105 subjects, 41 with HCM (31 male, 62±15 yrs), 40 with severe AS (19 male, 77±7 yrs, transaortic maximum velocity 4.8±0.6 m/s, aortic valve area index 0.46±0.12 cm²/m²), and 24 controls (12 male, 54±18 yrs) underwent STTE (Vivid E9). Apical 4-, 2-, and 3-chamber views for GLS and parasternal short-axis views of the mitral valve, papillary muscle, and apex for GCS were acquired. GLS was defined as all 17 averaged LV segments.

Results: Whole, endocardial, and epicardial layer GLS were significantly smaller in HCM than in controls (all p<0.001), and were significantly smaller in severe AS than in controls (all p<0.001). There were no significant differences in endocardial GCS at any site among the 3 groups. Endocardial GCS at the mitral valve and papillary muscle was significantly positively correlated with LVEF (R=0.447 and 0.34, respectively) in HCM. Similarly, in severe AS, endocardial GCS at the mitral valve and papillary muscle was significantly positively correlated with LVEF (R=0.472 and 0.556, respectively).

Conclusions: In HCM and severe AS with preserved LV EF, all GLS values were significantly smaller than in controls. We speculate that in such subjects, endocardial GCS is maintained in compensation for GLS decrement, and may contribute to maintaining LVEF.

P3530 | BEDSIDE
Impact of global and segmental hypertrophy on 2D and 3D strain in hypertrophic cardiomyopathy: comparison with healthy subjects
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Objectives: We studied the impact of hypertrophy on global and regional 2D and 3D strain in primary HCM as compared with controls.

Methods: A comprehensive resting 2D and 3D echocardiography was performed in 40 HCM and in 53 controls with a comparable distribution of age, gender, and left ventricular ejection fraction (LVEF). LV global (G) and segmental (S) measurements of all 2D and 3D peak strain components (longitudinal: GLS, GCS, radial: GRS, SRS and area: GAS, SAS) and 3D indexed LV end-diastolic myocardial mass (3D LVED mass) were obtained from all patients. LV wall thickness (LWWT) was assessed in short-axis views and classified in 4 quartiles (<10.5 mm, 10.5–13.0 mm, 13.0–16.5 mm and >16.5 mm).

Results: For global and regional 2D and 3D strain analysis results were consistent. However, reproducibility of 3D strain was similar or greater and more consistent for all strain components as compared to 2D strain analysis (table 1). There was a significant correlation between 2D LVED mass and all 3D strain components (from r=0.71 for 3DGLS to r=0.63 for 3DGCS, all p<0.05). 3D GCS had the strongest association with 3D LVEF (r=0.50, p<0.001). For segmental deformation, as compared to controls, HCM patients had lower 3D longitudinal function whatever the LWWT (controls: r=−0.57 vs. 1st quartile: r=−0.16, p=0.05) whereas circumferential was increased in none- and poorly hypertrophied segments (controls: r=−0.25±0.6 vs. 1st−21.2±0.6 and 2nd quartile: r=−0.8±0.5, both p<0.05).

Conclusion: 3D strain is a reliable technique to assess myocardial deformation. Myocardial mass is related with 3D strain components in HCM patients. circumferential deformation, as compared to longitudinal, seems to be the main determinant of the systolic function in HCM patients.

P3531 | BEDSIDE
Global myocardial mechanics with 3-Dimensional speckle tracking echocardiography in hypertrophic cardiomyopathy
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Background: Interstitial fibrosis as well as myocardial fibre disarray and non-

Conclusions: In HCM and severe AS with preserved LV EF, all GLS values were significantly smaller than in controls. We speculate that in such subjects, endocardial GCS is maintained in compensation for GLS decrement, and may contribute to maintaining LVEF.
uniformity shortening are common histological features of HCM even in the presence of normal left ventricular ejection fraction. Abnormalities in 2D speckle tracking echocardiography-derived parameters have been described in HCM patients showing a significant correlation with myocardial fibrosis. However values of 3D speckle tracking parameters in this population have not been fully studied. The aim of our study was to evaluate LV 3D speckle tracking parameters in HCM patients and its relation to functional parameters.

Methods: Twenty-four patients with HCM and thirty controls were included in the study. All subjects underwent conventional and 3D speckle tracking echocardiography (3DST) using the Scanner Artida 4D System. Global 3D longitudinal, circumferential, radial strains and area tracking were investigated.

Results: Patients with HCM showed attenuated global longitudinal (GLS) and circumferential strain (GCS) compared to controls (HCM vs. controls, GLS: −19.88±1.9% vs. −21.02±1.4%; GCS: −34.9±4.4% vs. −39.4±4.4%; p<0.001 for both). 3D area tracking (AT) was also significantly impaired compared to controls (HCM vs. controls, −33.6±7.5% vs. −47.9±4.8%, p<0.001). Left atrial (LA) volumes were moderately correlated with AT (r=−0.46, p<0.05). Additionally, the degree of LV obstruction was also correlated with GCS (r=−0.43, p<0.05).

Conclusions: 3D speckle tracking LV deformation parameters are impaired in patients with HCM providing novel insight into the pathophysiology of the disease. The relation between AT and LA volumes may reflect some degree of diastolic dysfunction. Its role over 2D speckle tracking echocardiography as well as its potential to predict clinical outcomes needs further evaluation.

Conclusions: LAe'sr function evaluated by LA strain rate was a promising parameter for LA dysfunction in patients with acute ischemic stroke.

### P3534 | BEDSIDE

Age- and Gender-related Differences on Left Ventricular Systolic Mechanics in Asymptomatic Asian Population: Special Focus on Torsion


Background: Gender may play an important role in left ventricular (LV) geometry and further contribute to LV mechanics with aging. The influence gender in age-related LV remodeling and torsion in asymptomatic Asian population remains largely unknown.

Methods: We consecutively enrolled asymptomatic subjects who underwent cardiac magnetic resonance imaging in our institution. LV mechanical function, method, and 2D-based speckle-tracking including strains and twist/torsion were all analyzed.

Results: Totally 4,100 subjects were analyzed (mean age: 49.9±10.8 years, 52.7% females). Advanced age quintiles was associated with greater wall thickness, higher LV mass index (all trend p<0.001). Compared to men, women showed both higher global longitudinal (−19.88 vs. −21.02%) and circumferential strains (−21.79 vs. −21.14%), greater torsion (2.13 vs 2.34° /cm) and better LV ejection fraction (0.46 vs 0.40, p<0.05). LAe'sr was correlated with LA ejection fraction (r=0.29, p<0.05) and E/E' (r=0.35, p<0.05).

Multivariate logistic regression analysis showed that LAe'sr was an independent predictor of LAA dysfunction (odds ratio 3.30, p<0.05).

Conclusions: Impaired LAe'sr function evaluated by LA strain rate was a promising parameter for LA dysfunction in patients with acute ischemic stroke.
**P3535 | BENCH**
The long noncoding RNA MALAT1-derived masrRNA is highly enriched in immune cells and regulates monocyte-macrophase functions.

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**Background:** Next generation sequencing revealed that the majority of the human genome is transcribed but has no coding function. It is estimated that >30,000 long noncoding RNAs (lncRNAs) are expressed in humans but their functions are largely unknown. We searched for lncRNAs influencing antiviral capacity in patients with viral (CVBS) cardiomyopathy and assign immunoregulatory functions to a small tRNA-like processing product of the IncRNA MALAT1.

**Methods and results:** To identify functions of the MALAT1-masrRNA system in the context of cardiotropic viral infections, we investigated its expression in immune cells and cardiomyocytes. Whereas the primary transcript MALAT1 was expressed in all cells and tissues, the small tRNA-like product masrRNA was highly enriched in immune cells. Antisense oligonucleotide (ASO)-mediated masrRNA ablation in monocytes led to massive induction of FASLG, FAS, TNF-a, and IL6, indicating important immunoregulatory functions of masrRNA in this cell type.

**Figure:** Panel A shows highly efficient ablation of masrRNA in monocytes by treatment with locked nucleic acid (LNA) anti-masrRNA ASO vs. scrambled (control) ASO vs. transfection agent (TA) alone. Panel B depicts transcriptional activation of FAS and its ligand (FASLG), TNF-a, and IL6.

**Conclusions:** MALAT1-derived masrRNA has important immunoregulatory functions. Beyond this specific IncRNA, multiple others are associated with cardiov-vascular diseases, but have complex cellular functions and thus are difficult therapeutic targets. Strategies to address IncRNA products with restricted functions may appear more promising. masrRNA exemplifies a first target of this type and its modulation by mimetic or antisense drugs has cardiovascular therapeutic potential.

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**P3537 | BENCH**
Constitutively active phosphatase inhibitor-1 improves cardiac in pressure-overload

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Recently the phosphatase-inhibitor-1 (P1) was identified as a distal and positive-acting modulator of β-AR signaling, which inhibits cardiac hypertrophy. The objective of the present study was to test the hypothesis that P1 reduces cardiac hypertrophy in pressure-overload (PO) settings.

**Methods:** Cardiac-specific expression of P1c in wild-type mice. We conclude, that in heart failure rather down-regulation of P1c may therefore be a potential strategy to treat heart failure.

**Figure:** Panel A shows highly efficient ablation of P1c in monocytes by treatment with locked nucleic acid (LNA) anti-P1 ASO vs. scrambled (control) ASO vs. transfection agent (TA) alone. Panel B depicts transcriptional activation of P1a and its ligand (P1b) in monocytes.

**Conclusions:** P1c demonstrates a first target of this type and its modulation by mimetic or antisense drugs has cardiovascular therapeutic potential.

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and there is limited evidence of translational buffering. Remarkably, we observe hundreds of strain-specific differences in gene expression that are apparent only at the translational level, almost doubling the number of differentially expressed genes detected between strains. Genome-wide protein synthesis rates measured by ribosome profiling are a better proxy for protein levels compared to RNA sequencing. Integration of genetic, transcriptional and translational datasets identifies distinct signatures in 3’UTR variation, RNA binding protein motifs, and mRNA expression that are associated with translational regulation of gene expression. Intriguingly, many genes regulated at the translational level have been implicated in human disease in genome-wide association studies (GWASs). Taken together these data document novel and extensive translational control of important cardiac and metabolic genes and pathways and show that a large number of genes associated with heart and liver traits by GWAS are regulated translationally. Cap-tured inter-individual differences in the translated genome will lead to new insights into the genes and regulatory pathways underlying disease phenotypes.

P3530 | BENCH
Mice with cardiac specific overexpression of hDSC2 develop a biventricular cardiomyopathy associated with severe fibrosis and calcification
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Mutations of DSC2 cause arrhythmogenic cardiomyopathy (AC). DSC2 is localized within the cardiac desmosomes and contributes to the Ca2+-dependent adhesion of cardiomyocytes at the intercalated disc. However, the molecular and cellular mechanisms induced by DSC2 mutations leading to AC are widely unknown. So far, no DSC2 mouse model mimicking an AC is described. Therefore, the aim of this study was to establish and characterize an adequate transgenic mouse model to investigate the underlying pathomechanisms in vivo. We developed and characterized a transgenic mouse model with a cardiac-specific overexpression of hDSC2. Echocardiography and (immuno)histology were used to characterize the functional and structural defects in our DSC2 mouse model. These experiments were complemented by Western blot analysis and qRT-PCR experiments to characterize the molecular expression changes of other desmosomal genes.

Analysis using echocardiography revealed that transgenic mice shortly after birth develop a severe cardiomyopathy with significantly reduced fractional shortening and ejection fractions compared to non-transgenic control mice. Thus, the established cardiac specific overexpressing hDSC2 mice are viable but develop a progressive biventricular cardiomyopathy mimicking the clinical phenotype of patients with arrhythmogenic cardiomyopathy. This novel mouse model might contribute to further understanding of the molecular and cellular pathomechanisms leading to arrhythmogenic cardiomyopathy.

P3540 | BENCH
Next generation sequencing in thoracic aortic aneurysms and dissections - eight novel mutations in known genes (ACTA2, FBN1, MYH11, SKI, SMAD3, and TGFBR1)
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Background: Thoracic aortic aneurysms and dissections (TAAD) are significant cause of morbidity and mortality and occur either as isolated manifestation or as a part of syndromic condition.

Purpose: The aim of our study was to define genetic background of TAAD.

Methods: In the years 2012–2014 we studied 40 unrelated TAAD patients (pts; 25–50). 4 orthotopic heart transplantation autopsy samples (all males) were used as healthy controls. 30 candidate genes were selected for the study. mRNA expression was determined by ribonculus sequencing. Integration of genetic, transcriptional and translational datasets identified 14 causative mutations in 14 pts (35%), 8 of them were novel. Analysis revealed 6 mutations in FBN1 gene: 3 missense variants in EGF-like calcium-binding domains (1 affecting cysteine residue), 1 nonsense, 1 splice site, and 1 in-frame deletion. Single missense mutations were found in each of TGFBR1 and TGFBR2 genes, both affecting their serine/threonine protein kinase catalytic domains. In addition, missense mutations: 1 in highly conserved of MH2 domain in SMAD3, 1 within a hot spot in SKI, 2 in ACTA2, and 2 in MYH11. All detected mutations were absent from 1000Genomes, ESP, and ExAC databases with exception of TGFBR1 (p.<0.00002 in EXAC) and both MYH11 variants (p.<0.001 in ESP and ExAC). In familial TAAD, all relatives with TAAD carried identified variants. Based on combined clinical and genetic data, syndromic TAAD was diagnosed/confirmed in 9 pts (7-Martan syndrome, 1-Loeys-Dietz syndrome, 1-Sprintzen-Goldberg syndrome), and nonsyndromic TAAD in 5 pts. Furthermore, we identified 17 mutation carriers among relatives. Summary: Genetic testing supports the diagnosis of inherited, both syndromic and nonsyndromic TAAD. Identification of novel causative mutations adds to heterogeneity of the genetic background of TAAD.

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P3541 | BENCH
Gene expression in myocardial tissue and peripheral blood cells: potential RNA-biomarkers for myocarditis identification
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Introduction: Myocardial inflammation following by cardiomyocyte necrosis is accommodated by altered gene expression in affected cells. Development of the pathology modifies gene expression in myocardial tissues, but also might affect transcription in peripheral blood cells.

Purpose: The study was devoted to investigate modulation of gene expression in myocardial tissues and PBC of patients with myocarditis and to identify potential biomarkers for this pathology.

Methods: 15 endomyocardial biopsy (EMB) samples (M: 10, F: 5, age: 37–62) and 10 PBC samples (M: 6, F: 4, age: 26–50) were obtained from patients with myocarditis, 6 PBC samples were obtained from healthy donors (M: 3, F: 3, age: 25–50), 4 orthotopic heart transplantation autopsy samples (all males) were used as healthy controls. 30 candidate genes were selected for the study. mRNA expression profiles in EMB from male and female groups. An absence of expression profiles in EMB from male and female groups.

Results: A minimal set of reference genes (GAPDH and HPRT1) for normalization of qPCR results was determined. RT-qPCR confirmed expression of 24 out of 30 genes in EMB samples and all 30 genes in PBC. Significant difference was found in expression profiles in EMB from male and female groups. An absence of female healthy myocardial tissue forces us not to use the data to further analysis. Expression of 10 candidate genes (NF-KB, IL2, NOTCH3, GLIPR, TMOD3, SEC24A, FCER1G, ITGB2, SIGLEC1, ADCY7) out of 30 studied was altered in myocardial tissue and PBC of patients with myocarditis and to identify potential biomarkers for this pathology.

Conclusions: Significant alteration of transcription was found for 10 genes in EMB samples of male patients with myocarditis. 6 out of 10 genes were identified in the present study, transcription level of 4 genes matched to the disease progression. Analysis of transcription in PBC revealed only 2 genes with altered expression; no correlation was found for expression of target genes in PBC and EMB samples.

P3542 | BENCH
Strategies to normalize zebrafish specific cardiac phenotypes resembling different human myosin binding protein C3 mutations using RNA approach
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Mutations in the gene encoding myosin binding protein C3 (MYBPC3) are one of the most common causes of cardiomyopathies and can produce varying phenotypes. The exact disease mechanisms responsible remain unknown. Zebrafish model offers unique opportunities to study human cardiovascular disease mechanisms in vivo.

Analysis using echocardiography revealed that transgenic mice shortly after birth develop a severe cardiomyopathy with significantly reduced fractional shortening and ejection fractions compared to non-transgenic control mice. Histopathology demonstrated that the myocardium is significantly replaced by fibrosis and fatty tissue. Furthermore, a severe calcification is detected within the myocardium. In addition, we showed that the expression of other desmosomal genes are significantly reduced in EMB samples. Significant alteration of transcription was found for 10 genes in EMB samples of male patients with myocarditis. 6 out of 10 genes were identified in the present study, transcription level of 4 genes matched to the disease progression. Analysis of transcription in PBC revealed only 2 genes with altered expression; no correlation was found for expression of target genes in PBC and EMB samples.

Conclusion: Significant alteration of transcription was found for 10 genes in EMB samples of male patients with myocarditis. Preliminary results suggest that expression profile can be considered not only as a biomarker of myocarditis, but also for assessment of therapeutic effects and the long-term outcome prognosis for patients with myocarditis.

Results: At the time of genetic inquest mean age of the study population was 43.5±13.4 years, 18 had familial TAAD. In 15 pts acute aortic dissection at mean age of 42.3 years was first symptom of TAAD, and 13 pts with thoracic aortic aneurysm had planned aortic surgery as first intervention at mean age of 42.8 years. Associated abnormalities included: BAV – 8 pts, 1 CoA, 1-ASD. We identified causative mutation in 14 pts (35%), 8 of them were novel. Analysis revealed 6 mutations in FBN1 gene: 3 missense variants in EGF-like calcium-binding domains (1 affecting cysteine residue), 1 nonsense, 1 splice site, and 1 in-frame deletion. Single missense mutations were found in each of TGFBR1 and TGFBR2 genes, both affecting their serine/threonine protein kinase catalytic domains. In addition, missense mutations: 1 in highly conserved of MH2 domain in SMAD3, 1 within a hot spot in SKI, 2 in ACTA2, and 2 in MYH11. All detected mutations were absent from 1000Genomes, ESP, and ExAC databases with exception of TGFBR1 (p.<0.00002 in EXAC) and both MYH11 variants (p.<0.001 in ESP and ExAC). In familial TAAD, all relatives with TAAD carried identified variants. Based on combined clinical and genetic data, syndromic TAAD was diagnosed/confirmed in 9 pts (7-Martan syndrome, 1-Loeys-Dietz syndrome, 1-Sprintzen-Goldberg syndrome), and nonsyndromic TAAD in 5 pts. Furthermore, we identified 17 mutation carriers among relatives. Summary: Genetic testing supports the diagnosis of inherited, both syndromic and nonsyndromic TAAD. Identification of novel causative mutations adds to heterogeneity of the genetic background of TAAD.

Acknowledgement/Funding: Institute of Cardiology statutory grant 2A.18/V1/12
We have previously recapitulated in the zebrafish model four disease causing missense mutations of MYBPC3 domain C1: Mutation 1 (Arg177His), Mutation 2 (Ala216Thr), Mutation 3 (Glu258Lys) and Mutation 4 (Ser217Gly). Injection of splice donor site morpholino targets Mutation 1, 2 and 4 at exon 5 and Mutation 3 at exon 6 in zebrafish embryos induced hypertrophic cardiomyopathy similar to the human phenotype. Mutation 3 resulted in severe cardiac phenotype exhibited by 71% zebrafish morphant embryos with enlarged cardiac chambers and reduced heart rate compared to 46% of Mutation 1, 2 and 4.

Since it remains unclear whether specific cardiac phenotypes in these zebrafish embryos reflect primary or secondary responses of the heart caused by the accumulation of the mutant mybpc3 RNA, further studies are necessary in order to determine the early changes occur specifically in response to mutation in MYBPC3. Therefore, we assessed the RNA-based approach as a potential correction of HCM. The human MYBPC3 was cloned into pcDNA-DEST47 vector. Site-directed mutagenesis was used to create corresponding mutations mentioned above in the human cDNA followed by generation of mRNA. The wild type human mRNA was co-injected with the morpholino targeting exon 6 to test the ability to suppress the accumulation of the mutant zebrafish mRNA and revert the embryonic zebrafish mutant phenotype. However, the co-injection resulted in aberrant cardiac phenotype and induced hypertrophic cardiomyopathy similar to the morphant embryos, suggesting that this specific cardiac phenotype produced by Mutation 3 might be a secondary response of the heart caused by activation of compensatory mechanisms after the alteration of cMyBP-C. Further work is needed to understand the exact pathogenic mechanisms of these mutations.

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P3544 | BENCH
Teratocarcinoma arising from induced pluripotent stem cell-derived cardiac tissue constructs can be diagnosed by FDG-PET to induce alloimmune rejection by cessation of immunosuppression
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Background: Tumorigenicity is a concern in cell therapy using induced pluripotent stem cells (iPSCs). Allogeneic transplantation of iPSCs under immunosuppression can be a safe approach with fully exploring the tumorigenicity before transplantation and inducing immune rejection of iPSC-derived tumor by cessation of the immunosuppression. However, imaging modality to identify the tumor so early as to induce immune rejection is poorly studied. We herein investigated tumor formation by CT, MRI, US and FDG-PET after transplantation of iPSC-derived cardiomyocytes (CM) in mice, and examined whether cessation of the immunosuppression could induce immune rejection of the tumor.

Methods and results: iPSCs established from C57BL/6N mouse and constantly expressing Luciferase were generated iPSC-CM sheets and transplanted on the cardiac surface of BALB/cJ mice with administration of tacrolimus. Histologically, the transplanted cells formed teratocarcinoma at day 7. FDG-PET demonstrated high FDG uptake with significantly higher SUV max at day 7 or 10 than day 3 or 5 (p<0.05). CT, MRI and US were unable to detect tumor at day 7. Then, mice were divided in 2 groups with continuous or cessation of immunosuppression at day 7. During 2 months of observation with bioluminescence imaging, teratocarcinomas were detected in 6/9 mice in the continuous group, whereas all teratocarcinomas were vanished in the cessation group, which led significant improvement of the survival of mice (p<0.05). Proliferative response and IL-2 release capacity of lymphocytes recovered in the cessation group.

Conclusion: FDG-PET could detect iPSC-derived teratocarcinomas early, and subsequent cessation of immunosuppression improved the survival of mice with vanishment of the tumors, indicating usefulness of FDG-PET for clinical application.

P3545 | BENCH
Improved endothelialisation of synthetic dual peptide-conjugated vascular graft seeded with human pericytes
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Introduction: When autologous vessels are unavailable, synthetic vascular grafts are employed for coronary bypass. Since their rapid endothelialisation is key to reduce complications conjugation of active molecules have been employed to increase the performance; our lab has recently engineered a scaffold presenting a gradient of two different active peptides, allowing the spatial determination of the functional molecule. Seeding of vascular scaffolds with progenitor cells ben-
officially impacts the patency of grafts. Human saphenous vein-derived pericytes (SVP) are immuno-privileged cells from vein leftovers from bypass patients, and can be used both for autologous and for off-the-shelf solutions. They showed pro-angiogenic potential in vitro and after direct injection in vivo (ischemia and infarction).

Purpose: This study describes a novel approach to synthetic vascular graft design, based on the creation of a gradient of biochemically relevant peptides, combined with the seeding of SVP on the adventitial layer. Methods: Polycaprolactone (PCL) fibres conjugated with the osteopentin-derived adhesive fragment (SVV, luminal) and the growth factor capturing heparin-binding peptide (Hep, adventitial) were electrospun. SVP were seeded on the adventitial layer. Peptides and SVP effect on endothelial cell (EC) adhesion and migration was evaluated. Results: Alamar blue assay showed a 2.5 and 3.5 fold increase in EC adhesion on SVV-conjugated scaffolds, after 3 and 6 days of culture compared to control; the effect was specific for SVV. Histology of the gradient scaffolds (H/S) showed a gradient of binding of fluorescent heparin and VEGF compatible with Hep peptide distribution. SVP attachment on the adventitial side of the H/S was assessed by immunostaining (H/S+SVP). Seeded scaffolds were cryopreserved for up to 2 weeks, preserving 70% viability. Seeding of SVP on H/S scaffolds increased EC coverage on the luminal side by 4 fold, compared to H/S scaffolds alone. When SVP were seeded on CTF scaffold the increase was more modest, indicating a synergic effect. Animals were sacrificed and livers were excised and analysed with hematoxylin/eosin, and Masson’s and Gallego’s modified trichrome staining provided a clear visualization of vessel and nervous ultrastructures. SVP were used to study scaffold vascularization. Transmission electron microscopy confirmed the presence of vascular and nervous ultrastructures. Conclusions: We engineered a vascular scaffold combining progenitor cells and a gradient of functional molecules showing their synergistic effect in promoting EC coverage.

Methods and results: We engineered MSCs with integrin-linked kinase (ILK), a pleiotropic protein enhancing progenitor cells homing, reversing myocardial remodeling and improving cardiac function following MI. We evaluated the therapeutic potential of ILK-MSCs in a porcine MI model established by a 90-minute balloon occlusion. ILK-MSCs were labeled by cell surface CD45 immunofluorescence prior to injection. Cell homing was visualized using fluorescent markers (DiD and DiR) and MRI imaging was used to follow cell survival and at 37°C, and day 4 post-injection. ILK-MSCs reached a ventricular distribution as assessed by MRI imaging at 4 weeks post-injection. In vivo follow-up revealed increased viability in ILK-MSC treated minipigs versus vehicle treated controls. Conclusions: These data confirm the potential of ILK-MSCs to improve myocardial function following MI. ILK-MSCs reached a ventricular distribution as assessed by MRI imaging at 4 weeks post-injection. In vivo follow-up revealed increased viability in ILK-MSC treated minipigs versus vehicle treated controls.
HiPSC-derived CTS potentially ameliorate cardiac dysfunction of human-size infant heart.

**P3550 | BENCH**

Human amniotic fluid stem cell secretome protects cardiomyocytes against doxorubicin toxicity

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**Conclusion:** HiPSC-derived CTS potentially ameliorate cardiac dysfunction of human-size infant heart.

**Methods:**

1. c-kit positive hAFS were isolated from amniotic fluid collected during second trimester diagnostic amniocenteses that had proved negative for disease.

2. Cells were cultured in serum-free medium for 24 hours in normoxia (20% O2) or hypoxia (1% O2).

3. The rat cardiomyoblast cell line, H9c2, and primary mouse neonatal cardiomyocytes (nCM) were pre-treated for 3 hours with hAFS-conditioned medium (hAFS-CM) before being exposed to pro-senescent (0.1μM) and pro-apoptotic (1μM) concentrations of doxorubicin for 3 and 18 hours, respectively.

4. Cell senescence and apoptosis, two main features of doxorubicin cardiotoxicity, were evaluated by staining for senescence associated (SA) β-galactosidase.

5. Intracellular signaling pathways were investigated by immunofluorescence and/or western blot. Experiments with specific kinase inhibitors were performed.

6. Both cell senescence and apoptosis caused by doxorubicin were significantly counteracted by hAFS-CM, the effect being more intense with hAFS-CM obtained in hypoxic conditions. Positivity for SA-β-galactosidase was decreased by 39.5% and 51% by normoxic and hypoxic hAFS-CM, respectively. A reduction in apoptosis by 30% and 50%, respectively, was also observed. The capability of hypoxic hAFS-CM to prevent doxorubicin-triggered senescence and apoptosis was confirmed in nCM (47% and 43% inhibition, respectively). Protection by hAFS-CM was associated with phosphorylation of Akt and ErK1/2. Consistently, pre-treatment with LY294002—which blocks phosphatidylinositol 3-kinase and thereby Akt signaling—and the ErK1/2 inhibitor, PD98059, significantly attenuated hAFS-CM antagonism of doxorubicin-induced senescence and apoptosis.

**Conclusion:** Our results provide unprecedented evidence that paracrine factors secreted by hAFS protect cardiomyocytes against doxorubicin toxicity, raising new prospects for therapy of chemotherapy-related cardiac disease.

**P3551 | BENCH**

A model of anthracycline-induced cardiotoxicity using induced pluripotent stem cell-derived cardiomyocytes

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**Purpose:** Doxorubicin (DOX), an effective chemotherapeutic drug, is limited in its clinical applications due to cumulative dose-dependent cardiotoxicity. The mechanisms of anthracycline-induced cardiotoxicity (ACT) are still not fully understood. The ability to generate human induced pluripotent stem cells (hiPSCs) provides a unique opportunity for modeling heart disease. We aimed to investigate the effects of DOX on iPS-derived cardiomyocytes (iPSC-CMs) to establish a human in vitro model of ACT for understanding the underlying pathomechanisms.

**Methods and results:** iPSCs from healthy human individuals were directly differentiated into functional iPSC-CMs (95%) for two months and exposed to 0.1, 0.5, 1, 5, and 10μM DOX for 24 hours. Surviving cells were cultured in normoxia (20% O2) using Annexin V/ PI staining resulting in a mortality rate of 30% after 5 μM DOX. Furthermore, a higher percentage of iPSC-CMs treated with DOX showed abnormal sarcomeric α-actinin distribution in comparison to untreated cells, suggesting disorganized myoflament structure. Since titin (TTN) serves as a template for sarcomeric assembly, we analyzed its isoform expression and degradation as a function of DOX treatment. We found no changes in cardiac TTN isoforms, but a decreased overall TTN expression on mRNA level after DOX-treatment. In addition, the TTN degradation pattern altered dose-dependently in DOX-treated iPSC-CMs, shown by western blots, suggesting TTN degradation as early event in ACT. Since TTN is susceptible to calcium-dependent protease degradation, we hypothesized that TTN degradation is dependent on diastolic calcium concentration. We found a dose-dependent decreasing expression of the calcium ion channels RYR2, SERCA, and NCX in DOX-treated iPSC-CMs. These results are in line with a significantly increase in diastolic calcium after DOX-treatment in iPSC-CMs using Fluor4. Furthermore, we found that DOX leads to an increased generation of reactive oxygen species (ROS) in iPSC-CMs, which could be explained by a DOX-dependent differential expression of NADPH-oxidase subunits that we showed in iPSC-CMs.

**Conclusion:** We demonstrate that DOX-treated iPSC-CMs recapitulate the abnormalities that were found in individuals with ACT. We show evidence for a DOX-induced apoptosis of iPSC-CMs and ROS-production in iPSC-CMs leading to sarcomeric disassembly and calcium-dependent titin degradation. HiPSCs should therefore be used as an in vitro model of ACT to investigate the influence of the genetic background on ACT for the development of therapeutic and protective strategies on a patient-specific level.

**References:**

- Kondo N, Nagai T, Takahashi M, Kanda M, Matsumura I, Komuro Y, Kobayashi C. Chiba University Graduate School of Medicine, Chiba, Japan; 2 Tokyo Women's Medical University, Institute of Applied Immunology and Science, Tokyo, Japan; 3 University of Tokyo, cardiology, Tokyo, Japan.
Physiologically trained cardiac adipose tissue derived progenitor cells within fibrin scaffolds to improve cardiac function

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Purpose: Cardiac tissue engineering aims to develop biostructures capable of re-establishing physiological organization and function of the infarcted myocardium. Cardiac cells are subjected to mechanical and electrical forces, which regulate gene expression and cell function. Therefore, it is important to obtain in vitro stimulation that could further integrate the therapeutic cells into the myocardium. Our goals were: 1) study the viability of a tissue engineered construct with cardiac adipose tissue-derived progenitor cells (cardiumATDPCs); and 2) examine the effect of electromechanical stimulated cardiacATDPCs within a myocardial infarction (MI) model in mice.

Methods: CardiumATDPCs were electromechanically stimulated, harvested and labelled to generate the 3D fibrin construct. The electromechanical stimulation protocol was designed to mimic the physiological heart environment; 2ms pulses of 50mV/cm at 1Hz and 10% straining during 7 days. Cell viability was evaluated through a Life & Dead assay. The cellular construct was implanted in the murine heart and animals were sacrificed after 3 weeks post-implantation. 40 animals were randomly distributed: without cells (control MI, fibrin MI) and with stimulated or non-stimulated (stimulated MI and sham). Echocardiography, gene and protein analysis were also carried out.

Results: In vitro electromechanical stimulation on cardiacATDPCs showed increased expression of cardiac transcription factors, structural genes and calcium handling related genes. After 3 weeks of in vitro culture in the fibrin construct, cells exhibited high viability and remained labeled. Cell treatment resulted in functional improvement of left ventricular ejection fraction (LVEF) relative to post-infarction values; indeed, stimulated cardiacATDPCs produced a 4.7% average increment compared to non-stimulated cells, as revealed by echocardiography. On the contrary, control MI and fibrin MI presented a decrement in LVEF (4.1% and 3% reduction, respectively). Finally, histology showed cell proliferation and main cardiac markers expression of implanted cardiacATDPCs, but also scarce migration to the border zone to MI was observed.

Conclusions: The electromechanical protocol designed enhances cardiac properties of therapeutic cells at genetic and protein level. Furthermore, the construct used in our study confers a suitable environment for cell viability, proliferation, cardiac maturation and migration to infarcted myocardium. All together, electromechanical stimulation of therapeutic cells previous implantation could be a valuable tool for cardiac regeneration approaches.

Allogeneic cardiac-reparative cell therapy for acute myocardial infarction. Preliminary results of the CAREMI clinical trial

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Results:

<table>
<thead>
<tr>
<th></th>
<th>Control MI</th>
<th>Fibrin MI</th>
<th>StIMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>CK-MB (ng/mL)</td>
<td>281.3±100.6</td>
<td>3.5±3.3</td>
<td>3.5±3.2</td>
</tr>
<tr>
<td>hs-CRP (ng/mL)</td>
<td>5438±1440.9</td>
<td>1346.2±1034.3</td>
<td>1339.8±1732.3</td>
</tr>
</tbody>
</table>

Cardiac enzymes profile (p<NS)

Enzymes

Peak post-infusion

| CK (U/L) | 186.7±123.1 | 164.3±85.9 |
| CK-MB (ng/mL) | 3.5±3.3 | 3.5±3.2 |

Methods and results: This trial was conducted to evaluate the following hypotheses: 1) the safety of cardiumATDPCs in the context of MI; 2) the preservation of the viability of cardiumATDPCs during the in vitro electromechanical stimulation; and 3) the restoration of myocardial function by cardiumATDPCs. The study was carried out at the University General Hospital Gregorio Maranon, Department of Cardiology, Madrid, Spain.

Conclusions: CardiumATDPCs are a viable therapeutic option for acute myocardial infarction. Further studies are needed to evaluate the long-term efficacy and safety of this approach.

Stem cells and cell therapy II

Improvement in ADMa and oxidative stress after stem cell therapy in patients with critical limb ischemia

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Background: Asymmetric dimethylarginine (ADMA), an endogenous inhibitor of nitric oxide synthase, acts as an inhibitor of angiogenesis, and is associated with an increased risk of cardiovascular mortality. Administration of stem cells has been shown to affect endothelial repair (24h, 1 week, 3 and 6 months) and 6-month efficacy data (by MRI) will be available during the conference.

Methods:

1. Sixty one patients (age 64±11 years, M:F 54:7) with advanced CLI (Rutherford category 5,6) not eligible for revascularization were treated by intramuscular injection of BM-MNCs application for advanced critical limb ischemia (CLI).

Results:

1. The concentrations of oxidative stress markers were analyzed before, 3 months, and 6 months after BM-MNCs delivery. Patients with limb salvage at 6-month follow-up were considered as responders to cell therapy. The concentrations of oxidative stress markers before, 3 months, and 6 months after BM-MNCs delivery were 51/61 (84%), and 46/61 (75%), respectively. In responders to cell therapy, the construct used in our study confers a suitable environment for cell viability, proliferation, cardiac maturation and migration to infarcted myocardium. All together, electromechanical stimulation of therapeutic cells previous implantation could be a valuable tool for cardiac regeneration approaches.
was significant decrease in ADMA concentration after 6 months (1.66±0.67 to 0.97±0.65 μmol/l, p<0.0004), accompanied by decrease in TNF-α (2.13±0.30 to 1.81±0.46 pg/ml, p<0.0002), increase in reduced glutathione (6.8±3.0 to 12.6±4.0 μmol/l, p<0.05). Importantly, the number of delivered BM-MNCs significantly correlated with decrease in ADMA concentration at 3-month follow-up (r=0.006, r=-0.45), and with decrease in TNF-α concentration at 6-month follow-up (r=0.009, r=-0.51). There was no correlation with number of applied CD34+ cells, or with dosage of administered atorvastatin.

Conclusions: Administration of BM-MNCs could potentially influenced angiogenesis and endothelial function by decrease of ADMA concentration and by attenuation of TNF-α level. Improvement of ADMA-NO axis and improvement of antioxidant status could participate on beneficial effects of stem cell therapy of cardiovascular diseases.

Acknowledgement/Funding: This study was sponsored with a grant from European Regional Development Fund (ITMS code: 26240200203).

P3557 | BENCH
Granulocyte colony-stimulating factor promotes the proliferation of cardiac side population cells by AKT-GATA4 pathway

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Background: Granulocyte colony-stimulating factor (G-CSF) was initially reported to induce myogenic regeneration by promoting mobilization of bone marrow stem cells or side population cells to the injured heart after myocardial infarction (MI). The role of population cells (CSPs) in the generation of new cardiac stem cells, has been reported to be able to differentiate into cardiovascular cells in vitro and in vivo. Our previous study showed that G-CSF improved cardiac function against ischemic-reperfusion injury by Stat3/HSF1 pathway in animal study. However, whether the cardiac-protection of G-CSF is associated with the effect on CSPs is unclear.

Purpose: We aim to study the effect and the potential mechanisms of G-CSF on CSPs.

Methods: MI model was established by ligation of left anterior descending coronary artery in mice. Mice were treated with recombinant human G-CSF (100μg/kg/day) or saline by subcutaneous injection for 7 days consecutively after MI. CSPs were sorted and counted from mice by fluorescence-activated cell sorting (FACS) analysis. In vitro, CSPs from neonatal rat were purified and cultured with or without G-CSF. The proliferation of cultured CSPs was analyzed by luminose cell viability assay.

Results: After MI, the ratio of CSPs was increased 2-fold compared to sham mice, and G-CSF greatly promoted the effect. In vitro, G-CSF significantly enhanced the proliferation of CSPs in concentration-dependent manner. Further analysis showed that G-CSF increased phospho-AKT expression and activation of GATA4 in cultured CSPs. AKT inhibitor dramatically suppressed G-CSF-induced proliferation of CSPs in vitro and in vivo. It also inhibited the upregulation of GATA4 and CSPs in cultured CSPs. In GATA4 knock-downed CSPs only severely damaged G-CSF-regulated expression of GATA4 by about 80%, but also partly abolished the phospho-AKT induced by G-CSF in cultured CSPs. In addition, G-CSF-induced proliferation of CSPs was greatly reversed by si-GATA4 in vitro. G-CSF-treated CSPs cultured in ischemic rat heart were better perfused than un-treated cells. Real-time reverse transcription polymerase chain reaction showed that the expression of AKT and GATA4 in cultured CSPs was up-regulated. Thus, G-CSF may exert cardioprotective effect against MI by promoting the proliferation of CSPs and support myocardial regeneration in injured heart.

P3558 | BENCH
Analysis of secretion profiles of pro-angiogenic paracrine factors in clinical trials of stem cell therapy for myocardial infarction

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Introduction: Great expectations were put on stem cell therapies for myocardial infarction (MI) over the last decade. However, inconsequent results of large clinical trials have hampered a wider application in patients who have suffered a MI. Whereas the REPAIR-AMI trial evidenced quite convincing results, no detectable effects of stem cell administration were found in the ASTAMI-trial. As paracrine mechanisms in stem cell therapy have received more and more attention recently, we sought to compare cell separation protocols of these trials with special emphasis on paracrine signalling.

Materials and methods: Mononuclear cells were obtained from peripheral blood and from bone marrow aspirates and were processed according to the ASTAMI and REPAIR-AMI protocols. In brief, cells in the ASTAMI protocol were suspended in sodium chloride solution supplemented with 20% of autologous plasma and were kept at 4°C, whereas in the REPAIR-AMI protocol cell cultures were cultured in X-Vivo 10 medium supplemented with 20% of autologous plasma at room temperature. Cell culture supernatants were analyzed for pro-angiogenic factors using ELISA (e.g. Interleukin-8, GRO-alpha, ENA-78, MCP-1, VEGF).

Results: Cells treated according to the REPAIR-AMI protocol secreted remarkably higher amounts of pro-angiogenic factors compared to the ASTAMI-protocol (e.g. Interleukin-8 9.7±9.7 pg/ml ± 2.9 SEM vs. 930.4 pg/ml ± 483.5 SEM, p<0.0022).

Conclusions: Here we could show that the REPAIR-AMI protocol was far superior regarding the secretion of pro-angiogenic factors. During the culture period these factors were enriched in great amounts in the supernatant when cells were treated in accordance to the REPAIR-AMI protocol. Based on recent studies showing that paracrine signalling represents a major influencing factor in stem cell therapy, we believe that the efficacy of clinical trials in MI patients could be increased by improved protocols for cell processing. The fact that almost no pro-angiogenic factors were present in the supernatant of cells processed according to the ASTAMI-protocol might explain the failure of the ASTAMI-trial.
P3551 | BENCH
c-kit/CreERT2 knock-in allele minimally tags c-kit positive resident endogenous cardiac stem cells and its cardiomyocyte progeny in the adult life

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Introduction: Recently, we have demonstrated that resident tissue-specific c-kit+ endogenous cardiac stem cells (eCSCs) represent an essential age-related cardiac repair mechanism in adult rodent hearts. However, the first mouse model for c-kit genetic fate mapping using a Cre knock-in the c-kit Exon1 +/+ does not reliably label the few c-kit+ cells minimally produce cardiomyocytes (CMs) either during development as well as in healthy or damaged adult hearts.

Purpose: We addressed whether a tamoxifen (TAM)-inducible Cre knock-in the c-kit Exon1 +/+ efficiently recombine c-kit+ eCSCs in the adult myocardium for reliable cell fate mapping.

Methods: Heterozygous c-kitCreERT2 (T2) +/+ mice were crossed with the global double membrane-estrogen receptor linked Cre recombinase (mER-Cre-mER) under the membrane-estrogen-receptor linked Cre recombinase (mER) locus to express a floxed (“cre erasable”) Stop sequence in front of the Diphtheria toxin A gene (R26-stop-DTA). Using double transgenic myh6-mER-Cre-mER/R26-stop-YFP mice, we established that daily i.p. administration of TAMeria toxin A gene (R26R-stop-DTA). Using double transgenic myh6-mER-Cre-mER/R26-stop-YFP mice, we established that daily i.p. administration of TAM:

Conclusions: Taken together these data demonstrate for the first time that the heart has an intrinsic robust and functionally productive regenerative capacity to recombine c-kitpos eCSCs in vivo. On the other hand, all animals from the groups with 2 or 3 TAM injections (corresponding to a cumulative total loss of 25 to 35% of CMs, respectively) survived and showed a significant LV dysfunction with LV dilation and reduced EF from 7 to 14 days. Cardiac performance started to improve at 21 days and was completely normalized at 28 days. Importantly, in response to pure CMs, only a minority of the animals showed a positive mononucleated CMs either during development as well as in healthy or damaged adult hearts.

P3552 | BENCH
An integrated approach using patient-specific induced pluripotent stem cells and protein biochemistry to study Vici syndrome-associated cardiomyopathy

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Vici syndrome with defective autophagy caused by EPG5 is a recessively inherited multisystem disorder characterized by callosal agenesis, cataracts, cardiomyopathy, combined immunodeficiency and hypopigmentation. Generation of induced pluripotent stem cells (iPSCs) from human patients provides a platform to study the disease mechanisms relevant to the identified genetic causes and modifiers in an in vitro cell culture system.

Purpose: In this study, we aim to generate iPSCs from Vici syndrome patients carrying EPG5 mutations (Vici-iPSCs) and analyze the cellular and molecular features of Vici-iPSC-derived cardiomyocytes (Vici-iPSC-CMs) and non-cardiomyocytes (Vici-iPSC-nCMs).

Methods and results: Skin fibroblasts from a Vici syndrome patient with EPG5 mutation (c.4952+1 G - A) were reprogrammed into Vici-iPSCs by using lentivirus containing four Yamanaka factors Oct4, Sox2, Klf4 and Myc. The generated Vici-iPSCs were proved for their pluripotency and verified with the EPG5 mutation by sequencing. Vici-iPSCs and control-iPSCs were directly differentiated into functional cardiomyocytes using a standardized serum-free protocol by modifying the Wnt pathway with GS3KO inhibitor CHIR90021 and Wnt pathway inhibitor IWP2. To study the CM phenotype, we measured the cell surface areas and found that Vici-iPSC-CMs were significantly bigger than control-iPSC-CMs, however, the volume of the cells demonstrated by flow cytometry analysis showed no differences. Preliminary data showed that the embryonic cardiac genes encoding atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) are elevated in Vici-iPSC-CMs whereas alpha-myosin heavy chain (αMHC) is downregulated and beta-myosin heavy chain (βMHC) is upregulated. Furthermore, Vici-iPSC-CMs did not reveal significant autophagosome accumulation compared to the control-iPSC-CMs while the Vici-iPSC-nCMs showed significant autophagosome accumulation than control cells by both Western blotting and immunofluorescence staining analyses. These findings suggest that the autophagy defects in Vici-iPSC-CMs are different with Vici-iPSC-nCMs.

Conclusion: Our data demonstrate that the differentiated cells from Vici-iPSCs can recapitulate the disease phenotype in vitro and can be used to study the underlying molecular mechanisms in Vici syndrome.

P3553 | BENCH
In situ activation of endogenous cardiac stem cells cells their secretome, miRNome, potentiating their regenerative capacity on the injured heart

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We examined the response of c-kitpos endogenous cardiac stem cells (eCSCs) to diffuse myocardial damage caused by an acute excessive dose of the synthetic beta-adrenoceptor agonist isoproterenol (ISO). Following ISO damage, eCSCs were isolated from one fourth of the CM content in just one month. The data strongly suggest that the heart has an intrinsic robust and functionally productive regenerative capacity to recombine c-kitpos eCSCs in vivo. On the other hand, all animals from the groups with 2 or 3 TAM injections (corresponding to a cumulative total loss of 25 to 35% of CMs, respectively) survived and showed a significant LV dysfunction with LV dilation and reduced EF from 7 to 14 days. Cardiac performance started to improve at 21 days and was completely normalized at 28 days. Importantly, in response to pure CMs, only a minority of the animals showed a positive mononucleated CMs either during development as well as in healthy or damaged adult hearts.

Purpose: To assess the endogenous cardiac capacity for CM replenishment after incremental amounts of pure CM death.

Methods: Transgenic mice mutant to express a Tamoxifen (TAM) inducible membrane-estrogen-receptor linked Cre recombinase (mER-Cre-mER) under the myh6 promoter were crossed with transgenic mice mutant in the RosA 26 (R26R) locus encoding a membrane-targeted green fluorescent protein (mG or GFP) after Cre (R26) locus a membrane-targeted tandem Tomato dimer (mT) prior to Cre expression in the ROSA cell fate mapping.

Conclusions: For the first time, we identified that activated eCSCs had a greater regenerative capacity than quiescent eCSCs. These miRs regulated a specific network of cell-cell communication and stemness genes as they were all either CD45+ or CD31 + cells. When gating the low expression in several pro-cell survival or cardiopoietic factors (IGF-1, HGF, peptide, VEGF-A) in activated eCSCs. MicroRNA array expression analysis of activated eCSCs identified up-regulation of mir-21*, mir-2 of 

ISO eCSCs were in S-phase or G2/M-phase, compared with a very small fraction of total c-kitpos bone marrow cells were recombined to express eGFP. The same high level of recombination was shown in c-kit+ cells of the known c-kit expressing cells even though at an expected different rate proportional to their expression in the adult life. In the adult myocardium for cell fate mapping.

Conclusions: Cre recombination in c-kitCreERT2 knock-in mice is dependent on c-kit expression. Cells that express high levels of c-kit are efficiently recombined. However, true c-kit-low eCSCs are only minimally recombined. Thus, using this fate map strategy, it is impossible to appropriately quantify the cardiac cell progeny, and CMs in particular, of c-kit+ eCSCs in vivo.

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Conclusions:
NF-κB and eNOS were highest in groups 1 and 5, lowest in group 2, and significantly
promoted the healing of mouse infarcted hearts.

Methods: We isolated CSCs from discarded specimens of transplanted hearts and
SVFs from vein leftovers of CABG patients. Cell surface phenotype, secre-
vice, molecular interactions and paracrine effects were investigated in vitro. To
assess the regenerative ability, CSCs, SVFs or CSCs+SVFs (300,000 cells of each
type/heart - n=6 mice per group) were delivered in the peri-infarct of a mouse
model. Sham (n=3) and Vehicle-injected mice (n=6) were used as control.
Mice were given 5-ethyl-2'-deoxyuridine - EdU (i.p., 500μg) every 2 days
over the recovery period and sacrificed 14 days post-MI.

Results: In vitro, SVFs and CSCs exhibit a similar mesenchymal phenotype
(CD44/90/105) and secrete similar paracrine factors (HGF, VEGF, FGF, SDF),
attesting to their potential for transplantation. In vivo, the addition of SVFs
imparted a molecular interaction involving DPP-4/SDF turnover and additively
ameliorated significant differences in LVEF (n=4, p<0.05 vs single cells). First, we show that DFF
modulation occurs post-transcriptionally and possibly involves DPP-4 (dipeptidyl
peptidase-4) inhibitors. Soluble DFF-4 levels are reduced in co-cultures vs CSC-single cultures
(n=4, p<0.05), with DFF-4 mRNA being downregulated in CSCs exposed to SVP-conditioned media (n=4, p<0.05 vs
control).

Cell transplantation similarly improved cardiac function at 14 days post-MI com-
pared to vehicle, with no additive effect by combined therapy. Importantly, only
when cells were delivered together in the recipient heart, we observed a reduc-
tion of the infarct scar (p<0.05 vs vehicle). Both cell types and their combination
were able to protect cardiomyocytes (CM) from apoptosis and recruit endogenous
CSCs, with no additive effect given from the combined therapy. EdU incorporation
studies showed that CSCs stimulate CM proliferation while SVFs promote endothelial cell
proliferation compared to vehicle. Interestingly, only CSC+SVF therapy induced the
phosphorylation of arterioles smooth muscle cells.

Conclusion: In vivo CSCs and SVFs cooperate to improve the healing of in-
farcted hearts in a complementary fashion. These data suggest that combinatory
cell therapies may improve cell therapy efficacy, opening novel opportunities
for cardiac repair.

P3567 | BENCH
Quantitative analysis of cardiomyocyte contractile kinetics and force
distribution using an automated morphologic similarity measure
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Background: Stem cell-derived cardiomyocytes are increasingly used for study-
ing cardiac physiology and pathophysiology in vitro. However, current techniques
for functional assessment of CMs are optimized for mature myocardial cells and
are not well suited for the study of stem cell derived CMs that lack distinct cellular
cues and well-developed sarcomeres.

Purpose: To develop an unbiased automated methodology for the quantitative
assessment of force generation and contractile kinetics of cardiomyocytes at dif-
ferent developmental states concurrently with other physiological measures such
as intracellular calcium cycling in response to isoproterenol and

Methods and results: We have performed pairwise statistical similarity mea-
sures between all frames in a video of human stem cell-derived cardiomyocytes
contracting on a flexible substrate. We then generated a similarity matrix that rep-
resents a comprehensive assessment of change in cell morphology over time to
calculate the contraction kinetics. In adult cardiomyocytes this approach produced
contraction curves highly similar to those generated by traditional edge detection
technology with a Pearson's correlation coefficient of 0.98. We further calculated the
contractile force generated during myocyte contraction with a novel mechan-
ical model and IPS-produced this approach based on extending fluorescent microsphere
based traction force microscopy. Both methods yielded highly similar results with
a mean difference in peak force of 0.01 μN (95% limits of agreement −0.05μN to
0.03μN). Addition of the cardiac indicator Fluo-4 allowed for the detection of sub-
tle changes in contractility and calcium cycling in response to isoproterenol and
verapamil. Likewise, the addition of the membrane potential dye Fluo-4 allowed for
the assessment of the cardiotoxicity of doxorubicin. We show that characteriza-
tion of contractility and action potential together detected more variation in peak

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amplitude than action potential alone after application of dofetilide (29.4% vs. 1.3%; p=0.0084).

Conclusions: We have developed a highly versatile novel methodology for the simultaneous quantitative analysis of contraction kinetics, force generation, calcium cycling, and electrophysiology in human cardiomyocytes. This novel approach has the potential for application in the study of cardiac disease, drug discovery and drug cardiotoxicity screening.

Acknowledgement/Funding: (NH/NHLBI) U01HL100408-01 and NIH/NHLBI 1K08 HL091209, E Dekker Student Scholarship Dutch Heart Foundation

Mitrval valve disease

P3568 | BEDSIDE
Echocardiographic and clinical long-term outcome of real world patients undergoing percutaneous edge-to-edge mitral valve repair
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Background: There is no data on long-term echocardiographic follow-up regarding the durability of mitral regurgitation (MR) in real-world patients undergoing percutaneous edge-to-edge mitral valve repair (pMVR).

Methods and results: From August 2009 to 2011, 137 consecutive patients with severe MR were treated with pMVR in two high volume university centers. Mitral regurgitation could be successfully reduced to grade ≤2 in 84.7% of patients (116/137 patients). In 2014 we scheduled all patients for clinical and echocardiographic examinations. Long-term follow-up (up to 5 years) revealed a mortality rate of 36.5% (50/137 patients). Twenty patients (14.6%) received a concomitant CABG and 10 patients underwent conventional MVR. Clinical follow-up (>3 years after pMVR) was achieved in 91.8% (87/93 patients, median follow-up 48 months). Of these, 34 patients presented with NYHA functional class ≤II (64.2%). In survivors with available long-term echocardiographic follow-up (>3 years after pMVR, 53/73 patients, median echocardiographic follow-up of 47 months), MR grade ≤2 was present in 86.8% of patients (46/53 patients). More detailed echocardiographic parameters will be presented at the congress.

Conclusions: In patient undergoing pMVR between 2009 and 2011 long-term echocardiographic follow-up showed a good long-term durability of the intra-procedurally induced reduction of MR in survivors. Furthermore, the majority of survivors presented with NYHA functional grade ≤II. Hence, pMVR represents an alternative non-surgical approach reducing symptoms and the grade of MR sustainable in selected real-world patients with severe symptomatic MR.

P3569 | BEDSIDE
Prevalence of severe mitral regurgitation eligible for transcatheter edge-to-edge mitral valve repair
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Background: Transcatheter edge-to-edge mitral valve (MV) repair of advanced mitral regurgitation (MR) is a non-surgical treatment option in inoperable and high-risk patients. It is unknown how many patients are potentially eligible for transcatheter edge-to-edge MV repair since several anatomical prerequisites of the MV apparatus have to be met for optimal treatment results. We assessed the prevalence of MR qualifying for transcatheter edge-to-edge MV repair in our institution.

Methods: Using a novel clinical Data Ware House we searched for all patients attached to our Department of Internal Medicine from 01/2008 to 01/2012 (prior to the timepoint when transcatheter edge-to-edge MV repair became available) with significant MR and aged ≥18 years. The current status of their treatment regime and eligibility for transcatheter edge-to-edge MV repair was assessed and re-evaluated according to current guidelines and echocardiographic criteria.

Results: The search of electronic medical records amongst 43,690 patients identified 331 patients with significant MR who had undergone echocardiographic assessment at our institution. Of these, 125 (38%) received MV surgery and 206 (62%) medical therapy only. Most patients not undergoing surgery had functional MR (70%). After evaluating echocardiographic data of medically treated patients (n=206), 81 (39%) of those were potential candidates for transcatheter edge-to-edge MV repair, and 90 (44%) died during the median follow-up time of 23 [7,23] months.

Conclusion: A large fraction of patients with significant MR but not operated was detected. Medically treated patients had a bad prognosis and about 40% of these were potential candidates for transcatheter edge-to-edge MV repair.

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P3570 | BEDSIDE
Influence of ischemic and nonischemic cardiomyopathy on mortality and regurgitation after MitraClip results from the Dresden MitraClip-registry
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Aims and background: Severe mitral regurgitation (MR) is the second most common valvular heart disease after aortic stenosis. The MitraClip is an interventional percutaneous method of repair of the mitral valve that mimics the surgical edge-to-edge Alfieri technique through mechanical coaptation of the mitral leaflets. Through surgical risk mitral valve replacement (MVR) is the treatment of choice. The purpose of this MitraClip-registry is to compare the safety, clinical efficacy, and in-hospital and short-term survival outcomes of MitraClip implantation in patients with severe MR of ischemic or nonischemic etiology.

Methods and results: From July 2012 to January 2015, a total of 140 patients were included in the Dresden MitraClip Registry. In presence of a positive vote from ethics commission, all patients gave informed consent to the procedure and authorized data collection. Severity of MR was examined using 3D-TEE (phillips). Decision upon MitraClip procedure was made in the interdisciplinary heart team individually. Patients follow up was 3 and 6 months after successful procedure with transorhalar and transesophageal echo (TTE, TEE) and clinical examination.

Baseline characteristics showed a mean age of 78 years (57–97 years), with an ejection fraction of in the ischemic cardiomyopathy group (69%). Of all patients, 64 (46%) suffered from ischemic cardiomyopathy (ICM), with a mean left ventricular ejection fraction (LVEF) of 30.8% and elevated Euro-2- score of 21%. Patients with dilative cardiomyopathy (DCM) and degenerative mitral valve disease (DMD) had LVEF of 52.3% and decrease Euro-2- score in the two groups were 15 and 13%. Implantation of the MitraClip was successful in 96% of patients. Procedural complication rate was low with 0.7% for stroke and myocardial infarction and the 6 month mortality rate was 23.9% for patients with ischemic cardiomyopathy (vs. 14.9% in patients with DCM and 5.8% in patients with DMR, respectively).

Conclusion: Percutaneous mitral valve repair with the MitraClip system is feasible in patients with ischemic or nonischemic cardiomyopathy with similar procedural results. Two times mortality was two times higher in patients with ICM, especially in those with severely reduced LVEF <30%. A prospective reassessment with transthoral and transesophageal measured ejection fraction and log. EuroScore2 helps to identify patients with high mortality in this community of surgical high risk patients.

P3571 | BEDSIDE
New cutoffs are needed for the assessment of functional mitral regurgitation severity using three-dimensional echocardiography
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Background: Two-dimensional echocardiography (2DE) and 2D PISA method have limitations for the assessment of the functional mitral regurgitation (FMR) severity because of a dynamic range of regurgitant orifice (EROA) and PISA during the cardiac systole. The assessment of MR severity using three-dimensional echocardiography (3DE), which determines the true volume of the PISA, enables itself as a more accurate method for measuring the EROA and the regurgitant volume (RVol).

Purpose: To assess the agreement between the severities of the FMR determined using 2DE and 3DE PISA analysis.

Methods: 25 pts (age 58±13 years, 18 males with mild, moderate and severe FMR underwent 2DE using a commercially available system (Acuson SC2000, Siemens, CA). A 3D color full-volume of the MR jet was separately recorded at baseline 30–40 cm/sec, encompassing the PISA throughout the regurgitant period. The severity of FMR was firstly assessed accordingly to current guidelines (using 2DE analysis, 44% of the patients had mild, 25% moderate, and 31% severe FMR). Using 2DE analysis, 44% of the patients had mild, 25% moderate, and 31% severe FMR. Using 3D PISA, EROA and RVol were measured offline at each frame of the MR flow, using dedicated software package (ePISA PISA, SC2000, Siemens, CA). Peak and mean 3D PISA during the cardiac systole, EROA and RVol were also measured. The severity of the FMR was then classified as mild, moderate and severe, using the same current guideline cut-offs for EROA and RVol.

Results: 2D EROA showed good correlation with both peak and mean 3D EROA (r=0.90 and r=0.80, p<0.001), whereas 2D RVol showed lower correlation with peak and mean RVol (r=0.84 and r=0.64, p<0.001). According to the standard 2D analysis, 44% of the patients had mild, 25% moderate, and 31% severe FMR. Using 3D peak PISA and mean cut-offs, 6% of the patients had mild, 19% moderate, and 75% severe FMR, with a low inter-rater agreement with the 2DE analysis (k=0.24, CI 0.03–0.42). Using 3D mean PISA, 63% of the patients had mild, 25% moderate and 8% severe FMR, with a moderate inter-rater agreement with the 2D analysis (k=0.60, CI 0.26–0.92).

Conclusions: 3D PISA analysis reclassifies the severity of the MR when using current cut-offs for FMR, and varies greatly with the method used (mean or peak
the all-cause mortality was comparable between patients with DMR and FMR.

Purpose: We aimed to clarify the difference in the characteristics and long-term outcomes of patients underwent mitraclip between DMR and FMR.

Method and result: In a total of 206 consecutive patients after the mitraclip implantation, 87 patients (42%) had DMR, whereas 119 patients (58%) had FMR. Male gender was more common in FMR. Patients with DMR were older than those with FMR. The prevalence of hypertension, diabetes mellitus, and chronic kidney disease was comparable between the two groups. Baseline MR severity and New York Heart Association (NYHA) class was similar between the two groups. N-terminal pro-B-type natriuretic peptide (NT-pro BNP) was still higher in FMR patients at 6 months and 12 months after the procedure, MR severity and NYHA class similarly improved in patients with DMR and FMR. However, NT-pro BNP was still higher and LVEF was lower in patients with FMR. Logistic euro SCORE was comparable between the two groups. Six months and 12 months after the procedure, MR severity and NYHA class similarly improved in patients with DMR and FMR. However, NT-pro BNP was still higher in FMR patients at 6 months and 12 months after the mitraclip implantation. Kaplan–Meier curves and the log-rank test revealed that the all-cause mortality was comparable between patients with DMR and FMR.

Conclusion: Despite the various differences of clinical characteristics, the improvements of MR severity and heart failure symptom, and the long-term survivals after the mitraclip implantation were comparable between DMR and FMR.

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P3572 | BEDSIDE
Comparing the clinical characteristics and long-term outcomes of patients undergoing MitraClip with degenerative versus functional mitral regurgitation

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Background: Percutaneous edge-to-edge mitral valve repair by using the mitraclip system is a new treatment option for severe mitral regurgitation (MR) in patients whose condition is inoperable or who are at high conventional operative risk. MR has two different etiologies; degenerative MR (DMR) and functional MR (FMR). The clinical presentations and prognosis after the mitraclip implantation in DMR and FMR patients still remain unclear.

Purpose: To compare the clinical characteristics and long-term outcomes of patients undergoing mitraclip between DMR and FMR.

Method and result: In a total of 206 consecutive patients after the mitraclip implantation, 87 patients (42%) had DMR, whereas 119 patients (58%) had FMR. Male gender was more common in FMR. Patients with DMR were older than those with FMR. The prevalence of hypertension, diabetes mellitus, and chronic kidney disease was comparable between the two groups. Baseline MR severity and New York Heart Association (NYHA) class was similar between the two groups. N-terminal pro-B-type natriuretic peptide (NT-pro BNP) was higher and LVEF was lower in patients with FMR. Logistic euro SCORE was comparable between the two groups. Six months and 12 months after the procedure, MR severity and NYHA class similarly improved in patients with DMR and FMR. However, NT-pro BNP was still higher in FMR patients at 6 months and 12 months after the mitraclip implantation. Kaplan–Meier curves and the log-rank test revealed that the all-cause mortality was comparable between patients with DMR and FMR.

Conclusion: Despite the various differences of clinical characteristics, the improvements of MR severity and heart failure symptom, and the long-term survivals after the mitraclip implantation were comparable between DMR and FMR.

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P3573 | BEDSIDE
Transfemoral closure of mitral paravalvular leak in the presence of metallic aortic valve

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Background: The Use of retrograde femoral access to close Mitral Paravalvular Leakage (MPVL) in patients with the combination of aortic and mitral metallic prostheses has considered contraindicated.

Purpose: The aim of this study was to assess the safety and feasibility of Percutaneous Closure of MPVL in patients with double aortic and metallic prostheses.

Methods: Consecutive patients with double prosthesis (DP) who underwent percutaneous MPVL closure in our institution were included. Anterograde and retrograde approach consisting of crossing the wire across the aortic prosthesis in order to accede and cross the pervalvular mitral leak were used. Arterious venous loop (AVL) were also performed in all cases but one. The devices used in all interventions were Amplatzer Vascular Plug III. Immediate and mid-term follow-up results were analyzed.

Results: From February 2009 to December 2014, 56 patients underwent MPVL in our institution. Twenty five patients (44.6%) had double prosthetic mitral and aortic valve (DP). Mean age was 69±11. 40% were male. The mean clinical follow-up was 416.5±323.1 days. Retrograde approach with AVL was performed in 17 patients (38%). All procedures were hemodinamically well tolerated. Technical success rates were 88%, (2 patients needed two procedures). One patient had device embolization that was punctaneously captured and a second device was successfully implanted in the same procedure and 1 patient needed emergency surgery due to disc intolerance. At follow-up 50% of the patients presented significant NYHA functional class improvement. Seven patients (28%) died during follow-up due to persistent cardiac failure.

Conclusion: Percutaneous Closure of MPVL in patients with double aortic and mitral prosthesis can be done safely considering few tips are taking into consideration during the procedure.

P3574 | BENCH
Non-invasive ultrasonic chordal cutting

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Objective: Chordal cutting targeting leaflet tethering has been described to improve the efficacy of annuloplasty during ischemic mitral regurgitation surgery. Histotripsy is a novel ultrasonic based technique for tissue fragmentation through the cavitation generated at the focus of a very intense ultrasonic pulse. In this study we investigate the feasibility of using histotripsy for chordal cutting to avoid cardiopulmonary bypass and invasive surgery in infarcted heart.

Methods: Experiments were performed in vitro in explanted sheep heart (N=5) and in vivo in sheep beating heart (N=3, 40±4 kg). In vitro, the mitral valve basal chordae was removed, fixed on a holder in a water tank. The ultrasound pulses were emitted from the therapeutic device (1-MHz focused transducer, pulses of 8us duration, peak negative pressure of 17 MPa, repetition frequency of 100Hz) placed at 64 mm from the valve. We performed 500 pulses in each location and systolic chamber was applied on the thorax cavity was filled out with water. We analysed MV coaptation and chordae by real time 3D echocardiography before and after chordal cutting. The animals were sacrificed at the end of the procedure, for postmortem anatomical exploration to confirm the section of the basal chordae and the integrity of the remaining marginal chordae.

Results: In vitro, all the basal chordae were completely cut. The mean procedure time was 6 (±3) minutes. The thickness of the chordae was the main criteria affecting the duration of procedure. In the sheep, central basal chordae of anterior leaflet were completely cut. The mean procedure time was 19 (±9) minutes. By echography, the sectioned chordae was visible and no mitral valve prolapse was found. All the postmortem anatomical exploration of hearts confirmed the section of the basal chordae. No additional lesions were objectified.

Conclusions: Non invasive ultrasonic histotripsy succeed to cut mitral valve basal chordae in vitro and in vivo in beating heart. Future investigation will be needed to test this noninvasive technique on its ability to decrease ischemic or functional MR secondary to leaflet tethering. If positive, this will open the door of completely noninvasive technique for MV repair especially in case of functional MR.

AORTIC VALVE INTERVENTION

P3575 | BEDSIDE
Blood culture-negative infective endocarditis due to Tropheryma whipplei - biomarker suggest intestinal barrier dysfunction and systemic immune activation

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Background and aims: Blood culture-negative infective endocarditis (IE) is associated with a high mortality and morbidity. However, initial diagnosis is frequently challenging in these patients and a special diagnostic workup is necessary to identify causing microorganisms. Recent data suggest that Tropheryma whipplei, the infectious agent of Whipple's disease, is the most commonly found pathogen associated with culture-negative IE. The pathogenesis of IE due to intracellular microorganisms is still a matter of debate. Since chronic inflammation may promote endothelial damage and therefore IE, the aim of the present study was to evaluate gut derived microbial translocation as a chronic immune stimulus in the pathogenesis of Tropheryma whipplei-induced IE (TWIE), a rare and life threatening (n=15) and disease controls (n=13).

Methods: Markers of microbial translocation and systemic immune activation, bacterial derived Lipopolysaccharide (LPS), endotoxin core antibodies (EndoCAb), LPS binding protein (LBP) and soluble CD14 (sCD14), were determined in the serum of TWIE patients (n=6) at time of diagnosis and after antimicrobial treatment and compared to healthy (n=15) and disease controls (n=13).

Results: The diagnosis of TWIE was based on the analysis of cardiac valve tissue and serum cytokines and/or histological methods and the absence of gastrointestinal symptoms. We found significantly increased levels of LBP and sCD14 in TWIE patients as compared to healthy controls (LBP-p=0.0161, sCD14-p=0.0019). Values of sCD14, that did not differ from patients with intestinal barrier dysfunction (p=0.3356), remained still high after therapy induction (p=0.0222), indicating sustained immune response. Low levels of LPS (p=0.04) in the context of high EndoCAb titres (p=0.0015) illustrate a long lasting exposure to endotoxin and prolonged immune activation.

Conclusion: An increased gut derived microbial translocation may promote chronic systemic inflammation favouring endothelial damage and therefore the
development of TWIE. In TWIE patients, markers of microbial translocation should be considered in the diagnostic and monitoring workup.

P3576 | BEDSIDE
Profile and outcome of patients with left-sided infective endocarditis with surgical indication who did not undergo surgery
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Introduction: In most of the series, around 60% of patients with left-sided infection underwent surgery during the index hospitalization or remained infected for more than 40%, some have an uncomplicated clinical course and do not have surgical indication and others should be operated but intervention is not performed for different reasons. This last group has not been systematically studied.

Objectives: To describe the main features of non-operated left sided infective endocarditis patients despite having surgical indication, and to look for their predictors of bad prognosis.

Methods: Multipurpose registry including all definite episodes of left-sided infective endocarditis admitted in three tertiary care hospitals from 1996 to 2014. We considered as surgical indications heart failure, uncontrolled infection and prevention of embolisms. We described the profile of patients with surgical indication who did not undergo surgery and performed a multivariate logistic regression analysis to determine their predicting factors of mortality.

Results: Among 1101 patients with left-sided infective endocarditis, 273 had surgical indication but were not operated (25%). Mean age was 67±14 years, 60% were male. Comorbidities were frequent: 27% chronic anemia, 20% chronic renal failure, 27% diabetes and 14% cancer. Staphylococcus aureus was the most frequent microorganism (30%), followed by coagulase-negative Staphylococci (18%) and enterococci (15%). On echocardiogram, vegetations were detected in 88% of the patients, perianium complications in 23% and moderate or severe valve insufficiency in 63%. Clinical course was complicated with heart failure in 68%, renal failure in 61%, stroke in 16%, septic shock in 31%. In hospital mortality was extremely high (53%). Staphylococcus aureus infection (OR 3.8, 95% CI 2–7.4, p<0.001), referral from other centers (OR 2.0; 95% CI 1.1–3.6, p=0.021), Streptococcus viridans (OR 0.2; 95% CI 0.1–0.6, p<0.001), renal failure (OR 2.3; 95% CI 1.3–4.3, p=0.006) and septic shock (OR 3.1; 95% CI 1.1–8.6, p<0.028) were the independent risk factors for hospital mortality in these patients.

Conclusions: One quarter of patients with left-sided infective endocarditis with surgical indications did not undergo surgery in our series and had a dismal short-term prognosis. Staphylococcus aureus, referral patients, renal failure and septic shock increased their mortality whereas Streptococcus viridans protected them.

P3577 | BENCH
In vivo long-term serial tracking of living mesenchymal stem cells seeded on bioengineered artificial pulmonary valve scaffold in sheeps
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Background: Tissue engineered heart valve (TEHV) with adaptive self-growing efficiency: 55%. Static cultivation of scaffold with the PET-MSCs led to successful ingrowth of the PET-MSCs into the scaffolds, (average cell number of 3x105 with efficiency: 55%).

Methods: Decellularized TEHV scaffolds were seeded with cultured MSCs transplanted with PET-reporter gene (PET-MSCs) using Lipofectamine (transfection efficiency: 55%). Static cultivation of scaffold with the PET-MSCs led to successful ingrowth of the PET-MSCs into the scaffolds, (average cell number of 3x105). In vivo long-term serial tracking of living mesenchymal stem cells (MSC) on the TEHV via serial in vivo non-invasive PET-CT imaging.

Results: After the injection of 10 MBq/kg [18F]-FBHG 3h, 6h, 24h and 3 weeks after valve implantation.

Conclusions: For quantification of survived cells in the TEHV post implantation, vials containing 5x104, 2x105 and 4x105 pET-MSCs were mixed with PET tracer for 1h. After wash-out of the non-bound tracer, the vials were in vitro scanned with PET-CT.

Results: In vitro PET-CT image of the TEHV showed the accumulation of the seeded cells at the base of the leaflets (Figure). PET-CT images of sheep’s heart after injection of the TEHV demonstrated a clear signal of PET-MSCs, with a mean estimated number of living cells of 1.2x106 with no meaningful decrease of cell number at 6h or 24h. Three weeks after valve implantation, PET-CT image showed living PET-MSCs in the TEHV (estimated cell number 6x105). Immunofluorescence at 1-month follow-up showed alpha-smooth muscle actin positivity on valve surface of TEHV.

Conclusion: This is the first report on serial non-invasive in vivo tracking of long-term survival of MSCs seeded onto TEHVs and percutaneously implanted into sheep. An immunofluorescence study at one month follow-up was performed showing positive alpha-smooth muscle actin positivity on the leaflet surface of TEHV.

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P3578 | BEDSIDE
Predictive value of plasma osteopontin level as a new biomarker in patients with rheumatic heart disease
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Background: Osteopontin (OPN) is an adhesion molecule that is increased in heart failure (HF) irrespective of its underlying cause. HF is a common complication of rheumatic heart disease (RHD). The probability of using OPN as a biomarker of RHD-relates HF is unknown.

Purpose: Is to assess the role of plasma OPN as a predictor biomarker of HF in patients with RHD.

Patients and methods: A cross-sectional study included 60 RHD patients diagnosed with rheumatic aortic valve stenosis who underwent aortic valve replacement surgery by the modified Adult Treatment Panel III of National Cholesterol Education Program criteria. A total of 307/749 (40.9%) patients showed MR at baseline. Major adverse cardiac and cerebrovascular events (MACCE; including death, myocardial infarction, cerebrovascular accident, prosthesis dysfunction, and need for re-operation) were investigated.

Results: Plasma OPN level was significantly higher in patients with RHD-associated HF compared to either RHD patients (without HF) or normal control (89.3±87.6, vs. 43.4±19.0, 45.1±9.9, p<0.001 respectively). OPN cut-off value of ≥16.25 ng/mL was able to predict the presence of HF by a probability of 73.3%. OPN level is negatively correlated with left ventricular ejection fraction (r=−0.321, p=0.012).

Conclusion: Plasma OPN could be a useful biomarker for diagnosis of RHD-related HF, and it is positively correlated with the severity of HF in those patients.

P3579 | BEDSIDE
Metabolic syndrome affects outcomes of heart valve surgery
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Background: Recently, synergic effects leading to a pro-thrombotic state has been demonstrated in the contest of Metabolic syndrome (MetS), which has been implicated in both accelerated native aortic valve stenosis and progression of bioprosthetic valve degeneration.

Purpose: Aim of the present study was to assess the impact of MetS on postoperative outcomes of patients undergoing heart valve surgery.

Methods: A consecutive series of 749 patients undergoing elective first-time heart valve surgery at one institution was studied. Metabolic syndrome was diagnosed using the modified Adult Treatment Panel III of National Cholesterol Education Program criteria. A total of 307/749 (40.9%) patients showed MetS at baseline. Major adverse cardiac and cerebrovascular events (MACCE; including death, myocardial infarction, cerebrovascular accident, prosthesis dysfunction, and need for re-operation) were investigated.

Results: At a mean follow-up of 37±16 months, mortality was 19/307 (6.2%) vs. 17/442 (3.8%) in patients with and without MetS, respectively (p=0.04). At three years, freedom from MACCE was significantly poorer among patients with MetS (47.5±5% vs. 59.8±5%, p<3.82; p<0.004). Of note, the occurrence of every single component of the composite outcome “MACCE” was significantly increased among MetS patients; particularly, freedom from prosthetic valve dysfunction (because of thrombosis, endocarditis or paravalvular leak) was 82.4% in the MetS subgroup vs. 91.1% for patients without MetS (p=4.03; p=0.02).

Conclusions: MetS is associated with poorer outcomes after heart valve surgery. Given its modifiable nature, MetS should be recognized as an independent preoperative variable to identify high-risk patients and, moreover, should be corrected with lifestyle modifications and pharmacologic therapy to improve the results of valvular surgery.

P3580 | BEDSIDE
Impact of a per procedure electrophysiologic study during transcatheter aortic valve implantation
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Conduction disorders are a frequent complication after transcatheter aortic valve implantation (TAVI).
Aortic valve intervention

P3581 | BEDSIDE
Evaluating conventional surgery risk scores and the TAVI2-SCORE to predict 1-year mortality after transcatheter aortic valve implantation with a self-expandable prosthesis

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Background: Several recent studies concluded that conventional surgery risk scores are not able to accurately predict 1-year mortality after transcatheter aortic valve implantation (TAVI). Recently the TAVI2-SCORE has been developed for this purpose and showed superior predictive ability in comparison with surgery scores. However, this tool has been validated in patients treated with a balloon-expandable transcatheter aortic valve (CoreValve) system. In this study we want to evaluate the ability of conventional surgery risk scores and the TAVI2-SCORE to predict high or low mortality risk at 1-year after patients with a CoreValve prosthesis.

Methods: 225 consecutive patients (80.4±7.4 years, 54.7% female) with severe symptomatic aortic stenosis and a high surgical risk according to the Heart Team underwent TAVI using a CoreValve system. Demographic, clinical, biochemical, echocardiographic and angiographic data were collected to calculate logistic EUROSCORE I, EUROSCORE II, STS-score and TAVI2-SCORE. Differences between groups (alive vs. dead at 1 year) were compared with the Student T-test, Mann Whitney U-test, Chi Square or Fisher’s Exact test as appropriate. The cumulative survival rate according to high vs. low scores was assessed with the Kaplan-Meier method.

Results: 1-year all-cause mortality was 18.4%. Patients who survived at 1 year had lower STS-scores than patients who died (median (Q1-Q3): 4.61% (3.33–7.38) vs. 6.03% (3.66–10.54), p<0.03), but there was no statistical difference between patients who died stratifying logistic EUROSCORE I (<20% vs. >20% (81.1% vs. 82.0%, p=0.9) and EUROSCORE II (<8% vs. >8% (81.3% vs. 81.8%, p=0.9). Furthermore, Kaplan-Meier analysis showed no significant difference in survival between patients with a TAVI2-SCORE <3 vs. TAVI2-SCORE >3 (82.2% vs. 77.1%, p=0.46).

Conclusions: A high STS-score was predictive for worse 1-year survival after TAVI in contrast with logistic EUROSCORE I and EUROSCORE II. The newly developed TAVI2-SCORE did not discriminate high vs. low mortality risk at 1 year in our cohort of patients treated with a CoreValve system.

P3582 | BEDSIDE
Impact of mitral regurgitation in mortality of patients undergoing transcatheter aortic valve implantation

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Introduction: Among patients undergoing transcatheter aortic valve implantation (TAVI) for the treatment of symptomatic severe aortic stenosis, it is currently under investigation whether the presence of mitral regurgitation (MR) has a significant impact on mortality.

Methods: We evaluated the contribution of MR in all-cause mortality of patients undergoing TAVI. Clinical and echocardiographic data from patients that prospectively underwent TAVI in our center were retrospectively examined. Patients were divided into two groups: with none/mild and with moderate/severe MR before the procedure. After clinical follow-up, statistical analysis of all-cause mortality events was performed with the Kaplan-Meier method and results were further evaluated for with Cox proportional hazard analysis.

Results: We included 119 patients in the analysis. Seventy-six patients (63.9%) were classified to none/mild and 43 (36.1%) to moderate/severe MR. The median follow-up time was 23 months (mean 22±13 months). During follow-up period the cumulative probability for all-cause mortality was significantly different between two groups (14.5% for none/mild versus 34.9% for moderate/severe MR, p=0.006). Independent predictors of mortality were moderate/severe MR [HR: 2.78, 95% CI (1.09, 7.03), p=0.032] and low stroke volume index [HR: 5.1, 95% CI (2.19, 12.05), p=0.001]. Results were independent to low ejec tion fraction (EF <40%) [HR: 1.03, 95% CI (0.362, 2.93), p=0.957].

Conclusion: Patients with symptomatic severe aortic stenosis and moderate/severe MR before TAVI had increased mid-term risk for mortality in comparison to patients with none/mild MR, irrespectively to EF. Low flow state contributed to mortality independent to MR degree.

P3583 | BEDSIDE
Post-operative first degree atrio-ventricular block as a new predictor of complete atrio-ventricular block or sudden death after balloon-expandable transcatheter aortic valve implantation

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Background: Many studies have described predictive factors of permanent pacemaker implantation (PPI) after transcatheter aortic valve implantation (TAVI). However, pacemakers' indications may vary among centers and are not yet well established in this setting. True predictors of atrio-ventricular block (AVB) after TAVI still need to be assessed.

Purpose: We aimed to evaluate the true predictors of AVB following TAVI, using clinical follow-up and pacemakers' memories.

Methods: Between January 2011 and November 2013, 213 consecutive patients without previous PPI underwent TAVI with a SAPIEN XT balloon-expandable valve using femoral approach, at our institution. All patients underwent continuous cardiac rhythm monitoring at least 24 hours after TAVI. Electrocardiogram (ECG) was performed the following 2 days after TAVI, and 1 month later. Median clinical follow-up was 13 months, and 8 months for pacemaker interrogation. Multivariate analysis was performed including the most relevant ECG criteria.

Results: Complete AVB occurred in 4 patients (1.9%) during TAVI, in 7 patients (3.3%) the days after, and in 11 patients (5.2%) after discharge. Sudden death occurred in 8 patients (3.7%) during the follow-up period. Pacemaker was implanted in 26 patients. Twenty of them (77%) recorded complete AVB episodes or >2% ventricular pacing, despite the use of a minimizing ventricular pacing algorithm. As shown in the table below, complete AVB or sudden death occurred significantly more often in the patients with preexisting right bundle branch block (RBBB), in those with new persistent (>48h) left bundle branch block (LBBB) after TAVI, and those with first degree AVB after TAVI.

Results of the multivariate analysis

<table>
<thead>
<tr>
<th>No complete AVB, and no sudden death (%)</th>
<th>Complete AVB or odd ratio (95% CI)</th>
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</thead>
<tbody>
<tr>
<td>Preexisting RBBB 5 (8) vs 20 (75)</td>
<td>0.14 (0.04–0.49)</td>
</tr>
<tr>
<td>New persistent LBBB 14 (8) vs 85 (68)</td>
<td>10.1 (2.46–41.67)</td>
</tr>
<tr>
<td>Complete AVB after TAVI 34 (16) vs 179 (84)</td>
<td>3.49 (1.08–11.24)</td>
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Conclusions: Our findings confirmed preexisting RBBB and new persistent LBBB as predictors of AVB following TAVI. We also demonstrated here for the first time, first degree AVB was an independent predictive factor of severe conduction disorders after TAVI. This has important implication for selecting the appropriate patients for PPI following TAVI.

P3584 | BEDSIDE
Impact of diabetes mellitus and hemoglobin a1c on patient outcomes following transcatheter aortic valve implantation

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Background: Transcatheter aortic valve implantation (TAVI) is an alternative to surgery for patients with symptomatic severe aortic stenosis who are inoperable or in a high operative risk. The incidence and prognostic impact of diabetes mel-
litus (DM), especially insulin treated, on short- and mid-term outcomes following TAVI remain to be defined.

**Purpose:** The aim of our study was to evaluate the clinical characteristics and the impact of DM status on the updated valve academic research consortium-2 (VARC-2) defined outcomes of TAVI, as well as to stratify patients outcomes according to their initial HBA1c levels.

**Methods:** In the present study, 586 consecutive patients who underwent TAVI at our institutions were enrolled and stratified according to DM status. All-cause mortality at 30 days or in hospital and at follow-up was the primary end point, whereas periprocedural complications, rates of myocardial infarction, stroke, and reinterventions at follow-up were the secondary ones.

**Results:** In all, 586 patients were enrolled: 348 (59%) without DM and 238 (41%) with DM. Thirty-day mortality was not significantly higher in patients with DM compared with patients without diabetes (3.3% vs. 2.9% p=0.974). Bleedings, vascular complications, post procedural acute kidney injury, and periprocedural strokes were not significantly different in the two groups. In a subanalysis of DM patients, complications were not significantly different in patients with orally treated DM compared to insulin-treated DM. At 1 year follow-up, patients with DM had a non-significantly higher mortality rate (17.6% vs 12.3%; p=0.114) if compared with patients without diabetes. In order to define the prognostic power of HbA1C among these patients, the cohort was divided into 3 groups according to HbA1C levels (<5.7, 5.7–6.4, >6.5). HR for HbA1C >6.5 was 2.571, p=0.033 (CI 95% 1.077–6.136) compared with HbA1C <5.7. Multivariate Cox regression analysis revealed that DM was not independently correlated with death.

**Conclusions:** History of DM does not significantly effect rates of complications in patients who underwent TAVI, however a less controlled disease as manifested by elevated HbA1C may be associated with increased mortality.

**AORTIC VALVE DISEASE**

**P3585 | BEDSIDE**

Rapid progression of mild to moderate aortic stenosis in patients with end stage renal disease

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**Background:** We aim to explore progression of mild to moderate AS in ESRD confirmed by TTE.

**Methods:** A total of 32 patients (23 males, 73±9.6 years) of ESRD on hemodialysis (mean duration: 7.1±5.6 years) with mild to moderate AS were enrolled. Propensity score matching was done to select age, sex and initial AS severity matched control (n=32). Comprehensive TTE was performed at baseline and during follow up. Severity of AS was assessed by peak systolic pressure gradient (PSPG), mean systolic pressure gradient (MSPG), and aortic valve area (AVA) calculated by continuity equations according to current guideline.

**Results:** Mean follow up duration was 32.7±24.3 months. Change of AVA and severity of AS were significantly higher (p<0.05) compared to their initial HBA1c levels (<5.7, 5.7–6.4, >6.5). HR for HBA1c >6.5 was 2.571, p=0.033 (CI 95% 1.077–6.136) compared with HbA1C <5.7. Multivariate Cox regression analysis revealed that DM was not independently correlated with death.

**Conclusions:** History of DM does not significantly effect rates of complications in patients who underwent TAVI, however a less controlled disease as manifested by elevated HbA1C may be associated with increased mortality.

**P3586 | BEDSIDE**

Significance of aortic regurgitation pre-transcatheter aortic valve implantation


**Aim:** The significance of aortic regurgitation (AR) pre-transcatheter aortic valve implantation (TAVI) implantation is unknown. The present study aimed to assess the clinical repercussion of AR in patients undergoing TAVI.

**Population and methods:** Retrospective analysis of 150 patients (mean age 81±7 years old, 43% male), from a tertiary centre prospective registry of 185 consecutive TAVI procedures, between November 2008 and November 2014. The indication for TAVI was, aortic stenosis in 145 pts and homograft dysfunction in 2 pts. AR was found in 122 (75%) pts and was moderate to severe in 33 (22%). We evaluated the clinical differences after the presentation and at a median follow up of 22 IQ [2–38] months, stratified by the presence of moderate to severe AR, using the following tests: Qui2, t-student and Mann-Whitney.

**Results:** Patients with moderate to severe AR presented more frequently with a NYHA functional class IV (21% vs 8.5%, p=0.04) and with a higher median NT-ProBNP (5190 IQ [1041–11457]pg/ml vs 1765 [795–3632] pg/ml, p=0.02). During the follow up, they showed a greater decrease of NT-proBNP (3295 IQ [962–5183] pg/ml vs 1796 [719–3749] pg/ml, p=0.02). The presence of AR was not associated with 30-day and 1-year mortality. Seven pts with moderate to severe AR developed moderate to severe leak. There was no differences between these pts and the overall patients stratified according to their initial HBA1c levels (p>0.05). The prevalence of AR was associated with moderate to severe leak without significant clinical repercussion.

**Conclusions:** Patients with moderate to severe aortic regurgitation have a worse baseline clinical status and improve more significantly after transcatheter aortic valve implantation. The presence of AR was associated with higher incidence of moderate to severe leak without significant clinical repercussion.

**P3587 | BENCH**

Effect of statins on tissue factor expression and calcification in human aortic valve interstitial cells


**Background and introduction:** It has been shown that in aortic stenosis (AS) tissue factor (TF) dependent coagulation pathway may play a significant role in the process of fibrosis and valves calcification. The valvular interstitial cells (VICs) activation and their transformation into osteoblastic phenotype seem to be the crucial step in AS development. Statins, which are very effective in atherosclerosis treatment, have been found to be generally ineffective in delaying the AS progression. The objective of this study was to evaluate the effects of statins on TF expression and calcification process in proinflammatory stimulated VICs.

**Methods:** Primary cultures of VICs derived from collagenase-digested stenotic aortic valves were stimulated with lipopolysaccharides (LPS), 200 ng/mL, peptidoglycan (PGN), 10μg/mL or TNF-α (10 ng/mL) for 8 h to induce inflammation response. Some of stimulated VICs were treated with atorvastatin (0.1–10μM) or rosuvastatin (0.01–1μM) for 24 h with or without the addition of 1mM mevalonic acid (crucial in a protein prenylation pathway). The relative mRNA expression of TF was measured by real-time PCR. Calcification was determined by alizarin red S measurement, after 14 days of cell culture in osteogenic medium.

**Results:** The relative TF mRNA expression by VICs was significantly increased by LPS, PGN and TNF-α stimulation (9.6-fold, 8.8-fold and 12.7-fold, respectively, p<0.01). Proinflammatory stimulators also increased calcification process (8.4-fold, 7.4-fold and 10.4-fold, respectively, all p<0.01). Preincubation with 1 and 10 μM atorvastatin for 24 h reduced the TF expression for all stimulators by average 24% and 89%, respectively (all p<0.01) as well as calcification process by 24% and 82%, respectively (p<0.01). Similar effects were observed for 1 and 1 μM rosuvastatin (TF mRNA reduction by 31% and 91%, respectively, and calcification by 42% and 92% respectively, all p<0.01). The lowest atorvastatin (0.1 μM) and rosuvastatin (0.01 μM) concentrations had no effects on TF mRNA expression and calcification severity. Addition of mevalonic acid totally abolished the reduction of TF mRNA expression and calcification induced by atorvastatin and rosuvastatin.

**Conclusion:** This in vitro study highlights a potential role of statins in reduction of TF expression and calcification in VICs. Although, lack of effect of statins in clinical observation may suggest that early initiation of treatment is required to reveal clinical benefit.

**Conclusion:** AS in ESRD progress in more accelerated manner compared to those without, even in mild to moderate AS. More frequent follow up than current guideline may benefit this group of patients in terms of determining timing of intervention.
P3589 | BEDSIDE
His bundle recording during and after TAVR to predict early and late atrio-ventricular block

Background: Early and late atrioventricular blocks (AVB) are frequent during trans-aortic valve replacement (TAVR) leading to permanent pacemaker (PPM) implantation. Whether His Bundle recording (HBR) during and after TAVR can predict AVB remains a matter of debate.

Objective: To correlate HV interval during and after TAVR with early and late AVB occurrence.

Methods: Between January 2013 and December 2014, HBR was assessed prospectively before balloon inflation (HV1), 15 minutes after (HV2), and at day 2 and 5 for Sapiens and CoreValve (HV3) in all pacemaker-free patients undergoing TAVR. PPM was implanted when permanent AVB persisted over day, or if paroxysmal AVB occurred within the first 5 days or if HV3 >80ms. Logistic regression was performed to assess if HVB could well predict early (from day 1 to day 5) or late (from day 5 to day 30) AVB occurrence.

Results: 86 patients aged of 85±8,2 years old, with a Euroscore of 15,3±9,3 and of whom 50 (79%) were female were recruited. Corevalve was predominantly used (59 (66%)). HV1, HV2 and HV3 were 56±19ms, 70±19ms and 63±14mrespectively. In total, 29 (34%) PPM were implanted before discharge of which 18 (19,7%) for documented AVB, 8 for prolonged HV interval and 3 for sick sinus syndrome. 12 patients (13,9%) showed AVB during follow-up after discharge, all implanted for early AVB. There was no AVB recorded in PPM for prolonged HV interval, programmed with a diagnostic atrio-ventricular conduction preservation algorithm. HV1 and HV2 were neither associated with early AVB occurrence (p=0,79 and p=0,34 respectively) nor with late AVB occurrence either (p=0,54, p=0,9 and p=0,91 respectively).

Conclusion: High degree AVB is a common finding after TAVR and can occur late. Repeated HBR before and after TAVR did not show any significant predictive value for early and delayed AVB.

P3589 | BENCH
Bisphosphonates inhibit 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. The aim of the present study was to evaluate the anticalcific action of bisphosphonates on the aortic valve in an experimental model of aortic stenosis.

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 aortic valve area (AVA). Subsequently eight animals were treated with local delivery of a mixture containing 50 μg zoledronate that was delivered on the cusps of 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 were embedded in paraffin waxes. Serial sections 4 μm thick were obtained and routinely stained with eosin –hematoxylin and von Cossia stain for calcified tissues. The stained slides were digitized using a light microscope. The files were processed for histomorphometric analysis using Image Pro Plus, version 5.1. The calculated areas were expressed as the percentage to the total area. Statistical analyses were carried out with the Statistical Package for the Social Sciences release 13.0.

Results: At baseline, all animals developed aortic valve stenosis with severe calcification. No differences regarding AVA were recorded between both groups. (21.3±1.76 vs 21.98±3.12, p=0.53). In all animals the local delivery of zoledronate and placebo mixtures was successful and uncomplcated. 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 (16.40±0.90 vs 26.92±1.80% 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 (16.40±0.90 vs 26.22±1.69% of the area, p<0.0001). No differences were observed between the cusps of the placebo group and the controls. (26.92±1.60 vs 26.22±1.69, p=0.23)

Conclusion: Local delivery of bisphosphonates on the aortic valve can inhibit calcification in an experimental model of aortic stenosis.

P3590 | BEDSIDE
Screening of GATA family reveals genetic variants in GATA5 gene in individuals with bicuspid aortic valve
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Background: Bicuspid aortic valve (BAV) is one of the most common heart diseases, with prevalence between 1–2% in the general population. It has a proposed genetic etiology and mutations have been described in several genes, as GATA5 gene, potentially involved in the development of BAV, as evidenced by the null mutant mouse.

Purpose: The aim of this study was to analyze the genetic variation of several members of GATA family in a series of patients with BAV and tricuspid aortic valve (TAV) to find variants associated with this defect.

Methods: We prospectively recruited a total of 275 individuals, 122 patients with BAV (mean age 52.7±15.8 years, 77.9% male) and 153 with tricuspid aortic valve (TAV) (mean age 72.1±9.4 years, 56.2% male), diagnosed by transthoracic echocardiography. DNA was obtained from peripheral blood and stored in the Biobank of our center. Exon 1 and following introns of GATA4, GATA6 and GATA6 genes were analyzed by Sanger sequencing. Polyhetero and SIFT programs were used to predict the pathogenic potential effect of the non synonymous variants found.

Results: We identified 7 polymorphisms in GATA4, 7 in GATA5 and 4 in GATA6 genes. Out of them, only rs41305803 (p.Asp203Gly) in GATA5 resulted significantly associated with the presence of BAV (OR=2.2; 95% CI [1.23–3.95]; p=0.024).

Interestingly, a non-synonymous variant in the contiguous amino acid was found (p.Arg202Gln). The mutated amino acid lies within one of the zinc fingers of the protein and is highly conserved in different species. Computer analyses consider this change as potentially pathogenic. Moreover, another two variants not previously described, but synonymous, each in an individual with TAV (p.H274= in GATA5 and p.Asn458= in GATA6) were identified.

Conclusion: A new GATA5 potentially pathogenic variant and a common polymorphism appear to contribute to the development of BAV. Our results support the involvement of this gene in the presence of BAV.
Conclusions:
for heart failure were consistent across all the groups. At 1-year, an improvement in the NYHA class as well as the rate of hospitalization independently predicts mortality. After adjustment, persistent severe PHy after 1 month was an independent predictor of mortality. At 1 year, the systolic pulmonary pressure (SPP) decreased of at least 10 mm Hg (severe PH: 129 patients, 13%). Patients were followed up for 1 year. As compared to patients in group 1, patients in group 2 and 3 had a higher one-year overall mortality: [HR 1.5 (1.2–3.1), p=0.01, and HR 2.3 (1.9–2.9), p=0.001, respectively].

Methods and results: 990 consecutive patients included in the CoreValve Italian Registry were included in 8 high volume centers and divided as follows: group 1, sPAP < 40 mm Hg (none/mild PHy: 376 patients, 38%); group 2, sPAP 40 to 55 mm Hg (mild-to-moderate PH: 485 patients, 49%); and group 3, sPAP < 55 mm Hg (severe PH: 129 patients, 13%). Patients were followed up for 1 year. At 1 year, the systolic pulmonary pressure (SPP) decreased of at least 10 mm Hg in 25% and 35% of the patients in group 2 and 3, respectively.

After adjustment, persistent severe PHy after 1 month was an independent predictor of mortality. At 1 year, an improvement in the NYHA class as well as the rate of hospitalization for heart failure were consistent across all the groups.

Conclusions: Moderate to severe PHy is associated with higher 1-year all-cause mortality after TAVR. The persistence at 1 month post-TAVR of severe PHy independently predicts mortality.

P5093 | BEDSIDE Baseline Mitral Regurgitation in Transcatheter Aortic Valve Replacement Patients: Does it Impact 1 Year Mortality?


Background: The prevalence of concomitant moderate to severe Mitral Regurgitation (MR) in patients with severe aortic stenosis undergoing transcatheter aortic valve replacement (TAVR) ranges from 13% to 48%. In patients undergoing TAVR, the MR is often left untreated.

Purpose: As percutaneous devices and methods to treat significant MR in high risk patients have been approved, the impact of MR in patients undergoing TAVR needs to be revisited.

Methods: Data was retrospectively analyzed from an existing database. The study cohort (total N=588) was divided into 2 groups based on the degree of baseline mitral regurgitation: Group 1 ≥ Moderate MR (n=71), and Group 2 < moderate MR (n=517). The two groups were compared in regards to baseline clinical, echo and procedural characteristics. In-hospital, 30 days and 1 year outcomes were assessed. Univariate and multivariate Cox regression analyses were performed to test the independent effects. Kaplan-Meier assessment was completed for 1-year follow-up (Figure).

Results: Patients with ≥ Moderate MR had a higher mortality rate vs. patients with less than moderate MR during the initial 30 days follow-up after TAVR (unadjusted, log-rank p=0.01). The mortality rates at 1 year follow-up were similar (HR=0.42 [0.11–1.61]). The only multivariate predictor of mortality at 1 year was baseline pulmonary artery systolic pressure. Among Group 1 62.5% and 77.7% of the patients had improved to below moderate MR at 30 days and 1 year, respectively.

Conclusions: The presence of pre-TAVR moderate to severe MR is not associated with an increase of mortality within one year of TAVR. Baseline concomitant MR in TAVR patients may not be a causal pathway for mortality within one year and may be left untreated.
tion. In the murine model of CVB3 myocarditis MDSC were found to contribute to the suppression of NK cell function early in infection, thus leading to a severe acute CVB3 myocarditis and chronic inflammatory heart disease in ABY/SnJ mice compared to C57BL/6 mice. These findings might help to develop new therapeutic immune regulatory strategies for the prevention of chronic myocarditis and, thus of dilated cardiomyopathy at later stages of the disease.

P3598 | BENCH
NOD2 knock down induces cardiobiological effects in murine Coxsackievirus B3-induced myocarditis
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Introduction: The cytoplasmatic pattern recognition receptor, nucleotide binding oligomerization domain 2 (NOD2), belongs to the innate immune system and is among others responsible for the recognition of ssRNA.

Hypothesis: So far, the role of NOD2 in viral myocarditis has not been unraveled. In this study, we examined whether or not NOD2 regulates cardiac inflammatory signaling in CVB3-induced myocarditis.

Methods: NOD2−/− and C57Bl6/j-wild type (WT) mice, acute myocarditis was induced by intrapertralional injection of 5x10e5 p.f.u. of CVB3 (Nancy strain). Seven days after infection, left ventricular (LV) function was evaluated by conductance catheter measurements. Cardiac fibrosis, inflammation, and apoptosis were determined via immunohistochemistry and real-time PCR. NOD2 was knocked-down in HL-1 cardiomyocytes by small interference (si) RNA. Subsequently, the cells were infected with CVB3 at a MOI 2 and 14 hours (h) and 24 h later collected for the analysis of CVB3 copy number, and mRNA expression or caspase 3/7 activity, respectively.

Results: NOD2−−/− vs. CVB3 mice exhibited an improved LV function compared to WT CVB3 mice. Cardiac infiltration of CD4+ , CD8+ , CD11b+ and CD68-positive cells was less pronounced in NOD2−/− vs. WT CVB3 mice. Concomitantly, NOD2−/− mice displayed a 3.9-fold, 2.9-fold, 5.3-fold, 8.0-fold, 1.4-fold, and 2.3-fold (P < 0.05) reduced LV mRNA expression of TNF-α, IL-1β, INF-γ, INF-α, RIPK2 and NLRP3 compared to WT CVB3 mice, respectively, and lower TLR4 and MyD88 mRNA expression. Furthermore, cardiac fibrosis in CVB3-infected NOD2−/− mice was less pronounced versus the infected WT group, as indicated by a 1.7-, 1.8- and 1.6-fold (P < 0.05) reduced LV mRNA expression of Col1a1, Col3a1 and TGF-β, respectively, and a decreased Col I to Col III ratio. In addition, cardiac viral load and apoptosis were 12.5-fold and 19-fold (P < 0.05) lower in NOD2−/− CVB3 versus WT CVB3 mice, respectively. In line with the in vivo data, NOD2 knockdown in HL-1 cells was associated with a decreased inflammatory response, a 1.4-fold (P < 0.05) lower CVB3 copy number, 1.2-fold (P < 0.05) reduced caspase 3/7 activity and 3.4-fold (P < 0.005) reduced TLR4 protein expression and underlying signalling.

Conclusion: NOD2 knock down improves left ventricular function and attenuates pathophysiological key mechanisms in acute CVB3-induced myocarditis mice. Modulation of NOD2 might represent a promising therapeutic strategy to treat viral myocarditis.

P3599 | BEDSIDE
Pentaglobin treatment in viral myocarditis - An update
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Background: Treatment of viral heart disease is a matter controversy

Patients and methods: We updated our treatment registry of 162 consecutive pts with biopsy proven viral myocarditis (~14 infiltrating cells/mm²) by endomyocardial biopsy (EMB). In 102 pts parvovirus B19 (63%), in 36 pts adenoviruses (22%), in 14 pts HHV6 (9%) and in 10 pts EBV (6%) were assessed by PCR as causative viral pathogens. All virus positive patients were treated with 10 g/day Pentaglobin® i. v. (enriched IgG, IgM and IgA preparation, Biogenet) at day 1 and 3. After six months all patients were reevaluated clinically, 75 patients (46%) in addition by EMB.

Results: After Pentaglobin therapy 141 pts improved by at least one NYHA class also increased exercise capacity. Mean LVEF increased from 48.7 to 61.2%, p < 0.005) independent from the respective virus. In 53 of the 75 (71%) rebiopsied pts inflammation had resolved. In all rebiopsied ADV-positive pts the inflammation had resolved and ADV-DNA had reached subthreshold levels. In Parvo B 19 myocarditis inflammation had resolved in 36 of the rebiopsied 46 pts (78%), Parvo B19 DNA viral load was substantially diminished in only 22 out of 46 pts (48%). In patients in whom both virus and inflammation were eliminated enddiastolic LV dimension had decreased and EF had improved (p < 0.001).

Conclusion: Treatment with Pentaglobin is highly effective in resolving myocardial inflammation independent of the underlying viral etiology. Virus eradication was most effective for adenoviruses less effective in Parvo B19 infection.

Acknowledgement/Funding: Cardiac Promotions Society Marburg

P3599 | BEDSIDE
Patients with acute myocarditis more often develop beta1-receptor autoantibodies than patients with post-infarction myocardial inflammation: first results from the prospective ETiCS-study
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Heart failure (HF) is a main cause of mortality & morbidity in Western countries. In the last decade evidence for a key role of autoimmunity in the pathogenesis of HF has emerged; particularly, autoantibodies targeting the cardiac beta1-receptor (beta1-aabs) are thought to be able to induce HF. However, the events triggering the formation of beta1-aabs and their effects on the course of HF are unknown.

Methods: Exposure of beta1-receptors & other cardiac antigens after inflammation or necrosis might trigger formation of beta1-aabs. Therefore, 13 European centres prospectively recruit 200 pts. with a 1st acute myocardial infarction (FAMI), and 180 pts. with acute biopsy-proven myocarditis (AmiTis) into the ETICS-study. At baseline (BL), after 3, 6, and 12 months pts. receive thorough clinical evaluation (incl. echo & cMRI’s at BL and 12 months) and blood sampling to follow the course of cardiac aabs. Activating beta1-aabs are assessed by a cell-based cAMP-assay that detects beta1-mediated cAMP-increases by measuring the change in fluorescence-resonance energy transfer (FRET) within a cAMP-sensor molecule.

Results and conclusion: The first 8 ETiCS-patients with complete follow-up (n=4 AmiTis/4 FAMI) were assessed for beta1-aabs and corresponding LVEF’s (echo). The 4 FAMI-patients did not develop aabs, but 2/4 (50%) of the AmiTis-patients developed activating beta1-aabs 6 months after cardiac injury. In beta1-aab pos.(+) patients cardiac function did not recover, whereas LVEF almost fully recovered in beta1-aab neg.(-) AmiTis (n=2/4) or FAMI-patients (n=4/4; see Figure).

FRET-activity and LVEF: AmiTis vs. FAMI

We assessed whether myocarditis rather than post-infarction inflammation trig-
TLR3, TLR4, TLR7, TLR8; p = 0.78, p = 0.05). A total of 78 pts with acute myocarditis were included (81.5% male, average value of LGE mass in this population. For the acute phase, with documentation of its highest value. We used the student t test for independent samples and the Pearson correlation and the receiver operating characteristic curve (ROC) to establish an accurate cut-off of TnI and CK for acute myocarditis. However, their role in the quantification of myocardial necrosis has not been established.

**Conclusion:** Myocardial gene expression profiling is a novel method to predict the presence of eosinophilic myocarditis in the myocardium, even without a direct histological proof. Thereby, the risk of sampling errors in small single EMB sections is reduced. Gene profiling also facilitates the discrimination of EOM from two other frequently fatal human myocardial diseases ICMG and CS, which require immediate and tailored differential therapy.

**P3601 | BENCH**

Acute myocarditis: correlation between myocardial necrosis biomarkers and delayed enhancement mass evaluated by cardiac magnetic resonance


**Background:** Cardiac magnetic resonance (CMR) with late gadolinium enhancement (LGE) has emerged as an in vivo marker of myocardial fibrosis, and is now a gold standard for myocarditis diagnosis, with an additional role in the prediction of clinical outcomes. Tropin I (TnI) and creatine kinase (CK) are myocardial necrosis biomarkers that are elevated in patients (pts) with acute myocarditis. However, their role in the quantification of myocardial necrosis has not been established.

**Purpose:** To evaluate the utility of the TnI and CK assay in the quantification of myocardial necrosis assessed by LGE mass in CMR.

**Methods:** Prospective, observational study of consecutive pts with acute myocarditis confirmed by CMR (Lake Louise criteria). All pts have performed a CMR study within 14 days from the onset of chest pain, heart failure, arrhythmias, ECG changes, with increased troponin levels. Diagnosis was corroborated by normal coronary angiography (n=44) and/or endomyocardial biopsy (n=22), and/or cardiac magnetic resonance findings (n=78). Short and mid-term survival and left ventricular function changes in fulminant versus non-fulminant acute myocarditis

E. Ammirati, M. Lilliu, M. Ciprani, A. Garasca, M. Brambatti, S. Nannoni, P. Pedrotti, F. Oliva, C.F. Russo, M. Frigerio. Niguarda Ca’ Granda Hospital, Milan, Italy

**Introduction:** Short and mid-term prognosis of acute myocarditis is still a matter of debate. Some reports suggested a better outcome in fulminant myocarditis (FM) than in non-fulminant acute myocarditis (NFAM), which seems contradictory with the dramatic presentation of FM.

**Aims:** To describe the outcome and changes over time in left ventricular ejection fraction (LVEF) in patients (pts) with FM compared with those with NFAM.

**Methods:** Between January 1, 2002 and May 31, 2014, acute myocarditis was diagnosed on the basis of clinical presentation (variable combinations of recent onset of chest pain, heart failure, arrhythmias, ECG changes, with increased troponin levels) in 102 pts. Clinical diagnosis was corroborated by normal coronary angiography (n=44) and/or endomyocardial biopsy (n=22), and/or cardiac magnetic resonance findings (n=78). Short and mid-term survival and left ventricular function changes in fulminant versus non-fulminant acute myocarditis

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**Results:** Mean age was similar (28±16 vs. 33±15 years, p=0.12), while female gender was more represented (50% vs. 13%, p<0.0001). Mean age was similar (28±16 vs. 33±15 years, p=0.12), while female gender was more represented (50% vs. 13%, p<0.0001). All but one events occurred during initial hospitalization (4 deaths, 3 heart transplantation [HTx]), one patient on LVAD under went elective HTx within one year. No patients with NFAM died or received HTx during follow-up. NFAM patients had worse outcomes compared with FM patients.

**Conclusions:** The ideal TnI cut-off of was 8.53 ng/dL, with a sensitivity of 79.31%, specificity of 89.66%, positive predictive value of 88.46%, negative predictive value of 81.25% and an overall diagnostic accuracy of 84.5%. The ideal CK cut-off was 305.5 U/L, with a sensitivity of 76.92%, specificity of 76.47%, positive predictive value of 71.43%, negative predictive value of 81.25% and an overall diagnostic accuracy of 76.7%.

**Conclusions:** In acute myocarditis pts the highest value of TnI and CK have a good correlation with the LGE mass (AUC=0.92 and AUC=0.75, respectively), allowing an easy, adequate and low cost quantification of myocardial necrosis, that can therefore have a potential prognostic value.

**P3602 | BEDSIDE**

Short and mid-term survival and left ventricular function changes in fulminant versus non-fulminant acute myocarditis

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**Aims:** To describe the outcome and changes over time in left ventricular ejection fraction (LVEF) in patients (pts) with FM compared with those with NFAM.

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**Results:** Mean age was similar (28±16 vs. 33±15 years, p=0.12), while female gender was more represented (50% vs. 13%, p<0.0001). Median follow-up was 880 days (259–1667). Kaplan Meier survival curves showed a significantly lower transplant-free survival in FM than in NFAM (78%vs.100%, log-ranked p<0.0001). All but one events occurred during initial hospitalization (4 deaths, 3 heart transplantation [HTx]), one patient on LVAD under went elective HTx within one year. No patients with NFAM died or received HTx during follow-up. NFAM patients had worse outcomes compared with FM patients.

**Conclusions:** The ideal TnI cut-off of was 8.53 ng/dL, with a sensitivity of 79.31%, specificity of 89.66%, positive predictive value of 88.46%, negative predictive value of 81.25% and an overall diagnostic accuracy of 84.5%. The ideal CK cut-off was 305.5 U/L, with a sensitivity of 76.92%, specificity of 76.47%, positive predictive value of 71.43%, negative predictive value of 81.25% and an overall diagnostic accuracy of 76.7%.

**Conclusions:** In acute myocarditis pts the highest value of TnI and CK have a good correlation with the LGE mass (AUC=0.92 and AUC=0.75, respectively), allowing an easy, adequate and low cost quantification of myocardial necrosis, that can therefore have a potential prognostic value.

**P3603 | BEDSIDE**

Short and mid-term survival and left ventricular function changes in fulminant versus non-fulminant acute myocarditis

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**Introduction:** Short and mid-term prognosis of acute myocarditis is still a matter of debate. Some reports suggested a better outcome in fulminant myocarditis (FM) than in non-fulminant acute myocarditis (NFAM), which seems contradictory with the dramatic presentation of FM.

**Aims:** To describe the outcome and changes over time in left ventricular ejection fraction (LVEF) in patients (pts) with FM compared with those with NFAM.

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**Results:** Mean age was similar (28±16 vs. 33±15 years, p=0.12), while female gender was more represented (50% vs. 13%, p<0.0001). Median follow-up was 880 days (259–1667). Kaplan Meier survival curves showed a significantly lower transplant-free survival in FM than in NFAM (78%vs.100%, log-ranked p<0.0001). All but one events occurred during initial hospitalization (4 deaths, 3 heart transplantation [HTx]), one patient on LVAD under went elective HTx within one year. No patients with NFAM died or received HTx during follow-up. NFAM patients had worse outcomes compared with FM patients.

**Conclusions:** The ideal TnI cut-off of was 8.53 ng/dL, with a sensitivity of 79.31%, specificity of 89.66%, positive predictive value of 88.46%, negative predictive value of 81.25% and an overall diagnostic accuracy of 84.5%. The ideal CK cut-off was 305.5 U/L, with a sensitivity of 76.92%, specificity of 76.47%, positive predictive value of 71.43%, negative predictive value of 81.25% and an overall diagnostic accuracy of 76.7%.
In HTx-free FM pts, a significant and greater improvement of LV EF is observed, but follow-up values remain lower than in pts with NFAM. However, after discharge overall prognosis appears good both in FM and in NFAM pts.

**P3604 | BENCH**

**Short and long-term outcome of acute myocarditis: what can we expect?**


**Introduction:** Myocarditis is a relatively common inflammatory disease that affects the myocardium. Current data suggest a good overall prognosis for patients with myocarditis. Our aim was to evaluate and report long- and short-term outcome of patients diagnosed with acute myocarditis in our tertiary referral center.

**Methods:** Retrospective analysis of 91 consecutive patients hospitalized with acute myocarditis between June 2006 and June 2014. Clinical features, complications, baseline and follow-up echocardiograms and cardiac magnetic resonance imaging were reviewed.

**Results:** The mean age of 33±10 years and 75 (82%) patients were men. Hypertension and dyslipidemia were present only in a few pts (17% and 15%, respectively). A viral prodrome was found in 76% of patients and chest pain was the commonest symptom (93%). All patients presented elevated levels of troponin I (mean peak level of 27±363 mg/ml). Mean BNP C-reactive protein values at admission were 204±571 pg/ml and 86±94 mg/dl, respectively. ST segment elevation (58%) was the most frequent ECG change. Coronary angiography performed in 38 (42%) patients was normal in all of them. Left ventricular (LV) systolic dysfunction (ejection fraction <55%) was present at admission in 23 patients (25%). Myocardial oedema was present in 62% and late gadolinium enhancement in 96%, predominantly subepicardial (63%), with an inferior-lateral location in most cases (39%) and involving 4 or more myocardial segments (58%). In hospital complications occurred in 5 patients (5%) and included cardiac shock (n=2); atrial fibrillation (n=2) and sustained ventricular tachycardia (n=1). There were no in-hospital deaths. After a mean follow-up of 36 months, residual LV dysfunction was reported in 3% without cases of heart failure. Recurrences occurred in 9% of cases. No other cardiac re-hospitalizations or deaths were recorded. In a multi-variate analysis, the presence of oedema in T2 weight imaging on admission was the only determinant of normalization of LV systolic function (p=0.042).

**Conclusion:** In this cohort, most of patients with acute myocarditis were male, at 3rd decade of life, without cardiovascular risk factors. Despite the favorable outcome, some patients do not fully recover LV function and others had recurrence of myocarditis. Myocardial oedema as defined by CMR was the only predictor of LV systolic function recovery.

**P3605 | BENCH**

**Identification of potential pathogenic epitopes in various cardiac proteins**

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**Purpose:** Heart diseases are the leading causes of death worldwide. Dilated cardiomyopathy (DCM) and myocarditis are basic heart diseases caused by various factors. The immune system is believed to play a central role after disease onset and during disease progression. Autoantibodies directed against various peptide-antigens present in cardiac tissue are found in these cardiac diseases.

**Methods:** Peptide Array analysis (PEPPERMAP) was performed against 26,364 different 15-mer peptides derived from 166 proteins associated with cardiovascular diseases. The sera used was obtained from 10 DCM, 10 myocarditis, and ICM patients and compared against that from 10 healthy, age-matched controls. A JOLA mice (n=8) were immunised on days 0, 7, 14 with peptide sequences (150±g) derived from proteins identified as autoantigens. On day 28, mice were sacrificed, histopathological evaluation of the heart and antibodies were determined within the sera.

**Results:** Statistical evaluation of the array identified novel antigen targets targeted by autoantibodies. In the myocarditis group various antigens were observed such as the giant sarcomeric signaling protein obscurin, the cytoplasmic protein dystrophin and laminin, as well as regulatory enzymes such as myosin light chain kinase and sodium/potassium transporting ATPase. The most promising candidate antigens in the DCM group were the structural proteins obscurin, dystrophin and laminin, as well as regulatory enzymes such as myosin light chain kinase and sodium/potassium transporting ATPase and the voltage-gated potassium channel KCNQ1.

Mice were immunised with peptides found in the myocarditis and DCM groups. We identified a peptide sequence within a dystrophin that induced inflammation and structural changes in immune cells.

**Conclusion:** In this study, various epitopes for autoantibody binding in different cardiac diseases were identified. Testing some of these peptide antigens in animal models identified novel pathogenic epitopes. These findings could help to establish testing methods for risk stratification in patients and to design more efficient and more specific treatment methods.

**P3606 | BENCH**

**The role of TWEAK and FN14 in autoimmune myocarditis**

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**Background:** Dilated cardiomyopathy (DCM) is a myocardial disease characterised by progressive depression of myocardial contractile function and ventricular dilatation. DCM can be caused by an inflammation of the myocardium triggered by autoimmune reactions. Our group developed a mouse model of experimental autoimmune myocarditis. Immunisation of Au mice with cardiac troponin I (cTnI) induces severe inflammation and subsequently fibrosis in the myocardium. Little is known about the role of the innate immune system in the pathogenesis of this autoimmune disorder. However, it was already observed that the cytokine tumor necrosis factor-like weak inducer of apoptosis (TWEAK) and its receptor FN14 play a pivotal role in different inflammatory diseases. Thus, we studied the impact of TWEAK and FN14 on the development of inflammatory cardiomyopathy.

**Methods and results:** Mice were immunised with cTnI to induce autoimmune myocarditis followed by cardiomyalgia, fibrosis and reduced ejection fraction (EF). Transthoracic echocardiography showed an improved EF in mice lacking FN14 (FN14−/−) compared to wildtype (wt) littermates (79±8% vs 75±10%). Histological examination of heart sections demonstrated less inflammation and fibrosis of the myocardium in FN14−/− mice in comparison to wt (inflammation score: 2.83±1.34 vs 3.56±1.50; fibrosis score: 2.67±1.80 vs 3.22±1.87). Moreover lower cTnI antibody titers were detectable in ELISA. In contrast TWEAK−/− mice displayed a decreased EF (79±5% vs 84±6%), severe inflammation and fibrosis (inflammation score: 3.43±1.59 vs 2.57±1.29; fibrosis score: 3.29±1.83 vs 2.43±1.40) and higher cTnI antibody titers compared to wt littermates.

**Conclusion:** TWEAK and FN14 may play an important role in the pathogenesis of autoimmune myocarditis. While FN14−/− mice showed a better disease outcome, mice lacking TWEAK suffered more from cTnI immunisation and showed reduced cardiac function compared to wt mice. This suggests other important FN14 ligands. Thus, inhibition of FN14 might represent a novel therapeutic strategy in the treatment of inflammatory cardiomyopathy.
**P3680 | BEDSIDE**

**Life expectancy of adults with congenital heart disease**

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**Background:** Contemporary estimates of survival in adults with congenital heart disease (CHD) are sparse.

**Methods:** We performed a survival analysis for 3,345 adult survivors with CHD prospectively followed up to 25 years. There were 1,688 males and 1,656 females. Median survival was 22 years (95% CI 17.5–27; p < 0.001). The median survival in group I (77.7 years [77–83]) did not differ from reference population. However, survival of patients was severely reduced (< 60 years) in the majority of patients in group III, and moderately reduced (60–75 years) for complete transposition and patients in group II (Table).

**Results:** Total follow-up was 37,934-person years. Median follow-up time was 10.6 years (1–18). At the end of the study 328 patients had died (prevalence 9.8%; annual incidence 0.86%). Female subjects died at a median age of 77.5 years (95% CI 76–81) and male subjects at a median age of 70.6 years (67–74) (p < 0.001). The median survival in group I (77.7 years [77–83]) did not differ from reference population. However, survival of patients was severely reduced (< 60 years) in the majority of patients in group III, and moderately reduced (60–75 years) for complete transposition and patients in group II (Table).

**Conclusions:** Contemporary life expectancy in adults with CHD is worse in male than in female, is lower than 60 years in the majority of complex CHD, between 60 and 75 years in complete transposition and in patients with moderately complex CHD and close to that of the reference population in patients with simple CHD.

**Acknowledgement/Funding:** Fondo de Investigaciones Sanitarias Exp P11/02099

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**P3689 | BEDSIDE**

**Population health science approaches to cardiovascular disease in Marfan syndrome**

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**Background:** Marfan syndrome is the commonest inherited connective tissue disease, and is associated with increased risk of aortic complications. The magnitude of this risk (overall, and in various age-sex groups) is not known precisely, and may have been under- or overstated by selective reporting from institutions with specialist interest in the condition. Furthermore, the risks of non-aortic cardiovascular complications are uncertain.

**Methods:** Large scale datasets of routinely collected statistics of all hospital admissions, and linked datasets of all registered deaths, in England 1999–2011 were used to define a cohort of 4,468 patients with Marfan syndrome. Risks of aortic dissection and of non-aortic cardiovascular complications were quantified in this cohort, and in a cohort of 10,119,152 controls, stratified for a number of background characteristics, including age and sex, over a mean follow-up period of 6.9 years.

**Results:** The relative risk of aortic dissection in the Marfan syndrome cohort compared to controls was 188 (95% CI 160–220, p < 0.0001). The relative risk was spectacularly increased (-1000-fold) in some age-sex groups. Risks of non-aortic cardiovascular disease were also increased; rate ratio for coronary artery disease was 3.2 (p < 0.0001), for myocardial infarction 1.5 (P < 0.01), and for stroke 3.9 (p < 0.0001).

In a separate analysis, Marfan syndrome was listed as a contributing cause of death in 352 deaths in England between 2001 and 2010. We found no evidence for any particular trend in the rates of such deaths over the 10 year period but unexpectedly, deaths attributed to Marfan syndrome were almost twice as frequent in men as in women (p < 0.0001).

The study is the largest cohort of patients with Marfan syndrome yet reported, and uniquely exploits a very large control population of over ten million people to provide reliable estimates of the risk of aortic and non-aortic cardiovascular complications in a contemporary population.
ment with a reasonable low complication rate. The prevalence of atrial tachycardia was not affected in the total cohort.

P3612 | BEDSIDE
Cardiac outcomes and prevalence of coronary stenosis in adult patients after arterial switch operation for transposition of the great arteries

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Background and introduction: There is limited data about long-term outcome of patients with transposition of the great arteries (TGA) repaired with the arterial switch operation in the adult population. The aim of this study was to report our experience and to assess in a large series the prevalence of coronary artery disease.

Methods: A retrospective analysis of 263 adult patients from 1990 to 1998 in a tertiary referral centre (n=68). Six patients were lost to follow up and the remaining 62 patients constitute the study population. Complex anatomy (ventricular septal defect or subpulmonary obstruction requiring repair) was present in 20 patients (32%) and 9 patients (12%) underwent palliation before ASO. On one late death (1%) was documented: sudden cardiac death during exercise in a 16-year-old. After a mean follow-up of 19.2±2.1 years, all the patients were in NYHA functional class I with a mean left ventricular ejection fraction of 63.2±6%. As for long-term complications, neoaortic root dilatation (~40 mm) was present in 25 patients (40%), moderate to severe aortic regurgitation in 4 (6%), right ventricular outflow tract obstruction (RVOTO) at any level in 19 (31%) and arrhythmias in 9 (1 patient with sustained ventricular tachycardia (1.6%)). No acute coronary syndromes were documented during follow-up, and 16 patients (26%) had undergone a high-resolution computed tomographic scan at a mean of 19.2±2 years after ASO procedure that did not reveal any coronary obstruction. A total of 17 reinterventions (13 surgical and 4 percutaneous) were required in 11 patients (18%), the most frequent indication being RVOTO root (8 reinterventions, 47%) and only one case (6%) of Bentall-Bono procedure for severe aortic regurgitation and neoaoartic root dilatation. Complex anatomy (60% vs 31%, p=0.029) and age at time of ASO (27±54 days vs 95±134 days, p=0.036) were predictors of neoaoartic root dilatation.

Conclusions: Long-term outcomes of patients with TGA who survive arterial switch operation are good in terms of mortality and functional class. Coronary stenosis and coronary events in the long run are rare. Patients with complex anatomy and those older at time of ASO are more prone to develop neoaoartic root dilatation.

P3613 | BEDSIDE
Late outcomes in adults following anatomic repair of congenitally corrected transposition of the great arteries

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Introduction: Anatomic repair (double switch operation) for congenitally corrected transposition of the great arteries (ccTGA) is associated with good short- to mid-term outcomes. An increasing number of these patients are surviving to adulthood. There is a paucity of data in adults regarding late sequelae. We sought to determine the long-term outcomes in older patients who have previously undergone a double switch operation for ccTGA.

Methods: A retrospective analysis of 16 patient records from 2001 to 2015 from a single institution was conducted. Median age was 23 years (range 18–56 years). Five patients underwent a double switch operation for ccTGA performed between 1990 and 1998 in a tertiary referral centre (n=68). Six patients were lost to follow up and the remaining 62 patients constitute the study population. Complex anatomy (ventricular septal defect or subpulmonary obstruction requiring repair) was present in 20 patients (32%) and 9 patients (12%) underwent palliation before ASO. On one late death (1%) was documented: sudden cardiac death during exercise in a 16-year-old. After a mean follow-up of 19.2±2.1 years, all the patients were in NYHA functional class I with a mean left ventricular ejection fraction of 63.2±6%. As for long-term complications, neoaortic root dilatation (~40 mm) was present in 25 patients (40%), moderate to severe aortic regurgitation in 4 (6%), right ventricular outflow tract obstruction (RVOTO) at any level in 19 (31%) and arrhythmias in 9 (1 patient with sustained ventricular tachycardia (1.6%)). No acute coronary syndromes were documented during follow-up, and 16 patients (26%) had undergone a high-resolution computed tomographic scan at a mean of 19.2±2 years after ASO procedure that did not reveal any coronary obstruction. A total of 17 reinterventions (13 surgical and 4 percutaneous) were required in 11 patients (18%), the most frequent indication being RVOTO root (8 reinterventions, 47%) and only one case (6%) of Bentall-Bono procedure for severe aortic regurgitation and neoaoartic root dilatation. Complex anatomy (60% vs 31%, p=0.029) and age at time of ASO (27±54 days vs 95±134 days, p=0.036) were predictors of neoaoartic root dilatation.

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P3615 | BEDSIDE
Outcome of adult survivors of congenital heart lesions after 25 years follow-up estimates of the standardized mortality ratio

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Introduction: The absolute and relative risk of developing congestive heart failure, atrial fibrillation and myocardial infarction was markedly increased in children and young adults with congenital heart disease compared to the general population. Despite the more positive prognosis for these patients, cardiovascular mortality is very high compared to healthy controls.

Methods: In a cohort of 3,345 adults with CHD followed up to 25 years, the standardized mortality ratios (SMR) were calculated using age at diagnosis and sex adjusted death rates. For mortality analysis, data provided by the National Death Index of Spain were used. One-sample log-rank test with online available software (http://biostatistics.mgh.harvard.edu/biostatistics/resources.htm) was used.

Results: Median age at first examination was 22 years (18–39) and median age at death was 44 years (33–56) for men and 50 years (40–59) for women. Follow-up time was 10.8 years (1–24.3). The SMR for males, 1,565 females, 1,348 patients had a simple CHD (group I); 1,606 patients had moderate complexity CHD (group II); and 393 patients had CHD of great complexity (group III). A total of 328 patients had died (9.8%) at the end of the study. The SMR was calculated as 1.6 (95% CI 1.3–2.0; p<0.001) in male subjects and 1.8 (95% CI 1.2–2.1; p<0.001) in female subjects. For the patients of group I, the SMR

<table>
<thead>
<tr>
<th>Main diagnosis</th>
<th>No. of cases</th>
<th>SMR</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventricular septal defect</td>
<td>355</td>
<td>0.67</td>
<td>0.49–0.95</td>
<td>0.019</td>
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<tr>
<td>Bicuspid aortic valvulopathy</td>
<td>515</td>
<td>0.91</td>
<td>0.75–1.11</td>
<td>0.314</td>
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<td>Atrial septal defect</td>
<td>383</td>
<td>1.21</td>
<td>0.89–1.64</td>
<td>0.068</td>
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<td>Subvalvular aortic stenosis</td>
<td>114</td>
<td>1.52</td>
<td>0.97–2.4</td>
<td>0.038</td>
</tr>
<tr>
<td>Eisenmenger complex</td>
<td>175</td>
<td>0.97</td>
<td>0.84–1.11</td>
<td>0.67</td>
</tr>
<tr>
<td>Coarctation of the aorta</td>
<td>355</td>
<td>2.90</td>
<td>1.85–4.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Tetralogy of Fallot</td>
<td>325</td>
<td>3.11</td>
<td>1.92–4.8</td>
<td>&lt;0.001</td>
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<tr>
<td>Transposition of the great arteries</td>
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<td>8.02</td>
<td>4.4–14.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Eisenmenger syndrome</td>
<td>49</td>
<td>12.5</td>
<td>7.3–21</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Single ventricle physiology</td>
<td>100</td>
<td>14.5</td>
<td>9.0–24</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
was not significantly different than that of the reference population (1.08; 95% CI 0.9–1.3; p=0.38). However, the SMR for the group II was 1.9 (95% CI 1.6–2.4; p < 0.001) and for the group III 10.2 (95% CI 7.8–13; p < 0.001). The excess in mortality rate increased progressively with complexity of CHD (table).

Conclusions: The global excess of mortality, was 60% for males and 80% for females with important differences depending on complexity. These data may be used as a prognostic index in adult survivors with CHD.

Acknowledgement/Funding: Fondo de Investigaciones Sanitarias Exp PI14/02095

ACUTE PULMONARY EMBOLISM

P3616 | BEDSIDE

The influence of age on the prognostic value of the clinical prediction rules in patients with pulmonary embolism

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Introduction: Value of the Revised Geneva Score (RGS) and the Wells Score (WS) in prognostic stratification was tested in patients with acute pulmonary embolism (PE), especially in elderly. There is no data concerning younger patients.

Purpose: To investigate whether the initial assessment of clinical probability of PE has the same prognostic accuracy in terms of the long-term mortality among younger (<50 years old) and older (≥50 years old) patients with PE.

Methods: 238 consecutive patients with proven PE were retrospectively classified into three probability subgroups according to the simplified Geneva and Wells scores. Follow-up was conducted up 115 months.

Results: Younger patients accounted for the 19.7% of the study cohort. Overall three-year mortality (30.3%) and hospital deaths and 63 (26.2%) deaths during follow-up. According to both probability rules younger patients significantly more likely than older were classified into the low-probability subgroups and less likely into the high-probability subgroup (p < 0.05). In older patients long-term mortality rates differed significantly depending on the RGA and WS – determined PE probability subgroup (p < 0.001; RGS; p=0.04 WS). Kaplan-Mayer curves for RGS differed markedly between the three probability categories, figure. WS well discriminated low-risk patients while the survival curves of patients at high and intermediate risk overlapped. On the contrary amongst younger patients, analysis of survival curves according to the initial probability of PE determined by the RGS and the WS failed to demonstrate their prognostic significance.

Conclusions: Initial RGS and WS assessed PE probability may have prognostic utility but only in older patients. In younger patients prognostic stratification according to both scales was not confirmed.

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Accuracy of a clinical-ultrasonographic score for the diagnostic stratification of patients with suspected pulmonary embolism

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Introduction: International guidelines recommend the use of validated clinical scores to estimate the pre-test probability of pulmonary embolism (PE). Point-of-care ultrasonography proved to be accurate in the diagnosis of deep venous thrombosis (DVT) and of many pulmonary pathologies.

As there is no certitude in the diagnostic accuracy of a clinical-ultrasonographic score (US-WS) with a clinical score as Wells score (WS).

Materials and methods: We calculated the traditional dichotomized WS (“PE likely” if >4 points, “PE unlikely” if <4) in adult patients suspected of PE presenting to four hospitals. Lung and venous US were performed by a physician blinded to clinical data. US-WS differs from WS in the following items: signs and symptoms of DVT, replaced by “DVT at venous ultrasonography” and “alternative diagnosis less likely than PE” replaced by “alternative diagnosis less likely than PE after lung ultrasonography”.

The latter item was positive (3 points) in presence of at least one subpleural infarct; in case of alternative ultrasonographic diagnosis the item was considered negative (0 points). In case of a normal lung US examination, the item was considered positive or negative referring to what assigned to the same item of WS. Final diagnosis was obtained by multidetector CT pulmonary angiography or scintigraphy.

Results: Among the 249 enrolled patients PE was finally diagnosed in 60 (24.1%). Among the 143 patients (57.4%) with WS ≤4, PE was present in 25 (17.5%) cases. In the 106 patients (42.6%) with WS ≥ 4, PE was diagnosed in 35 (33%) Pulmonary and venous ultrasonography was performed in 7±3 minutes. US-WS was ≤4 in 187 patients (75.1%, p < 0.05 vs WS), of which 18 (9.6%) had PE as final diagnosis. In the 62 patients with US-WS ≤ 4 (24.8%, p < 0.05 vs WS), PE was present in 9 (14.5%) patients (8.2%, 95% CI 5.6–11.2 and specificity (89.4%, 95% CI 84.1–93.4) were superior to those of traditional Wells score (sensitivity 58.3%, 95% CI 44.9–70.9, specificity 62.4%, 95% CI 55.1–69.4). The area under the curve of US-WS (88.4%, 95% CI 83.2–93.6), was significantly superior to that of WS (62.1%, 95% CI 53.5–70.7) (p < 0.05).

Conclusions: A clinical-ultrasonographic score (US-Wells score), rapidly feasible at the bedside, increases the proportion of low-risk patients with a better global accuracy compared to traditional clinical score.

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Prognostic impact of cardiovascular risk in pulmonary embolism


Introduction: For a long time, venous thromboembolism (VTE) and atherosclerotic disease were believed to be completely distinct entities. More recent studies contradict this theory, suggesting that cardiovascular risk factors (CVRF) are linked to a greater risk of VTE. It is further claimed that patients with pulmonary embolism (PE) are at greater risk for cardiovascular events. This positive association is highly relevant in clinical practice, mainly in primary and secondary prevention of VTE.

Objective: Ascertain if there is a link between PESI (Pulmonary Embolism Severity Index) and cardiovascular risk (CVR), and the extent to which CVR and each CVRF individually affects PE’s six-month outcome.

Methods: Retrospective, descriptive and correlation study extended to all patients (P) with PE hospitalized in our hospital, from January 2012 to November 2014. Basal clinical characteristics of the patients were analysed and stratification for CVR was carried out, computing the SCORE (Systematic Coronary Risk Evaluation Project) in two groups: low/mild CVR and high very high CVR. PE was stratified, computing the PESI, in low risk (class I-II PESI) and high risk (class III-V PESI). Uni and multivariate analysis of 6 months recurrence, re-hospitalization and overall mortality was performed. The statistical methods used were Mann-Whitney’s U test, Fisher’s exact test and chi-squared test.

Results: Within a population of 130 hospitalized P due to PE, PESI score was applied to 125 P (65.6% female; 68.4+15.8 years). 22.4% had diabetes mellitus type 2, 63.2% hypertension and 32% dyslipidemia. 54.4% P were classified as class 2; 63.2% hypertension and 32% dyslipidemia. 54.4% P were classified as class II PESI and 45.6% as high very high CVR. Each individual was not associated with PE outcome. Individuals with high CVR tend to have a higher PESI (86% vs. 14%, p=0.001). Patients with lower CVR deceased less, regardless of PESI (22.2% vs. 50%, p=0.002). CVR stratification appears to be more closely related to death in hospital (7.4% vs. 19.3%, p=0.046) than at 6 months (13.8% vs. 20.9%, p=0.343). A lower 6 months re-hospitalization rate was also determined for individuals with low CVR (16.9% vs. 36.4%, p=0.025). A statistically significant difference in the recurrence rate was not found.

Conclusion: Whereas overall mortality was higher in the group with greater CVR, this analysis indicates SCORE can be an asset in stratifying PE risk; thus, prospective studies aimed at validating this application are required.
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Time trends and case fatality rates of pulmonary embolism during 11 years of observation in Northern Italy

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Background: Pulmonary embolism (PE) is a common and increasingly diagnosed disorder with high mortality and morbidity rates. However, population-based information on its incidence and prognosis remains limited. We conducted a large epidemiology study collecting data on hospitalization for PE (from 2002 to 2012) in a population of about 13 million people in Northwestern Italy.

Methods: Patients were identified using the ICD-9-CM codes: 415.11, 415.19; gender and age specific incidence rate of PE during the study period were estimated using the resident population for each year of the study. Furthermore, time trends in the in-hospital PE-related mortality and case fatality rate were calculated. Results were adjusted for possible confounders.

Results: The overall crude incidence rate for the entire study period was 55.4 and 40.6 events per year per 100,000 inhabitants for women and men, respectively (p<0.001). However, this difference completely disappeared when the incidence rate in the two genders was standardized according to age. The mean case fatality rate was significantly higher in male patients compared to female patients (13.83 vs 12.95, p 0.002). Incidence of PE significantly increased in both genders during the study period. In-hospital case fatality rate significantly decreased throughout the study period (p<0.001) in women (from 15.6% to 10.2%) and in men (from 17.6% to 10.1%). The observed decrease of the in-hospital case fatality rate remained significant also after adjustment for possible confounders.

Conclusion: Time trends over an 11-year period show an increasing incidence of PE, but a significant reduction in mortality during hospitalization. Reduction in the case fatality rate remained significant after adjustment for these possible confounders.

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Low dose prolonged infusion of tissue type plasminogen activator therapy in massive pulmonary embolism

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Background: Pulmonary embolism (PE) has a high mortality but the in-hospital all-cause case fatality rates were lower in unstable patients who received thrombolytic therapy (TT) than those who did not. However TT is associated with major complications. The aim of the present study was to assess the efficacy and safety of low-dose (25mg) prolonged administration (in 6 hours) of tissue-type-plasminogen-activator (tPA) on in-hospital mortality and outcomes in patients with massive PE.

Methods: A total of 37 consecutive patients with massive PE were included in this study. The primary end-points consisted of in hospital all cause mortality, major complications, pulmonary hypertension and right ventricular dysfunction. Secondary end-points are all cause mortality, pulmonary hypertension and right ventricular dysfunction at 6 month.

Results: The mean age of the patients was 68.7±14.54. The mean pulmonary artery systolic pressure (PASP) (56.5±17.34 mmHg vs. 34.16±2.81 mmHg, p<0.001), right/left ventricle (RV/LV) diameter (1.37±0.12 vs. 0.96±0.12, p<0.001) were significantly decreased after the TT. Tricuspid annular plane systolic excursion (1.43±0.33 cm vs. 2.07±0.27 cm, p<0.001), Tei index (0.47±0.08 vs. 0.55±0.07, p<0.001), S' (9.62±8.2 vs. 15.3±2.6) were significantly increased after TT (Table 1). No major bleeding was observed. None of the patients had life threatening complications. In-hospital mortality was one and total mortality was three. Pulmonary hypertension was not developed during follow up.

Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>On admissiona</th>
<th>Post TTb</th>
<th>Pre-dischargec</th>
<th>6 monthsa</th>
</tr>
</thead>
<tbody>
<tr>
<td>PASB, mmHg</td>
<td>56.5±17.34</td>
<td>34.16±8.21</td>
<td>30.35±3.19</td>
<td>28.70±3.04</td>
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<tr>
<td>TAPSE, cm</td>
<td>1.43±0.33</td>
<td>2.07±0.27</td>
<td>2.17±0.22</td>
<td>2.21±0.22</td>
</tr>
<tr>
<td>MR, %</td>
<td>47.4±0.8</td>
<td>55.0±0.7</td>
<td>59.8±0.4</td>
<td>61.6±0.3</td>
</tr>
<tr>
<td>S', cm/sec</td>
<td>0.96±0.28</td>
<td>1.53±0.26</td>
<td>1.61±0.22</td>
<td>1.69±0.24</td>
</tr>
<tr>
<td>RV/LV</td>
<td>1.37±0.12</td>
<td>0.99±0.12</td>
<td>0.98±0.10</td>
<td>0.67±0.10</td>
</tr>
</tbody>
</table>

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.

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Withholding anticoagulation after negative CTPA is safe in patients with a likely clinical probability of PE

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Background: According to the 2014 ESC guideline on acute pulmonary embolism (PE), a negative multi-slice computed tomography pulmonary angiography (CTPA) alone is a controversial criterion to rule out symptomatic PE in those patients who have a likely pretest probability of PE, as assessed with a validated clinical decision rule (level B recommendation). Whether these patients should be further investigated thus remains controversial.

Aims: To determine the safety of withholding anticoagulation in patients with a likely pretest probability by the Wells score (≤4 points) in whom PE was excluded by negative CTPA alone, and whether this safety is modified by a history of symptomatic venous thromboembolism (VTE). We defined the upper limit of the range of death and VTE after a negative angiogram (2.7%) as the cut-off point for the safe exclusion of PE (van Beek, Clin Radiol 2001).

Methods: Patient-level meta-analysis from 4 large prospective diagnostic management studies in which PE was ruled out based on the combination of an unlikely clinical probability (Wells score ≤4 points) and a normal D-dimer, or a normal CTPA. All patients were followed during 3 months for the occurrence of symptomatic VTE. The 3-month incidence of symptomatic VTE after exclusion of PE was pooled using a random-effects model for all patients, for those with a likely pretest probability alone and from the latter cohort those with and without prior VTE separately.

Results: Data from 6,148 consecutive patients with suspected PE were pooled, with an overall PE prevalence of 25%. The failure rate in all 4,694 patients in whom PE was excluded was 1.2% (95% CI 0.5–2.6). In the 1,940 patients with a likely PE (Wells score ≤4 points) and normal VTE, the failure rate was 1.3% (95% CI 0.5–2.9). However, this difference completely disappeared when the incidence rate in the two genders was standardized according to age.

Conclusions: Withholding anticoagulation after negative CTPA is safe in patients with a likely pretest probability of PE and a negative CTPA alone. It could be debated whether patients with a likely pretest probability and a prior episode of VTE should be referred for additional diagnostic testing.
P3624 | BEDSIDE
Survival based on the transpulmonary and diastolic pressure gradient in end-stage COPD post-capillary pulmonary hypertension
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Background: Pre-capillary pulmonary hypertension is an established complication of advanced COPD. Post-capillary pulmonary hypertension (pcPH), defined by a mean pulmonary artery pressure (mPAP) >25 mmHg and a pulmonary artery wedge pressure (PAWP) >15 mmHg, is less well-characterized in COPD. The transpulmonary gradient (TPG = mPAP-PAWP) <12 mmHg has previously been considered a marker of ‘passive’ pcPH, while TPG >12 mmHg has been considered ‘reactive (out-of-proportion)’ pcPH. The diastolic pressure gradient (DPG = dPAP-PAWP) <7 mmHg has recently been introduced for ‘isolated pcPH’ (ipcPH), and DPG >7 mmHg for ‘combined pcPH’ (CpcPH).

Purpose: Although based on a strong pathophysiological reasoning, the role of the TPG and the DPG in predicting outcome remains uncertain. We have analysed the prognostic implications of a hemodynamic stratification based on the TPG and the DPG in COPD-pcPH.

Methods: 409 patients consecutive patients with end-stage COPD were assessed for lung transplantation including right heart catheterization during 1991–2010 (status follow-up january 2015) at Rigshospitalet, Copenhagen, Denmark. Fifty-two (13%) patients presented with pcPH. Patients were included in an analysis of pre-transplant survival based on the TPG and the DPG. Furthermore, 35 (7%) patients underwent transplantation and were subject to an analysis of post-transplant survival. Kaplan-Meier statistics with log-rank testing was utilized.

Results: Post-capillary PH patients were 56±7 years of age, presented with FEV1 22.9±7.4%, FVC 51±18.8%, TLC 118±27.7 and had preserved left ventricular systolic function (LVEF 62±9%). Hemodynamically pcPH patients presented with mPAP 32±6.2 mmHg, PAWP 18±2.5 mmHg, CO 5.8±1.1 l/min, PVR 2.6±1.5 WU. Survival analysis demonstrated a pre-transplant survival benefit for patients with a TPG <12 mmHg vs >12 mmHg (p<0.012), but not for patients with a DPG <7 mmHg vs >7 mmHg (p=0.134).

Conclusions: Transpulmonary gradient (TPG), but not the diastolic pressure gradient (DPG), seems to be a valid pre-transplant prognostic tool in post-capillary pulmonary hypertension related to end-stage COPD. In contrast, neither the TPG nor the DPG grouping affects post-transplant survival.

P3626 | BEDSIDE
Factors associated with operability of chronic thromboembolic pulmonary hypertension: insights of Spanish registry (REHAP)
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Introduction: The treatment of choice for chronic thromboembolic pulmonary hypertension (CTEPH) is the pulmonary endarterectomy (PE). However an important proportion of patients with CTEPH receive only medical treatment (MT) due to distal inoperable disease, comorbidities or no referral for asses operability. Aim: To analyze the factors associated with PE in CTEPH patients in Spain. Methods: Voluntary reporting of incident CTEPH cases from 2006 to 2013 were evaluated (n=349). PE were performed in 100 patients (29%) and 249 patients (71%) received only MT. Clinical parameters, 6-minutes walking test (6MWT) and hemodynamic variables were analyzed.

Results: Patients undergoing PE were younger (55 [43–68] vs 72 [58–80] years, p<0.001), higher proportion of men (58% vs 37%, p<0.001) and a greater distance walked in the 6MWT [390 (293–468) vs 319 (194–418) meters, p=0.004] than those receiving only MT. No significant differences were found in functional class (FC), or baseline hemodynamic parameters other than mean pulmonary arterial pressure (mPAP) 49±12 vs 45±12 mmHg (p=0.004); pulmonary vascular resistance (PVR) 10.2±4.5 vs 9.9±6.2 Wood Units; cardiac index (CI) 2.1±0.6 vs 2.3±0.6 l/min m⁻². The figure 1 shows the multivariate analysis for PE.

Conclusions: In Spain, independent factors associated with operability were having proximal lesions in angiography, a better physical status (6MWT) and an unexpectedly a higher mean pulmonary arterial pressure. While older age was an independent risk factor associated for non-operability.

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CVD prevention and outcomes
P3625 | BEDSIDE
Mortality trends from cardiovascular diseases in southern Brazil
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Introduction: Cardiovascular diseases (CVD) are the leading causes of death in Brazil. In recent decades, especially in the south and southeast, a decline in mortality from CVD has been seen. These findings has also been observed in Europe and the United States.

Objective: To analyze time-trend mortality from cardiovascular diseases, ischemic heart disease and cerebrovascular diseases in southern Brazil.

Methods: An ecological time series study was performed using data from the Mortality Information System of Health Ministry, with deaths of residents of Santa Catarina, from 1980 to 2012. The causes of death from 1980 to 1995 used the ICD-9 and the 1996 to 2012, ICD-10. Diseases of the circulatory system were identified as codes ICD-9 and the 1996 to 2012, ICD-10. Diseases of the circulatory system were identified as codes 390–459 and I00–I99. Analysis was carried out with the Mortality Trends Tool, from the Health Information System of the Ministry of Health.


Conclusion: Mortality from cardiovascular diseases in southern Brazil has decreased over the years, especially from 1980 to 1995. This trend continued from 1996 to 2012, but with a slight increase in the southern region.

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classified as 390–459 and 100 to 199, ischemic heart disease as 410–414 and I20 to I25, and cerebrovascular diseases, 430–438 and I60 to I69, respectively. The mortality rates were standardized by world standard age for each of the causes in general, presented by 100,000 inhabitants. The average focused on five points was calculated to reduce the oscillation of the coefficients mortality rate obtained. Later, a pinpoint regression was performed to estimate mortality trends for each case.

Results: During the study period there were 248,296 deaths, 51% of those in women. However all causes showed significant reductions in the mortality rate. For cardiovascular diseases, the mortality rate in the beginning was 256 deaths per 100,000 inhabitants and at the end, 145 deaths per 100 thousand inhabitants, with represents a reduction of 2% (95% CI: −2.4; −1.5) per year. The greatest reduction was observed in the 2005–08 period, 5.3% (95% CI: −8.0; −2.5) per year. For cerebrovascular diseases, a reduction of 1.6% (95% CI: −1.8; −0.9) per year, from 69 to 48 deaths per 100 thousand inhabitants. The largest reductions were in 1997–2001, 3.4% (95% CI: −4.9; −1.9) and from 2004 to 2010, 3.2% (95% CI: −3.7; −2.6) per year. In relation to cerebrovascular disease, the mortality rate decreased from 91 to 41 deaths per 100 thousand inhabitants, down 2.8% (95% CI: −3.2; −2.4%) per year; the largest reductions were 7% (95% CI: −9.3; −4.6) per year in the 2005–2008 period.

Conclusion: There was a progressive reduction in mortality from cardiovascular diseases, ischemic heart disease and cerebrovascular diseases. However, despite this reduction, high rates of death from these diseases still exist.

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Factors associated with grade-1 hypertension: a cross-sectional assessment and implications for hypertension care based on the Dietary Approaches to Stop Hypertension (DASH) approach in primary care
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Background and introduction: A Reference Framework for Hypertension Care was recently developed by Hong Kong government, and the Dietary Approaches to Stop Hypertension (DASH) regime was recommended for patients aged 40–70 years with grade 1 hypertension. However, few studies have been devoted to translating the Reference Framework into real primary care settings. Information on plausible determinants and dietary factors associated with grade 1 hypertension is particularly in the Chinese population were scarce.

Purpose: To follow the Reference Framework to screen subject with grade 1 hypertension in primary care settings, and explored factors associated with grade 1 hypertension (having systolic blood pressure [BP] of 140–159mmHg and/or diastolic BP of 90–99mmHg).

Methods: The study sample consisted of community dwellers (N=10,693) enrolled in a primary care programme in which participants overall had similar characteristics when compared to the Hong Kong population census. Invitation phone calls were given to a randomly selected subjects (N=2,673, 50% of total subjects aged 40–70 years) in 2013. Physical examination was performed for anthropometric measurements on blood pressure (BP) and body mass index (BMI) according to a standardized protocol. Questionnaires were used to collect information on socio-demographics, lifestyles, and family medical history. Multiple logistic regression analysis was performed to explore factors associated with the presence of grade-1 hypertension.

Results: A total of 679 out of 2,673 subjects agreed to participate in the screening, and 320 subjects were grade-1 hypertensive (47.2%, [320/679]). Unhealthy diet regime (adjusted odds ratio [aOR]=2.19, 95% CI 1.04–4.62), BMI >27.5kg/m2 (aOR=1.87, 95% CI 1.53–2.27), irregular daily meals (aOR=1.47, 95% CI 1.11–1.95), cigarette consumption (aOR=1.59 for amount; aOR=1.83 for duration), alcohol drinks (aOR=1.87 for amount; aOR=1.65 for duration), and positive family history of hypertension (aOR=1.08) were independently associated significantly with the presence of grade-1 hypertension. The increase in the number of risk factors combined significantly correlated with higher predicted probability of grade 1 hypertension.

Conclusion(s): The finding that dietary-intake factors were associated with grade-1 hypertension echoes the incorporation of dietary-related interventional approach into the Reference Framework for hypertension management in the current class of 2013. The association between aggregate risk factors and grade 1 hypertension should also be taken into consideration in long-term preventive strategy.

Acknowledgement/Funding: This study was funded by the Health and Health Services Research Fund, Food and Health Bureau, Hong Kong [Project DOI: 09100701]
Sub-specialization in cardiology care and outcome: should clinical services be redesigned, again?

Background: Inpatient management of cardiac patients by cardiologists results in reduced mortality and hospitalization. With increasing sub-specialization of the field due to growing management complexity and use of technological innovations, the impact of sub-specialization on patient outcomes is unclear.

Purpose: We sought to investigate whether management by subspecialty cardiologists impacts the outcomes of patients with subspecialty specific diseases and if so, whether this is due to clinical expertise or access to technological innovations in care.

Methods: All patients admitted to a tertiary centre over nine years with a diagnosis of heart failure, acute coronary syndrome (ACS) or primary arrhythmia were reviewed. The outcomes of these patients managed by cardiologists subspecialized in their admission diagnosis (heart failure specialists, interventionalists, and electrophysiologists) was compared with those treated by general cardiologists.

Results: Heart failure was diagnosed in 1,704 patients, ACS in 7,763 and arrhythmia in 4,398. There was no difference in length of stay (LOS) (p=0.26), mortality (p=0.006), however no difference in mortality (p=0.14). ACS patients managed by interventionalists were more likely to undergo coronary intervention (p<0.05). Electrophysiologists more frequently referred patients for catheter ablation and pacemaker implantation than general cardiologists (p<0.05).

Conclusions: The development of healthcare models which align cardiovascular disease with the subspecialist are likely to result in effective utilization of healthcare personnel and appropriate selection of patients who would benefit from technological innovations in care.

Cardiac rehabilitation program is effective improving functional capacity in post myocardial infarction patients with multivessel disease. Patients with complete revascularization had a better recovery of functional capacity in comparison with partial revascularization.

Background: Studies have shown that weekend and holiday admissions for patients with acute coronary syndrome (ACS) are associated with higher incidence of in-hospital mortality and major adverse cardiovascular events (MACE). This has been attributed to reduced staffing, fewer senior doctors, and the unavailability of certain diagnostic or therapeutic facilities and procedures. This has been attributed to reduced LOS and cardiovascular readmissions and mortality (all p<0.05). This reduction in mortality was seen mainly in low risk patients (p<0.05). There was a reduction in LOS and cardiovascular readmissions in arrhythmia patients receiving subspecialty management (both p<0.05), however no difference in mortality (p=0.14). ACS patients managed by interventionalists were more likely to undergo coronary intervention (p<0.05).

Methods: Ages ranged from 23–49 years, mean age was 40 (± 7.83). The CR group (n=143) versus MVI (139 patients), who were referred to a cardiac rehabilitation program.

Results: A total of 175 patients were included in this study. 59 were admitted on a weekend/holiday and 116 on a weekday. The mean age was 58.98±12.59, and mostly male (72.57%). Baseline characteristics did not differ between the two groups, except for a history of previous revascularization (0% vs 10%, p=0.010) and presence of both ischemia and infarct on ECG (57.6% vs 72.4%, p=0.048) in the weekday group. In-hospital mortality was significantly higher in the weekend group (27.1% vs 12.1%, p=0.0125). Multiple logistic regression identified a weekend admission and heart failure to be predictors of in-hospital mortality. Controlling other variables, a weekend/weekday hospital admission was found to be an independent predictor of in-hospital mortality (OR 7.69, 95% CI 1.78, 33.30; p=0.006).

Conclusion: For patients with ACS, a weekend admission was independently associated with increased in-hospital mortality. This finding has important quality-of-care implications. There is a need to explore the factors that contribute to this “weekend effect” in our setting by a prospective trial.

Conclusion: The study aims to establish whether a CR programme offered to young ICD patients (less than 50 years of age) helps improve their quality of life and reduces stress and anxiety levels. A comparison was made to a group of young ICD patients who had not yet completed a CR programme.

Methods: The sample size was twenty ICD patients with inherited cardiac conditions. Ages ranged from 23–49 years, mean age was 40 (± 7.83). The CR group (n=10) had enrolled on an eight week CR programme and completed a quality of life questionnaire and Hospital Anxiety and Depression Scale (HADS) at baseline and after the programme. The CR group (n=10) were asked to complete the same questionnaires. Retrospective questionnaire data was analysed pre and post CR using repeated measures and compared with prospective data collected from the non-CR group. Quality of life components included physical fitness, feelings, daily activities, social activities, pain, change in health, overall health, social support and quality of life.

Results: In total five patients in the CR group completed the CR programme within the study timeframe and 80% of patients in the non-CR group returned the questionnaires. None of the CR group quality of life scores were found to be statistically significant following CR. There was a reduction between pre and post questionnaire median scores in components “quality of life” (12.5%), “daily activity” (12.5%), and “physical fitness” (25%). A reduction of 14.29% was observed in the CR group depression scores, however differences in both anxiety and depression scores were not found to be significant (p=0.680, p=0.06 respectively). Post CR scores and non-CR group quality of life scores were not significantly different.

Conclusion: This exploratory study identified areas of quality of life where younger ICD patients experience problems and how CR may assist them in their initial recovery after ICD implant. A reduction was found in depression scores following CR, however it is not clear whether CR improves quality of life for this population. There may be scope for specific ICD follow up in the future as these patients currently have access to specialist advice from healthcare professionals within Cardiology.
P3634 | BEDSIDE
Effects of rehabilitation on endothelial function assessed through changes in nitric oxide metabolism and hypertensive response to exercise in patients with stable coronary artery disease

Purpose: To evaluate the effects of cardiovascular rehabilitation on the endothelial function, assessed through changes of circulating blood markers of endothelial function: the stable end product of Nitric oxide (NOx) and Xanthine Oxidase (XO); and on the levels of Unc Acid (UA), and its association with hypertensive response to exercise in patients with stable coronary artery disease.

Design and methods: 90 pts with stable CAD (59.41±5.62 years, all men), admitted at residential rehabilitation center, were studied. All patients underwent 3 weeks supervised comprehensive rehabilitation program. At baseline and after 3 weeks in all pts values of NOx, XO and UA were determined and exercise test was performed.

Results: After 3 weeks NOx increased (from 291.53±63.43 to 200.32±43.56 μmol/l, P<0.005) with mean decrease 91.21±36.13 μmol/l. Exercise capacity increased from 5.64±1.43 to 6.66±2.26 METs (mean increase was 1.01±1.43 METs), and SBP per minute changes during the first exercise test were 4.75±0.25 mmHg/min. Value of mean per minute changes during the second exercise test, at the level on which the first exercise test was ended was 3.66±1.95 mmHg/min (P=0.001, mean decrease 1.08±2.84 mmHg/min). A positive correlation was found between mean increase in NOx and mean decrease in UA (r=0.626, p<0.0005), as well as between mean increase in NOx and mean decrease in XO (r=0.700, p<0.0005). A positive correlation was also found between mean decrease in SBP per minute and mean NOx increase (r=0.808, p<0.0005) as well as between mean decrease in SBP per minute and mean decrease in UA levels (r=0.564, p<0.0005).

Conclusion: Cardiovascular rehabilitation induced improvement in endothelial function in patients with stable CAD, expressed through significant increase of NOx and significant decrease of XO; also significant decrease in UA and significant improvement in exercise capacity was achieved. Our results show an association between per minute changes during exercise test and changes in markers of endothelial function. Beneficial changes in NOx, XO and UA may induce favorable changes in vascular tone, and hence they might contribute to endothelial function improvement and SBP regulation during exercise.

P3635 | BEDSIDE
Avoiding unplanned admissions for patients with chronic pain of cardiac origin: analysis of the impact of the Liverpool Angina Management Programme
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Purpose: To assess the impact of the CB-CDMP on unplanned admissions in patients with stable coronary artery disease.

Methods: Of sixty six patients registered with the particular CCG were sent per-patient data to the CB-CDMP for all unplanned admissions identified as ICD-10 defined angina or chest pain unplanned admissions in the 360 days pre or post first presentation at the CB-CDMP. Reduction in frequency and duration in days of these unplanned admissions was calculated as 63.5% (p<0.01) and 78.1% (p<0.01) respectively. Reduction in frequency of unplanned admissions was significantly associated with cardiac misconceptions (p<0.01).

Conclusions: Analysis of the impact of the CB-CDMP demonstrates a significant reduction in frequency and duration of patients’ unplanned admissions. The CB-CDMP has an important role to play in meeting national and local targets for reducing unplanned admissions.

P3636 | SPOTLIGHT
Seasonal difference in angina attacks in patients with vasospastic angina
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Background: Patients with stable angina due to coronary artery atherosclerosis often suffer angina attack when they are in cold weather. On the other hand, there is little information about seasonal difference in angina attacks in patients with vasospastic angina, although cold pressor test is used to provoke vasospasms. The present study evaluated seasonal difference in angina attacks in patients with vasospastic angina.

Methods: Between April 2012 and December 2014, acetylcholine provocation test (ACh) was performed in 269 patients. They were divided into 4 groups according to seasons when ACh provocation test was performed: 1) spring (March to May), n=54; 2) summer (June to August, n=83); 3) autumn (September to November, n=68); and 4) winter (December to February, n=54).

Results: There were no significant differences in age, gender, and risk factors of coronary artery disease among 4 groups. Positive ACh provocation test was observed more frequently in winter compared to spring, summer, and autumn (72.2% vs. 46.2% vs. 45.2% vs. 39.7%, p<0.001). Multivariate analysis showed winter as an independent predictor of positive ACh provocation test (odds ratio CI: 2.74 [1.51–5.05]).

Conclusions: Angina attacks in not only patients with stable angina due to coronary artery atherosclerosis but also those with vasospastic angina may be observed more frequently in winter.

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P3637 | BEDSIDE
Eastern European immigrants with ischemic heart disease in southern Europe: Cardiovascular profile and risk of events
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Introduction: Previous studies have suggested a higher cardiovascular risk of eastern Europeans as compared to southern population in Europe. Genetic factors but also environmental and dietetic contributors could be behind this epidemiological profile.

Objective: We aimed to describe the profile, clinical presentation, degree of coronary disease and in-hospital outcomes of immigrants from eastern Europe undergoing coronary angiography, and compare them with patients in southern Europe. Conclusions: All patients from eastern Europe had worse outcomes than patients from the southern Europe. This higher risk may be explained by a seasonal difference in angiography between 2008 and 2014 because of heart failure, stable angina or acute coronary syndrome (ACS) were included. These presenting coronary artery disease (n=145) were compared with a cohort of patients in southern Europe consecutively admitted with the same syndromes within the same period (n=146).

Results: Mean age of immigrants from eastern Europe was 51±11 years and 83% were males. Clinical presentation was: STEMI 45%, NSTEMI 39%, stable angina 12%, and heart failure 4%. Coronariography showed left main disease in 3%, three vessels in 15%, proximal LAD in 32%, and RCA in 93%. Angioplasty was performed in 88% and coronary artery bypass graft in 10%, with complete revascularization in 68% patients, and in-hospital mortality of 0%. Compared to non-selected patients, eastern European patients were younger (51±11 vs 69±11 years, p<0.001), with less hypertension (48 vs 60%, p<0.041) and diabetes (19 vs 28%, p=0.063), and less heart failure (62 vs 21%, p<0.001), family history of ACS (4 vs 10%, p=0.044), LDL-cholesterol (117±35 vs 107±38mg/dl, p=0.047), and triglycerides (190±94 vs 140±88mg/dl, p<0.001) despite similar rate of former diagnosis of coronary artery disease. Compared to the 4 groups, Positive ACH provocation test was more frequent (44 vs 32%, p<0.036), but no differences in extension and severity of coronary disease or revascularization technique (surgical or percutaneous) were found. Drug-eluting stents were implanted less frequently (33 vs 59%, p<0.001). No differences in in-hospital complications, remaining LVEF, or in-hospital mortality were found.

Conclusion: Immigrants from eastern Europe in our environment present similar coronary disease compared to unselected patients, but at a younger age. Underdiagnosed risk factors as hypertension or dislipidemia, family history, and three times higher smoking rate led to a higher proportion of STEMI. However, in-hospital outcomes were similar maybe due to their younger age. Long-term outcomes will be reported at the congress.
CARDIOVASCULAR REHABILITATION: INTERVENTIONS AND OUTCOMES I

P3638 | BEDSIDE
Twelve weeks of successful smoking cessation therapy with varenicline improved spirometric lung age
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Purpose: Cigarette smoking makes an accelerated decline in forced expiratory volume in one second (FEV1), and a low FEV1 predicts morbidity and mortality from smoking-related illnesses including cardiovascular disease. There is extensive evidence that smoking cessation slows down the accelerated decline in FEV1 in smokers and improves pulmonary function. However, smoking cessation fails to improve lung function and the other lung parameters in smokers with chronic obstructive pulmonary disease (COPD) and emphysema. In obese subjects with COPD and emphysema, smoking cessation therapy with varenicline improves spirometric lung age. In this study, we evaluated the short-term effects of smoking cessation therapy with varenicline on respiratory function.

Methods: Participants included 93 consecutive subjects who received 12 weeks of smoking cessation therapy. All subjects were treated with varenicline, and no changes were made to their medications during treatment. At first and last visits, physical examination and spirometry was performed. Spirometric lung ages were calculated by the formula using height and FEV1 developed by Morris and related to years of smoking for the remaining patients who achieved weight and carbon monoxide-confirmed 4-week continuous abstinence, included 72 subjects, whereas the failure group, comprising those who did not achieve complete smoking cessation, included 21 subjects. The number of cigarettes consumed per day was reduced in all subjects in the failure group.

Results: Spirometric lung ages significantly improved from baseline to 12 weeks in the success group (61.5±20.0 vs. 59.3±19.4 mg/dL, respectively, p<0.01); however, spirometric lung ages significantly deteriorated in the failure group (62.9±20.1 vs. 65.7±21.3 mg/dL, respectively, p<0.01). The effect sizes (Cohen’s d) of spirometric lung age in the success and failure group were 0.35 and 0.84, respectively.

Conclusion: These findings suggest that successful smoking cessation therapy with varenicline improves spirometric lung age in the short term.

P3639 | BEDSIDE
Intensive aerobic exercise training on 3 days/week compared to 5 days/week in patients with coronary artery disease: Is less more?
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Background: Exercise training has been well documented to reduce cardiovascular disease (CVD) risk factors and improve capacity in patients with CAD. Despite effective established in cardiac rehabilitation programs, Studies comparing interval training and continuous training observed similar improvements in peak VO2. However, data are still lacking about the optimal exercise training extent. The aim of the study was to elucidate the impact of regular physical exercise on VO2 peak.

Methods and results: A total of 100 patients with CAD (mean age 66±7.3 years, 86% male) were randomly assigned to 4-week exercise training on 5 days per week (Monday-Friday) or 3 days per week (Monday/Wednesday/Friday) at our institution (moderate condition, 70–75% of peak heart rate). Primary study endpoint was the change of aerobic exercise capacity (relative maximum oxygen uptake, VO2 max) compared to 3 days/week for 4 weeks on aerobic exercise capacity in patients with CAD.

Results: Spirometric lung ages significantly improved from baseline to 12 weeks in the success group (61.5±20.0 vs. 59.3±19.4 mg/dL, respectively, p<0.01); however, spirometric lung ages significantly deteriorated in the failure group (62.9±20.1 vs. 65.7±21.3 mg/dL, respectively, p<0.01). The effect sizes (Cohen’s d) of spirometric lung age in the success and failure group were 0.35 and 0.84, respectively.

Conclusion: These findings suggest that successful smoking cessation therapy with varenicline improves spirometric lung age in the short term.

P3641 | BEDSIDE
The role of the individual hospital in adherence to medical guidelines after acute myocardial infarction
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Background: Adherence to pharmacotherapy guidelines after acute myocardial infarction (AMI) is not satisfactory, and studies concerning causes are insufficient. The data from Danish registries and audits concerning the implementation of guidelines and their adherence are mostly restricted to AMI survivors 30 days after an AMI in 2009–2012 identified. Information on medication use was obtained from a national register of prescriptions. Hospitals were analyzed individually and in groups depending on hospital characteristics: (a) location, determined by Danish main regions, (b) hospital size, according to AMI incidences, and (c) degree of specialization, determined by whether the hospital offers specialized cardiac functions. Multi-variable logistic regression was used to analyze treatment initiation of all three recommended drugs.

Conclusion: ACCES compared with controls, engaged twice as many patients in terms of adjusted odds of reporting standard of care to improve in and post-hospital care. This increase in service utilisation was achieved with no additional staffing. These findings have important implications for the many CR programs with limited staff resources or relatively low levels of uptake.

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P3642 | BEDSIDE
Comparison between moderate-high exercise and continuous exercise in a real-life cardiac rehabilitation setting - nine months follow-up

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It has been postulated that interval training is superior to the traditional continuous training in cardiac rehabilitation (CR). Yet, most of the studies included only heart failure patients with relatively small sample sizes and diverse training methodologies that are not always in concordance with real-life CR settings.

The purpose was to compare the outcomes between interval and continuous training in functional capacity, cardiac risk factors, quality of life, LV systolic and diastolic functions, respiratory muscle symptoms and exercise over 6 months follow-up. Methods: Following a 4-week adaptation to exercise period, eighty-four coronary artery disease patients were recruited and randomly assigned to an interval exercise group (IE) or a continuous exercise group (CE). Measurements were obtained at baseline, after 12 weeks of training, and at 9 months. Functional capacity was obtained by the oxygen consumption (VO2max) exercise test. Patients attended the CR twice a week for 60 minutes. Exercise intensity relied on the VO2peak and rating of perceived exertion (RPE).

Results: Both groups increased their VO2peak significantly after training with no differences between them. Maximal load improved more notably in the IE group (11% vs 9%, p<0.01) compared to the CE group (4.8%, p<0.05). Both groups demonstrated reductions in weight, body mass index, and resting heart rate. Glycosylated Hb decreased significantly within the IE group only. Both groups improved QOL variables substantially but similarly. The calculated left ventricular ejection fraction (LVEF) was significantly increased over time among all patients. No cardiac events were registered during the intervention, and no differences between the groups were noticed in cardiac symptoms. At 9 months no differences were observed between the groups. However, regardless of group affiliation, patients who had started in the CR maintained the physiological adaptations while patients who had left the program demonstrated reduced cardiopulmonary performance. Patients maintaining physical activity, further improved their LVEF (p<0.05).

Conclusion: Interval training in a real-life CR setting can produce similar cardiopulmonary, weight, QOL, and LV diastolic and systolic function benefits as continuous training. Regardless of training methods it seems that a prolonged CR program and exercise is more effective in preserving the benefits.

P3643 | BEDSIDE
Short term inspiratory muscle training associated with combined aerobic and resistance training is beneficial in patients undergoing CABG surgery in phase II cardiac rehabilitation program

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Background: The inspiratory muscle training (IMT) program has been the subject of several studies in the clinical setting of phase I cardiac rehabilitation. However, the efficacy of short-term inspiratory muscle training associated with combined aerobic and resistance training results in improvement in inspiratory muscle strength and functional capacity in patients undergoing CABG surgery in phase II cardiac rehabilitation program is largely unexplored and deserves further investigation.

Purpose: To investigate the efficiency of short-term IMT associated with combined aerobic and resistance training on respiratory muscle strength, functional capacity, and quality of life in patients undergoing CABG surgery participated in a phase II cardiac rehabilitation program.

Methods: Twenty-four patients undergoing CABG surgery were randomly assigned to a 12-week IMT program associated combined aerobic and resistance training (IMT + AE + RT, n=12) or to combined aerobic and resistance training (AE+RT, n=12). Before and after intervention, the following measures were obtained: maximal inspiratory and expiratory pressures (PImax and PEmax), peak oxygen uptake (VO2peak), and quality of life scores. For statistical analysis, Student t test and Chi-square test were used (p<0.05).

Results: Compared to AE+RT, IMT program associated aerobic and resistance training resulted in significantly large increments in PImax (p<0.001), PEmax (p<0.001), VO2peak (p<0.001) and quality of life scores (p<0.001).

Conclusions: The present study demonstrated that the addition of short-term IMT program possibly potentiated the effects of combined aerobic and resistance training and could be a potentially strategy in patients undergoing CABG surgery in phase II cardiac rehabilitation program. The clinical significance of these findings should be addressed in larger randomized trials.

P3644 | BEDSIDE
Effects of inspiratory muscle training in patients with atrial fibrillation

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Background and purpose: It has been previously shown that the specific inspiratory muscle training resulted in increased functional capacity, inspiratory muscle strength and endurance in patients with congestive heart failure. The aim of this study was to investigate the effects of inspiratory muscle training on pulmonary functions, functional capacity, quality of life and depression in patients with atrial fibrillation.

Methods: Thirty three patients with atrial fibrillation were participated to the study. Patients were randomly divided into two groups. Seventeen patients (training group) received inspiratory muscle training with Threshold IMT device for three months. Training was applied for 7 days/week, twice-daily for 15 minutes with intensity at 30% of maximal inspiratory pressure (MIP). Sixteen patients were in control group and received standard medical treatment only. Patients were evaluated with spirometer for pulmonary functions; mouth pressure device for respiratory muscle strength; six-minute walk test for functional capacity; SF-36 and Minnesota Living with Heart Failure questionnaires for quality of life and Beck Depression Inventory for depression at the beginning and at the end of the study.

Results: After the training, there was a significant improvement in MIP (p<0.0001), maximal expiratory pressure (MEP) (p<0.0001), FEV1 (p<0.0001), FEV1/FVC (p<0.002), FEF0.06 (p<0.0001), FEF0.01 (p<0.0001) and six-minute walk distance (p<0.0001) values in the training group. Physical (p=0.002) and mental dimension (p=0.0005) scores and all subgroup scores, except "bodily pain", in SF-36 index were improved. Minnesota Living with Heart Failure Questionnaire and Beck Depression Index scores were also improved in comparison to control group (p=0.0001).

Conclusion: In conclusion, inspiratory muscle training can improve pulmonary functions, respiratory muscle strength, functional capacity, quality of life and depression in patients with atrial fibrillation.

P3645 | BEDSIDE
Effects of home-based training with telemonitoring guidance in low to moderate risk patients entering cardiac rehabilitation

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Introduction: Home-based exercise training in cardiac rehabilitation (CR) has the potential to improve CR uptake and decrease costs of CR. In addition, patients are expected to develop self-management skills during home-based CR, which will help them maintain an active lifestyle. The FIT@Home study evaluates physical fitness and physical activity levels after home-based CR with telemonitoring guidance. In this interim analysis we discuss the long-term results of home-based CR on physical fitness.

Methods: This randomized controlled trial compared the long-term effects of a 12-week home-based (HB) training program with 12-week centre-based (CB) training program in low to moderate risk patients entering CR. The home-based group (n=45) received three supervised training sessions before they started training with a heart rate monitor in their home environment. They received individual coaching by telephone based on objective training data uploaded on the Internet. The CB group (n=45) received regular exercise of similar duration and intensity under direct supervision of a physical therapist. Physical fitness was assessed by a cardiopulmonary exercise test at baseline, 12 weeks and 1 year.

Results: Preliminary short term results show that exercise adherence of the HB group (n=36) was similar to the supervised CB group (n=40) in the first 12 weeks (HB: training frequency of twice a week, intensity of 73.6% of HRmax). Patients in the HB and CB group showed a significant improvement in peakVO2 after 12 weeks training (14% and 11% respectively), without significant between-group differences (p=0.75). By February 2015, 34 patients (HB=17; CB=17) had completed the long term assessment of physical fitness. In both groups, physical fitness levels were maintained one year after the start of CR, without a significant difference between groups (p=0.52).

Conclusion: This study shows that HB training with telemonitoring guidance has similar short-term effects on physical fitness as regular CB training in CR patients. Although data from only 34 patients were available, long term analysis indicate that both groups were able to maintain their physical fitness levels. This study demonstrates that home-based cardiac rehabilitation is an effective alternative compared to regular centre-based training for low to moderate cardiac risk patients.
Conclusion: We propose an algorithm to calculate the success of CRP therapeutically, with antithrombotic therapy (p=0.003 and p=0.003, respectively) and of patients in Group 1 and Group 2 taking statins (p=0.007 and p=0.02, respectively). The number of patients treated with ACE inhibitors/ARBs remained at the same level (from 97% to 82%, p=0.001) also decreased significantly in Group 2 with HBWT.

Methods: We identified 6 indicators of performance referring to current guidelines: heart rate (HR) <70 beats/min, blood pressure (BP) <140/90 mmHg, smoking cessation or non-smoker (SMK), left ventricular ejection fraction (LVEF) >40%, LDLc <100 mg/dl or <70 mg/dl if diabetic, on treatment with at least 3 drugs among ACE inhibitors or ARBs, Betablockers, Statins and ASA. To assess the relative contribution of each indicator in the definition of CR performance, we fitted a structural equation model employing “Stata 13” system.

Results: 839 consecutive patients (68% male, aged 69±11) included in our registry from 2009 and 2010, were analyzed. 49% had recent STEMI/NSTEMI and among ACE inhibitors or ARBs, Betablockers, Statins and ASA. Weights for each indicator in the PERFScore were 0.57 for HR, 0.40 for BP, 0.87 for LVEF, 0.57 for SMK, 0.42 for LDLc and 0.75 for drugs, multiplied by 1 if the target has been reached, otherwise by 0. The range is 0–36.

Conclusion: We propose an easy algorithm to calculate the success of CRP that could help the cardiologist to achieve therapeutic goals.

P3647 | BEDSIDE
Home-based walking training and adherence to medical therapy in patients undergoing coronary artery bypass grafting
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Aim: To evaluate the effects of home-based walking training on adherence to medical therapy in patients who have undergone coronary artery bypass grafting.

Material: 112 patients (mean age 56.8±5.5 years) with coronary artery disease (CAD), who have undergone CABG, were examined. One month after CABG (after supervised outpatient program), patients were enrolled into three groups, comparable in demographic and clinical characteristics: Group 1 with supervised cycling training (SC) (n=35), Group 2 – home-based walking training (HBWT) (n=36) and the comparison group (n=36). Subjects did 3 trainings per week for 3 months. Patients were examined 1 month and one year after CABG.

Methods: Echocardiography (ECHO-CG), bicycle ergometer (BE) and the assessment of adherence to medical therapy in patients undergoing coronary artery bypass grafting.

Results: One year after surgery the number of patients receiving β-blockers (from 97% to 80%, p<0.005), antithrombotic therapy (from 100% to 88%, p=0.0004) and statins (from 97% to 82%, p<0.0005) decreased in Group 1 with SC. The number of patients treated with ACE inhibitors/ARBs remained at the same level (73% and 75%, p=0.693). The number of patients treated with β-blockers (from 97% to 90%, p=0.001), antithrombotic therapy (97% to 82%, p<0.01) and statins (from 98 to 82%, p=0.001) also decreased significantly in Group 2 with HBWT. The number of patients treated with ACE inhibitors/ARBs decreased from 77 to 66%, p=0.005. A more significant decrease in the number of patients treated with β-blockers (from 100% to 70%, p=0.0001), antithrombotic therapy (from 100% to 64%, p=0.0001) and statins (from 98 to 57%, p=0.00001) was observed in the comparison group. The number of patients treated with ACE inhibitors/ARBs also tended to decrease (from 75% to 65%, p=0.07). Importantly, the number of patients in Group 1 and Group 2 taking statins (p=0.007 and p=0.02, respectively), antithrombotic therapy (p=0.003 and p=0.003, respectively) and β-blockers (p=0.01 and p=0.04, respectively) was significantly higher compared to the patients in the comparison group.

Conclusion: Home-based walking trainings have low effect on adherence to medical therapy, compared to supervised cycling programs. Thus, they are more effective compared to the results of patients without any physical training programs.

P3648 | BENCH
Inspiratory muscle training and aerobic training present similar effects on blood pressure and cardiovascular autonomic control in hypertensive patients
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Background: Inspiratory muscle training (IMT) and Aerobic training (AT) lead to beneficial effects on the cardiovascular autonomic control, reducing sympathetic modulation and blood pressure levels in hypertensive patients. However, the effects of both interventions have never been compared in this population.

Objective: We sought to observe autonomic cardiovascular control and blood pressure in hypertensive patients after IMT and AT protocols.

Methods: Hypertensive patients were randomized to perform 12 wks IMT (7 days/wk, 30 min/day, at 30%PImax) or TA (treadmill, 2 days/wk, 60 min/day, at 70% HRmax). Ambulatory blood pressure monitoring, spectral analysis of blood pressure and heart rate variability and microencephrography for assessment of muscle sympathetic nerve activity (MSNA) were performed.

Results: After 12 weeks of intervention, we observed reduction of SBP (IMT: 119±10.01 vs 112±1.5 mmHg, AT: 123±14.84 vs 118±7.77 mmHg) and DBP (IMT: 70±9.00 vs 67±8.9 mmHg, AT: 75±6.49 vs 72±7.04 mmHg). A significant reduction in total blood pressure was also observed (IMT: 192±15.2 vs 185±13.1 mmHg, AT: 197±14.0 vs 191±12.5 mmHg).

Conclusions: Both interventions showed beneficial effects on patients with hypertension, by reducing blood pressure levels, cardiac sympathetic modulation and peripheral sympathetic activity. So, we believe the effects of IMT and AT are similar in hypertensive patients and both interventions may be used in the treatment of hypertension, reducing complications this population.

P3649 | BEDSIDE
Five-repetition sit-to-stand test in heart failure patients. Reliability and correlation with the Six Minutes Walking Test
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Background: Five-repetition sit-to-stand test (5STS) is a test of lower limb function that measures the fastest time taken to stand five times from a chair with arms folded. The 5STS has been validated in healthy community-dwelling adults, in chronic obstructive pulmonary disease population, but not in chronic heart failure patients.

Objective: To determine the reliability of the 5STS and compare with six minute walk test (6MWT), a consolidated test of functional capacity and prognosis, in CHF pts during a cardiac rehabilitation program (CR)

Methods: 13 admission and at the end of the CR (last 15±8 days) 24 stable CHF pts (71% male, left ventricular ejection fraction 33±12%, mean age 66±13 yrs, 62% with non-ischemic cardiomyopathy) performed the 5STS and the 6MWT. Data on Body Mass Index (BMI) and EuroQol score as quality of life index were collected. During the tests pulse oxygen saturation (SpO2), heart rate and systolic blood pressure were measured. Rate pressure product (RPP) was calculated. In addiction severity of dyspnea and fatigue was assessed using the Modified Borg Scale. During hospitalization moderate intensity expenditure physical training program was performed.

Results: All pts were able to perform both 5STS and 6MWT. Comparing the admission with the pre-discharge tests a significant increase in 6MWT distance (370 vs 420 m, p=0.00001) without decrease in maximum RPP (10950 vs 10944 p=0.48) was recorded. A mild decrease in time for 5STS (13.9 vs 12.4 sec, p<0.11) and a significant decrease in maximum RPP (9558 vs 8967 p<0.0001) were documented. Maximum RPP was significantly lower in 5STS in comparison with 6MWT both in the test performed at the beginning and at the end of the CR (10950 vs 9558, p=0.0001; 10944 vs 8967, p=0.0001). Similarly, SpO2 and dyspnea and fatigue score according to Borg scales were reduced during 5STS compared with 6MWT (SpO2 95.8% vs 96.8%, p=0.03, Borg Fatigue 2.8 vs 1.57, p=0.01, Borg Dyspnea 1.9 vs 0.33 p=0.03). A significant inverse correlation between 5STS time and 6MWT distance was found (r=-0.71). During CR significant decrease in BMI (24.15 vs 23.7 70 beats/min, blood pressure (BP) <140/90 mmHg, smoking cessation or non-smoker (SMK), left ventricular ejection fraction (LVEF) >40%, LDLc <100 mg/dl or <70 mg/dl if diabetic, on treatment with at least 3 drugs among ACE inhibitors or ARBs, Betablockers, Statins and ASA.

Conclusions: Data demonstrate that 5STS is easy to perform and reliable in stable CHF pts. It induces less hemodynamic and respiratory stress compared to 6MWT. The correlation with 6MWT suggests a potential capacity of 5STS to determine functional status in CHF patients who are not able to perform 6MWT. Further studies are needed to validate the 5STS in CR setting.
Angiographic characteristics

Conclusions: Cardiac remote telemetry is a useful diagnostic tool in cardiac rehabilitation program, especially in patients after surgery in whom paroxysmal atrial fibrillation is common disorder. Our response time to emergencies is immediate.

P3650 | BEDSIDE
Impact of a cardiac rehabilitation programme on mortality and cardiovascular events after a percutaneous coronary intervention in patients with multivessel disease and incomplete revascularization

Hospital Universitario Virgen de Valme, Cardiology, Seville, Spain

Background: Multivessel coronary artery disease and incomplete revascularization is one of the most serious conditions in ischaemic heart disease. Although the benefit of cardiac rehabilitation programmes in patients with ischaemic heart disease after an acute event is recognised, it has never been studied in this subgroup of patients.

Purpose: Analyse the effect of a cardiac rehabilitation programme on long-term all-cause mortality and cardiovascular morbidity and mortality in patients with multivessel disease and incomplete percutaneous revascularization.

Methods: We performed a retrospective cohort study of 401 patients undergoing a percutaneous coronary intervention at our hospital between January 2006 and December 2010. We compared the course of individuals who followed a three-month cardiac rehabilitation programme (n=130) to patients not included in the programme (n=271), with a 2-year follow-up.

Results: Participation in these programmes is associated with a significant reduction in all-cause mortality (RR 0.273; 95% confidence interval [95% CI], 0.131–0.571; p<0.001) and coronary mortality (RR 0.571; 95% CI 0.112–0.657; p=0.002) as well as a no significant reduction in non-fatal acute myocardial infarction (RR 0.947; 95% CI 0.576–1.556; p=0.947) and restenosis of previously treated lesions (RR 0.831; 95% CI 0.429–1.611; p=0.583).

Descriptive characteristics

Conclusions: Our study shows that in patients with multivessel coronary artery disease and incomplete revascularization, a comprehensive cardiac rehabilitation programme is associated with a significant reduction in cardiac mortality and in all-cause mortality rates.

P3651 | BEDSIDE
Importance of in-hospital remote telemetry in cardiac rehabilitation units. Our centre experience

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Introduction: Cardiac rehabilitation helps heart patients re-cover quickly and improve their overall physical and mental functioning. A critical component of every cardiac rehab pro-gran is the monitoring of the patient’s ECG signal during exercise. Cardiac remote telemetry is the transmission of cardiac signals from a patient to a distant receiving location with a goal of rhythm monitoring to ST segment monitoring and sophisticated arrhythmia detection and diagnosis under surveillance of trained personal.

We aimed to investigate the usefulness of cardiac telemetry in patients’ admitted after coronary artery by pass surgery (CABG) or percutaneous coronary intervention (PCI) in our in-hospital cardiac rehabilitation center.

Materials and methods: Out of 2276 patients admitted for in-hospital cardiac rehabilitation, we studied two hundred eighty nine patients with previous CABG (53%) or PCI (47%), 62% males, aged from 26 to 83. Risk factors were noted, blood was sampled for analyses. Exercise test were performed on admission and after 21 days of in-hospital rehabilitation. According to the first test results patients were selected for exercises program: free walking, cycle and/or Nyllin steps. Duration of physical activity was measured after 21 days of in-hospital rehabilitation.

We aimed to investigate the usefulness of cardiac telemetry in patients’ admitted after coronary artery by pass surgery (CABG) or percutaneous coronary intervention (PCI) in our in-hospital cardiac rehabilitation center.

Results: Participation in these programmes is associated with a significant reduction in all-cause mortality (RR 0.273; 95% confidence interval [95% CI], 0.131–0.571; p<0.001) and coronary mortality (RR 0.571; 95% CI 0.112–0.657; p=0.002) as well as a no significant reduction in non-fatal acute myocardial infarction (RR 0.947; 95% CI 0.576–1.556; p=0.947) and restenosis of previously treated lesions (RR 0.831; 95% CI 0.429–1.611; p=0.583).

Descriptive characteristics

Conclusions: Cardiac remote telemetry is a useful diagnostic tool in cardiac rehabilitation program, especially in patients after surgery in whom paroxysmal atrial fibrillation is common disorder. Our response time to emergencies is immediate.

P3652 | BEDSIDE
Case management in patients after TAVI: are frailty and exercise capacity predictors for decision making process?

H. Vollier1, S. Eichler1, A. Harnath2, W. Kamke3, C. Butter1, M. Krahe3, M. Schikora1, J. Jachczyk1, A. Salzwedel1, 1University of Potsdam, Center of Rehabilitation Research, Potsdam, Germany; 2Sana Heart Center Cottbus, Cottbus, Germany; 3Medizinische Klinik Reha-Zentrum in Berlin, Germany; 4Brandenburg Heart Center, Bernau bei Berlin, Germany; 5Brandenburg Klinik Bernau bei Berlin, Germany

Purpose: For a decade, transcatheter aortic valve implantation (TAVI) has become a promising treatment modality. Up to now, there are no sufficient data about postinterventional treatment pathways. Therefore, we aimed to evaluate predictors for referring pat. to cardiac or geriatric rehabilitation (CR/GR). Additionally, the effect of the intervention itself and of CR on exercise capacity is investigated.

Methods: Since 10/2013, pat. with an elective TAVI are enrolled in the prospective multicentre registry. Conventionally, further pathways of patients are recorded. We documented sociodemographic, laboratory and echocardiographic parameters like LVEF, and comorbidities (e.g. stroke, renal failure). Functional testing (6-Minute-Walk-Test [6MWT], exercise stress test and Frailty-Index including frailty assessment of Daily Living Activities [FADL], State Exam, Mini Nutritional Assessment, Timed Up and Go, and a subjective pre-clinical mobility disability) were performed preinterventionally. In addition, CR was tested at admission and to discharge from CR.

Results: Up to 12/2014, 222 patients (60.6±1.5 years, 45.5% male) with EF 52.7±11.9% and NYHA III/IV 213 (96.4%) were enrolled. 212 (95.5%) underwent transfemoral and 10 (4.5%) transapical intervention. A pathologic Frailty-Index (>3 points) emerged in 110 of 204 (53.9%) patients. After TAVI, 126 (56.8%) patients were referred to CR and 36 (16.2%) to GR. 32 (14.4%) patients were discharged home and 28 (12.6%) were either transferred into a hospital, died or couldn’t be figured out. CR, GR and home group differ in preinterventional frailty (Frailty-Index >3 in 43.7% 4/15.7%, p<0.005) and in 6MWT at admission of CR compared to the preinterventional measurement (46.3±9.69 m 95% CI 24.2 - 68.5; p<0.001) and during CR (56.0±7.35m 95% CI 39.7 − 72.4; p<0.001). Exercise capacity is significantly improved by 0.15±0.22W/kg (p<0.001) during CR

Conclusions: The preliminary results of the TAVI registry provide information about the treatment pathways of patients after TAVI. More than two thirds of the patients are referred to rehabilitation for preventing nursing care. In this context, 6MWT and the Frailty-Index seem to be meaningful assessments for targeted assignment to further care. Furthermore, a benefit in exercise capacity for the CR patients results in the independence of long-term care.

P3653 | BEDSIDE
Cardiopulmonary exercise testing is predictive of return to work in cardiac patients after multicomponent rehabilitation

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Introduction: Return to work (RTW) is a pivotal goal of cardiac rehabilitation (CR) in patients after acute coronary syndrome or elective cardiac surgery. We therefore aimed to evaluate cardiopulmonary exercise testing (CPX) parameters as predictors for RTW at discharge after CR.

Methods: We analysed data from a prospectively collected registry of 489 working-age patients (51.5±9.8 years, 87.9% men) who had undergone inpatient CR between 06/2009 and 12/2011, predominantly after percutaneous coronary intervention (PCI, 62.6%), coronary artery bypass graft (CABG, 17.2%), or heart valve replacement (9.0%). Sociodemographic and clinical parameters, noninvasive cardiac diagnostic (2D echo, exercise electrocardiogram, 6MWT) and psychodiagnostic screening data, as well as CPX findings were compared with RTW data from the German statutory pension insurance program and analysed for prognostic ability.

Results: During a mean follow-up of 26.5±11.9 months, 373 (76.3%) patients returned to work, 116 (23.7%) did not, and 60 (12.3%) retired. Comorbidities (p=0.011) and physically heavy work (p=0.001) were negatively associated with RTW, whereas a higher exercise capacity at entry into CR (p=0.001) and effective PCI (p=0.02) increased the probability of RTW. After adjustment for covariates, maximum work load (in Watts) at CPX termination and the VE/VCO2-slope (pulmonary ventilation during exercise divided by the rate of carbon dioxide elimination) were the independent predictors of RTW. A higher work load increased the probability of RTW, while a higher VE/VCO2-slope decreased it (p=0.027) i.e. CPX even had prognostic value for retirement: the likelihood of retirement decreased with increasing anaerobic threshold (VO2AT) (p=0.016).
Conclusion: FMD is improved after CR in patients with PCI, and this beneficial effect was noted equally on both groups. Our results suggest that improvement of endothelial function is one of the important effect of CR reducing cardiovascular risk in patients with coronary disease.

P3657 | BEDSIDE
Multidisciplinary rehabilitation program in patients with advanced heart failure after cardiac resynchronization therapy

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Introduction: Cardiac resynchronization therapy (CRT) has been proven to improve functional class and systolic function in heart failure patients (NYHA class III-ambulatory IV) and additional cardiac rehabilitation program with exercise training in this high risk group remains to be determined.

Objective: The objective of this program was to assess further improvement of exercise capacity of patients with advanced heart failure after CRT through multidisciplinary cardiac rehabilitation program.

Methods: Twelve patients (5 women and 7 men; mean age 48, ranged 18–70) who received CRT (mean duration of 2.2 months) further completed an 8-week multidisciplinary cardiac rehabilitation program with aerobic exercise training (including 3 sessions/week with a total of 24 sessions & 40 minutes/session on treadmill walking & cycling) plus specific counseling services on heart failure disease with emphasis on patients’ self-management. Cardiopulmonary exercise test (CPET) and six-minute hall walk (6-MWT) were assessed and compared at baseline (before implantation of CRT), after CRT and after rehabilitation respectively.

Results: There were statistically significantly further improvement on the duration (seconds) of the CPET (614±166 to 743±4147, p<0.001), peak VO2 (4.19±1.37 to 5.73±1.53, p<0.001), oxygen pulse (948±3.76 to 10.58±3.36, p<0.05), VE/VCO2 (39.42±8.40 to 36.58±7.82, p<0.05) as well as 6-MWT (meters) (433±58.95 to 494.33±74.77, p<0.001) after the 8-week rehabilitation program. After physicians’ assessment, 4 subjects out of 6 (who were originally on heart transplantation wait list) were grounded into the heart transplantation waiting list due to the improvement of functional class to NYHA class II.

Conclusions: Well prescribed exercise training program specifically designed for heart failure patients who received evidence-based heart failure therapy is bene-

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P3656 | BEDSIDE
Beneficial effect of cardiac rehabilitation on endothelial function in patients who received coronary revascularization

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Background: It is well known that cardiac rehabilitation including exercise training has cardioprotective effects on patients with ischemic heart disease. Endothelial dysfunction can increase the risk of a coronary event. In this study, we investigated whether the endothelial function measured by using flow-mediated dilatation (FMD) was improved after CR in patients who had received percutaneous coronary intervention (PCI).

Methods: Consecutively 119 patients (104 males, mean age: 54.9±9.1 years) who had treated with PCI were included. The patients were divided into 2 sub-groups; 69 patients with acute coronary syndrome and 50 stable angina patients. All patients were examined on the second or third day after PCI, and 6 months from discharge. They received CR after discharge according to the standard exercise protocols which were previously described elsewhere.

Results: There was no significant difference of FMD at baseline (8.1% in angina vs. 7.7% in ACS, p=0.18) and 6 months follow-up (9.2% vs. 8.9%, p=0.61) between the patients with angina and ACS. However, FMD which was measured after 6 months CR was significantly improved on both groups (increase by 1.1% in angina; 95% CI: 0.1–2.0, p=0.03 vs. 1.1% in ACS group; 95% CI: 0.5–1.8, p<0.002). And also, peak oxygen uptake (VO2max) was improved on both groups (increased by 2.1 mL/kg/min in angina; 95% CI: 0.8–3.4, p=0.003 vs. 2.6 in ACS group, 95% CI: 1.1–4.2, p<0.001).

Conclusion: FMD was improved after CR in patients with PCI, and this beneficial effect was noted equally on both groups. Our results suggest that improvement of endothelial function is one of the important effect of CR reducing cardiovascular risk in patients with coronary disease.
P3658 | BENCH

Loaded breathing exercise increases cardiovascular sympathetic modulation acutely in patients with essential hypertension
J. Ferreira1, K.B. Scapini2, F. Santos2, P. Dal Lago3, F.M. Consolim-Colombo2, M.C. Irgoyen2, 1Universidade Federal de Ciências da Saúde de Porto Alegre, Porto Alegre, Brazil; 2Heart Institute, University of São Paulo Medical School, São Paulo, Brazil; 3Federal University of Health Sciences of Porto Alegre, Porto Alegre, Brazil.

Introduction: Inspiratory muscle training (IMT) reduces cardiac sympathetic modulation and blood pressure levels in hypertension. However, there are no reports about the acute effects of one single session of loaded breathing exercises (LBE) in this population.

Objectives: To compare the acute responses of the autonomic cardiovascular control components in patients with essential hypertension and healthy volunteers to a LBE session.

Methods: Hypertensive volunteers (GH) and healthy controls (GC) were recruited to perform a 30 min LBE session, at 30% of maximal inspiratory pressure (PI-MAX). Cardiac rate responses were monitored by oscilometric method and the autonomic modulation was evaluated by spectral analysis. The measurements were performed before and in the first hour after LBE sessions.

Results: One hour after the session, hypertensive volunteers showed increase of blood pressure variance (SD: GC: 51.51±37 vs 47.89±37 mmHg, p=0.85; GH: 4.42±1.61 vs 6.11±45 mmHg, p=0.01), heart rate variance (SD: GC: 51.88±17.15 vs 49.23±17.51, p=0.78; GH: 35.14±7.61 vs 41.42±27.00, p=0.05) and sympathetic peripheral modulation (LF/BS: GC: 14.90±16.51 vs 9.71±9.32 mmHg², p=0.46; GH: 16.07±15.19 vs 27.15±13.56 mmHg², p=0.02) as well as increase of cardiac parasympathetic modulation (HF/BS: GC: 1089.98±816.28 vs 1110.61±1048.16, p=0.96; GH: 667.75±547.43 vs 1079.52±1200.37, p=0.03). In addition, there was improvement of the baroreflex sensitivity (BRR): 56.5±5.4 vs 69.1±12.6, p<0.03 and changes in baroreceptor effective index (BIEB: 0.32 vs 0.27, p=0.01) after LBE, only in the hypertensive group.

Conclusion: Acute responses of the autonomic cardiovascular control components to a loaded breathing exercises session seem to be more evident in populations with impairment of such systems, as in hypertension. Considering the increase of sympathetic modulation is associated to increase of parasympathetic modulation, we believe that the beneficial effects observed after chronic IMT protocols, are obtained from the acute responses to single sessions of LBE.

Acknowledgement/Funding: CNPq

P3659 | BEDSIDE

Effect of long-term home based cardiac rehabilitation programme on recurrent chest pain, and mortality risk after coronary revascularization
E.B. Batamata, A.A. Griveco, S.S. Filimon, D.M. Lisit, L.G. Morov, Institute of Cardiology, Chisinau, Moldova, Republic of

Background: We compared readmission and mortality risk between cardiac revascularization participants (CRP) and nonparticipants.

Methods: A total of n=197 patients (61.5±0.8 years old) were randomized: group 1 – 91 pts; group 2 – 106 CRP performed a training and secondary prevention programme over 12 months. Clinico-functional assessment and the Seattle Heart Failure Model (SHFM) prediction of survival were obtained at baseline and follow-up.

Results: Rehospitalization rate during 12 months period in CRP group was 2.7 times lower than in the control group (29% vs 79%) (table). Only 2.9% and 2.2% of patients were hospitalized for other reasons, but the majority required cardiovascular interventions. Baseline mortality prognosis at one year in non-CRP group was estimated as 6.55% vs 3.35% in CRP group, at two years 12.7% vs 7.21% and 30.1% vs 16.53% at five years. After intervention these parameters were significantly lower.

<table>
<thead>
<tr>
<th>Group 1</th>
<th>Group 2</th>
</tr>
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<tbody>
<tr>
<td>Readmission All cause</td>
<td>19 (21.1)</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>69 (76.7)</td>
</tr>
<tr>
<td>Non-cardiovascular</td>
<td>2 (2.2)</td>
</tr>
</tbody>
</table>

Conclusion: Cardiac rehabilitation participation is associated with a markedly reduced risk of rehospitalization during first year after. 2. Partially supervised rehabilitation program improved long term estimative survival prognosis.

P3656 | BENCH

Implementation of Jacobson’s progressive relaxation in coronary bypass surgery patients before chest tube removal
M.R. Rupar, S. Kostic. Dedine Cardiovascular Institute, Belgrade, Serbia, Rehabilitation, Belgrade, Serbia

Introduction: The purpose of this study was to determine whether the use of a Jacobson progressive muscle relaxation, when used without opioid analgesia, decreases pain during chest tube removal (CTR) after coronary bypass surgery. Methods: A two-group quasi-experimental posttest design was used. A convenience sample of 100 subjects was divided into an experimental group (n=50), who received relaxation training 15 minutes before chest tube removal and a control group (n=50), who did not receive relaxation. All patients received 500mg of paracetamol 30 minutes before relaxation. Pain was assessed with verbal pain score (0–5). Analysis of variance was used to analyze the data.

Results: Significant decreases in pain were demonstrated as a result of implemented relaxation test: 2.63±0.725 vs 3.62±0.725, p<0.001. All experimental subjects stated that the relaxation technique was simple to perform.

Conclusion: This study supports the use of Jacobson progressive muscle relaxation for pain management during CTR among patients who have undergone coronary bypass surgery.

P3661 | BEDSIDE

Prognostic value of endothelial parameters changes during cardiac rehabilitation on recurrent chest pain in patients with coronary artery disease: 30 months follow-up
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Purpose: To evaluate the effects of cardiac rehabilitation on circulating blood markers of endothelial function: nitric oxide (NOx), Advanced Oxidation Protein Products (AOPP), and Xanthine Oxidase (XO), and their prognostic value on recurrent chest pain.

Methods: 47 patients (pts) (57.9±3.6 years, all men) were admitted to cardiac rehabilitation after myocardial infarction (MI). All pts underwent a supervised residential 3-weeks exercise training. At baseline and after 3 weeks of residential exercise training, NOx, AOPP and XO were measured. Clinical long-term follow-up (30 months) was performed. Medical therapy was documented, and for this analysis, we focused on recurrent anginal chest pain.

Conclusion: After 30 months there were no cardiovascular (CV) hard endpoints (CV death, MI, stroke), however 24 pts (51%) had episodes of typical anginal chest pain (AP group) while 23 pts (49%) were without anginal chest pain (no-AP group). During rehabilitation NOx increase in both groups (p<0.0005). The mean NOx increase in no-AP group was higher than in AP group (13.7±10.5 vs 4.03±4.7, p=0.009). AOPP levels were decreased in both groups, with higher mean NOx in no-AP group (27.85±17.59 vs 25.08±4.87, p=0.03) and in AP group (19.3±9.7 vs 17.1±2.8, p=0.03). Conclusion: NOx increase (OR 0.836, CI 0.745–0.938, p=0.02) was predictive of NOx, AOPP and XO were no significant predictors of NOx increase. AOPP and XO were not significant predictors of NOx increase. AOPP and XO were not significant predictors.

P3662 | BEDSIDE

Long-term healthcare costs after myocardial infarction in a clinical practice setting in Sweden: results from a contemporary nationwide registry study

Background: Nationwide data on healthcare costs after myocardial infarction (MI) are not widely studied, in particular beyond first year after MI. The aim was to investigate long-term healthcare costs after MI in a clinical practice setting.

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## IMPROVEMENT OF MEDICAL CARE IN CARDIOVASCULAR PATIENTS: SOCIAL AND ECONOMIC ISSUES

P3660 | BENCH

Implementation of Jacobson’s progressive relaxation in coronary bypass surgery patients before chest tube removal
M.R. Rupar, S. Kostic. Dedine Cardiovascular Institute, Belgrade, Serbia, Rehabilitation, Belgrade, Serbia

Introduction: The purpose of this study was to determine whether the use of a Jacobson progressive muscle relaxation, when used without opioid analgesia, decreases pain during chest tube removal (CTR) after coronary bypass surgery. Methods: A two-group quasi-experimental posttest design was used. A convenience sample of 100 subjects was divided into an experimental group (n=50), who received relaxation training 15 minutes before chest tube removal and a control group (n=50), who did not receive relaxation. All patients received 500mg of paracetamol 30 minutes before relaxation. Pain was assessed with verbal pain score (0–5). Analysis of variance was used to analyze the data.

Results: Significant decreases in pain were demonstrated as a result of implemented relaxation test: 2.63±0.725 vs 3.62±0.725, p<0.001. All experimental subjects stated that the relaxation technique was simple to perform.

Conclusion: This study supports the use of Jacobson progressive muscle relaxation for pain management during CTR among patients who have undergone coronary bypass surgery.
follow-up. CV-related hospitalizations contributed to the majority of these costs.

The study included 97,254 patients, with a total of 315,839 observation days. Results:

The mean 5-year cumulative healthcare costs from year 2 onward were €6,389. High-risk patients had higher healthcare costs both in the first year after MI and in the long-term follow-up. CV-related hospitalizations contributed to the majority of these costs compared with hospital outpatient care visits or drugs (Figure 1).

Conclusion: This nationwide registry study shows that healthcare costs after MI are primarily driven by CV-related hospitalizations, and that risk stratification has a substantial impact on healthcare costs, in particular in a long-term perspective.

Acknowledgement/Funding: Sponsored by AstraZeneca

P3664 | SPOTLIGHT

Bedside and out of hours admission to hospital with acute coronary syndrome confers poorer mortality and longer length of hospital stay

R. Poturi1, H. Uppal1, D. Lavi1, S. Chandran1

1 Astor University, ACALM Study Unit in collaboration with Aston Medical School, Birmingham, United Kingdom; 2 North Western Deanery, Department of Acute Medicine, Manchester, United Kingdom

Introduction - Acute Coronary Syndrome (ACS) is the most common cardiovascular diagnosis requiring hospital admission worldwide and in the UK. It is associated with substantial mortality and healthcare burden. Given the current five day working pattern in the UK, we hypothesise a significant variation in the outcomes of patients admitted with ACS during the standard working hours compared with out of hours and weekends.

Methods: Between 2006–2011, all patients admitted to hospital with ACS were identified using the ACALM (Algorithm for Co-morbidities, Associations, Length of stay and Mortality) study protocol. ACALM uses the ICD-10 and OPCS-4 coding systems to identify patients and the methodology has been used and published widely. Analyses were performed comparing mortality and length of hospital stay between admissions according to the day of the week and core working hours (0900 to 1700 Monday to Friday) and out of these hours.

Results: Of 25,9465 adult patient population there were 25,994 patients with ACS. Mean age 67 years; Male 64.2%. Over the study period, 38.2% of the patients died after ACS during their follow-up period. However, patients admitted on Saturday or Sunday had significantly higher values of 43.3% and 39.9% respectively. Patients admitted outside of the normal working hours had a value of 39.1% compared with 36.5% for patients admitted during working hours. The mean length of hospital stay (LOS) was significantly higher for patient admitted during the standard working hours compared with out of hours (p<0.05).

Table 1. Characteristics of ACS patients according to time of admission to hospital

<table>
<thead>
<tr>
<th>All patients</th>
<th>Patients admitted during normal working hours</th>
<th>Patients admitted out of normal working hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%)</td>
<td>25,994 (100)</td>
<td>10,466 (41.4)</td>
</tr>
<tr>
<td>Mean Age, years</td>
<td>67</td>
<td>67</td>
</tr>
<tr>
<td>Male, %</td>
<td>64.2</td>
<td>63.9</td>
</tr>
<tr>
<td>Number of patients who died during the study period (%)</td>
<td>9,654 (38.2)</td>
<td>3,854 (36.5)</td>
</tr>
<tr>
<td>Mean length of hospital stay (days)</td>
<td>7.0</td>
<td>5.9</td>
</tr>
<tr>
<td>Mean survival period, days</td>
<td>1,861</td>
<td>1,910</td>
</tr>
</tbody>
</table>

Denotes statistical significance, p<0.05.

Conclusion: Day and time of hospital admission confer significant variations in outcomes such as mortality and LOS in patient with ACS. These disparities further fuel the argument for 24/7 specialist care in the UK.

P3665 | BEDSIDE

Improvement in one-year survival after acute myocardial infarction according to socioeconomic position in Chile: the analysis of the period 2002-2011

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University of Chile, School of Public Health, Santiago, Chile

Background: CHD mortality has declined in the last decade. In 2005 acute myocardial infarction (AMI) was admitted to universal health coverage in Chile. To date it is unknown whether the benefit was similar in different socioeconomic groups. AIM: to evaluate changes in survival after AMI according to socioeconomic position (SEP) from 2002 to 2011 in Chile.

Methods: National hospital discharge database of the our Ministry of Health were used to identify all first cases of AMI hospitalized in public and private hospitals between 2002–2011 in Chile (ICD 10, I21-I22). Link with national mortality database were performed comparing mortality and length of hospital stay between admissions according to the day of the week and core working hours (0900 to 1700 Monday to Friday) and out of these hours.

Results: Of 2002–2011 adult patient population there were 25,9294 patients with ACS. Mean age 67 years; Male 64.2%. Over the study period, 38.2% of the patients died after ACS during their follow-up period. However, patients admitted on Saturday or Sunday had significantly higher values of 43.3% and 39.9% respectively. Patients admitted outside of the normal working hours had a value of 39.1% compared with 36.5% for patients admitted during working hours. The mean length of hospital stay (LOS) was significantly higher for patient admitted on Saturday and Sunday and outside of core working hours (p<0.05).

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<th>All patients</th>
<th>Patients admitted during normal working hours</th>
<th>Patients admitted out of normal working hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%)</td>
<td>25,994 (100)</td>
<td>10,466 (41.4)</td>
</tr>
<tr>
<td>Mean Age, years</td>
<td>67</td>
<td>67</td>
</tr>
<tr>
<td>Male, %</td>
<td>64.2</td>
<td>63.9</td>
</tr>
<tr>
<td>Number of patients who died during the study period (%)</td>
<td>9,654 (38.2)</td>
<td>3,854 (36.5)</td>
</tr>
<tr>
<td>Mean length of hospital stay (days)</td>
<td>7.0</td>
<td>5.9</td>
</tr>
<tr>
<td>Mean survival period, days</td>
<td>1,861</td>
<td>1,910</td>
</tr>
</tbody>
</table>

Denotes statistical significance, p<0.05.

Conclusion: Day and time of hospital admission confer significant variations in outcomes such as mortality and LOS in patient with ACS. These disparities further fuel the argument for 24/7 specialist care in the UK.
patients from low SEP. This could be attributed to the implementation of universal health coverage. These results will be useful to evaluating public policies implemented during the last decade in Chile.

Acknowledgement/Funding: School of Public Health grant

P3665 | BEDSIDE
Trends in social inequalities in the prevalence of major cardiovascular disease among adults in Germany
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Background: Social gradients in cardiovascular disease (CVD) and risk factors have been reported in many countries, but little is known whether these social inequalities have increased or decreased in recent years.

Purpose: To investigate whether there are social inequalities in the prevalence of major CVD in the adult population in Germany and whether these inequalities have changed between 1998 and 2010.

Methods: Using data from two German National Health Interview and Examination Surveys conducted in 1997–1999 (GHNIES98, n=4,170) and 2008–2011 (DEGS1, n=8530), we examined trends in the lifetime prevalence of major CVD (myocardial infarction, chronic ischemic heart disease, stroke or heart failure) according to socioeconomic status among adults aged 40–79 years in Germany. History of major CVD was assessed by structured computer-assisted physician interview. Socioeconomic status (SES) was classified as low, medium and high using an index based on information on education, occupational status and net equivalent income. Trends of social inequalities in CVD prevalence were examined in logistic regression models including interaction terms for survey*SES and adjusting for age, region, community size and behavioural risk factors (smoking, obesity, sports activities, alcohol intake).

Results: Between 1998 and 2010, age-standardised lifetime prevalence of major CVD decreased from 13.9% to 11.3% (p=0.03) among women but did not change significantly among men (16.0% and 17.5%, p=0.2). In 2010, prevalence of major CVD was significantly higher in low vs. high SES groups among women (17.0% vs. 5.2%) and men (24.1% vs. 12.8%). Adjusting for age, lower SES was associated with significantly higher odds of CVD among women (OR low vs. high SES 2.11 (95% CI 1.34–3.3)) and men (OR low vs. high SES 2.02 (95% CI 1.35–3.02); OR RII low vs. high SES 2.0 (95% CI 1.3–3.0); OR RII low vs. middle SES 1.7 (95% CI 1.2–2.5)). Among men, social inequalities have increased since 1998 (p for interaction survey*SES <0.05), with fully adjusted prevalences increasing by +3.2% among men with low and medium SES and decreasing by −4.6% among men with high SES. Among women, no significant change in social inequalities was found (p for interaction survey*SES <0.1), with fully adjusted prevalences decreasing similarly by about −3% in all SES groups.

Conclusions: There is a significant social gradient in the prevalence of major CVD among women and men in Germany. Between 1998 and 2010, social inequalities in CVD prevalence remained stable among women and increased among men.

P3666 | BEDSIDE
Burden of cardiovascular hospitalizations following myocardial infarction among older adults
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Background: Most research on post-myocardial infarction (MI) prognosis has focused on the time to first recurrent cardiovascular disease (CVD) event. However, given the chronic nature of the disease, patients may experience repeated CVD hospitalisations. This overall burden has not been well described.

Purpose: To examine the cumulative number of CVD hospitalisations following an MI.

Methods: Individuals age 66 and older enrolled in Medicare, a government health insurance system for older adults in the United States, who were hospitalised for MI in 2000–2010 were followed for up to 10 years. Data on CVD hospitalisations (stroke, MI, heart failure, MI, stroke, and other cardiovascular conditions) through administrative claims. The number of hospitalisations was annualised to account for variable follow-up.

Results: Among 136,153 individuals followed for 10 years after MI, 69,242 (50.8%) had ≥1 CVD hospitalisation, including 29,802 (21.9%) with ≥1 heart failure hospitalisation, 9,752 (7.2%) with ≥1 MI hospitalisation, 9,561 (7.0%) with ≥1 ischaemic stroke hospitalisation, and 938 (0.7%) with ≥1 haemorrhagic stroke hospitalisation. Of those who experienced at least one CVD hospitalisation, 63.7% had multiple CVD hospitalisations (Figure). Heart failure was associated with multiple recurrent hospitalisations; 50.5% of those experiencing a heart failure hospitalisation had multiple heart failure hospitalisations. The proportion of individuals experiencing multiple recurrent hospitalisations was 32.0%, 28.5%, and 26.8% for MI, ischaemic stroke, and haemorrhagic stroke hospitalisation, respectively.

Conclusion: Studies limited to the first recurrent CVD event following MI substantially underestimate the burden of disease on patients and healthcare systems.

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P3668 | BEDSIDE
Acute coronary syndrome perception: determinants and impact on medical care seeking
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Background: The interpretation of acute coronary syndrome (ACS) symptoms may influence the time to hospital admission. Long pre-hospital delay relates to lost opportunities for early risk stratification and management, leading to increased mortality and morbidity. We explored predictors of illness perception and its association with the delay in medical help seeking.

Methods: We assembled a cohort of all consecutive patients admitted to the Cardiology department of two tertiary hospitals of different regions with ACS diagnosis between September 2013 and January 2014. ACS perception was evaluated by personal interview in the first 48h of hospital admission with the question: “Did you consider the possibility of your symptoms being related to a cardiac problem?”. Clinical data was obtained from medical patient’s records and by interview.

Results: 311 patients (mean age 63.3±13.2 years; 71% male) were included; 59.5% with non-ST segment elevation ACS and 40.5% with ST-segment elevation ACS. A large proportion of patients (40.5%) did not perceive symptoms as cardiac until the doctor’s information. Previous ACS diagnosis influenced the symptoms perception: 87.3% of those with ACS past history compared to 53.5% in others (OR 5.81; 95% CI: 2.51–13.46; adjusted for age, sex, hospital localization and ACS type). No association was found between ACS perception and ACS type, age, sex, academic degree and income.

Perception of ACS was significantly related to earlier arrival for medical help, with a median time to hospital admission of 157 (interquartile range (IQR):72–329) minutes compared to 203 (IQR:101–560) minutes in non ACS perception group (p=0.021). The difference according to perception was pronounced in patients without previous ACS diagnosis (156 (69–321) minutes vs 201 (107–449) minutes, p=0.012) and non-significant in patients with previous ACS (170 (84–625) vs 207 (77–1577) minutes, p=0.570).

After adjusting for age, sex, ACS past history, ACS type and hospital location, perception of ACS was significantly associated with 30% shorter pre hospital delay (p=0.036).

Conclusions: The illness perception of patients with acute coronary syndrome needs to be improved, independently of socio-demographic factors. Mistaken ACS symptom interpretation was significantly associated with delay in treatment seeking. These results reinforce the need for better health education, focusing on the alert signs for ACS to improve hospital admission time and treatment in this setting.

P3669 | BEDSIDE
ST-segment Elevation Myocardial Infarction and primary angioplasty: the predictors of patient delay
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Introduction: Primary angioplasty (PPCI), is the best treatment for ST-segment Elevation Myocardial Infarction (STEMI) when performed earlier in the course of the disease. Despite the campaigns to raise general population awareness for STEMI symptoms, the time between symptoms onset and first medical contact
("patient delay") is still suboptimal. Therefore it is essential to understand the factors related to this delay in order to improve the performance of this healthcare intervention and patients’ outcomes.

Objective: To evaluate the factors associated with the "patient delay" in patients with STEMI.

Methods: We prospectively collected the data of 18 national interventional cardiology centers capable to perform PPIC in 24/7. A survey was conducted during one month for four consecutive years (2011–2014) in order to characterize all patients admitted for STEMI with indication for PPIC (~12 hours after onset of symptoms). Demographic and clinical characteristics were collected descriptively. Independent predictors of "patient delay" above the median value were analyzed through univariate and multivariate logistic regression.

Results: 865 STEMI patients were included for analysis (mean age of 62±13 years; 22% female; and 18% had diabetes). The overall median of "patient delay" was 106 min and 432 patients have exceeded such time. Annual data regarding "patient delay" did not show statistical significant differences among years (118 min in 2011, 102 min in 2012, 91 min in 2013 and 106 in 2014 min; p=0.067). Age, ≥75 years, female gender, the onset of symptoms during the night (midnight to 8 AM) and going to a primary healthcare facility before the first medical contact were found as independent predictors of increased "patient delay" in multivariate regression analysis. Patients from the North region, the contact through the emergency telephone number and the use of Emergency Medical Services were independently associated to a low "patient delay" time.

Conclusions: Our data shows that national "Patient delay" is still very high. Our findings suggest that the elderly population and women should be subject of specific programs and be taken as priority in the development of awareness programs. The result highlight the needs to reinforce that patients should not delay the call for aid, even if symptoms occur during the night. The contact should always be made through the emergency phone number.

P3670 | BEDSIDE

Gender differences in predictors of left ventricular myocardial relaxation in non-obese, healthy individuals

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Background: Previous studies indicate that individuals with metabolic syndrome (MetS) might be at risk for left ventricular (LV) diastolic dysfunction. However, little is known about which metabolic factors contribute to the development of LV dysfunction in individuals who are not obese or overweight and who do not have diabetes mellitus and/or cardiovascular diseases.

Methods: Participants without diabetes mellitus, systolic dysfunction, or other heart diseases underwent a thorough physical examination, including tissue Doppler echocardiography. A peak early mitral annular velocity (e') of 5.0 was considered as indicating abnormal LV myocardial relaxation (LVMR). We performed single and multiple logistic regression analyses of e' and cardiac risk factors, including MetS factors and indicators of major organ dysfunction.

Results: A total of 1055 individuals (mean age, 63±13 years) participated, of which 307 (30%) had MetS and 199 (18.9%) had abnormal LVMR. Several significant variables were found as independent predictors of increased "patient delay" in multivariate regression analysis. Waist circumference (WC), overweight or obesity (%) in women (OR 3.69, CI 1.99–6.86) and poor food choices. A series of multivariate logistic models were estimated, among others year-specific models and full model containing year of data collection as independent variable (with "repeated" contrast to check trend). All analyses were adjusted for age, sex, domicile, family structure and perceived family wealth.

Results: The proportions of teenagers with unhealthy lifestyle habits are presented in the Table. Time trends were similar in teenagers living in the city and in the countryside. Not living with both birth parents was related to smoking (OR 1.66 [95% CI 1.23–2.24] in 2002, 1.75 [1.30–2.35] in 2006, 1.97 [1.37–2.83] in 2010 and 2.38 [1.66–3.43] in 2014). Self-perceived poverty was related to the probability of smoking in 2014 (2.20 [1.15–4.21]) and in 2010 (2.25 [1.18–4.26]) but not in 2006 (1.58 [0.98–2.54]) nor in 2002 (1.26 [0.78–2.01]) and to low physical activity in 2002 only. The proportions of teenagers with at least three unhealthy habits was 5.9% in 2002, 7.1% in 2006, 9.0% in 2010, and 5.7% in 2014 (p=0.003).

Conclusions: We found favorable time trends in rates of smoking and low physical activity, strongly marked just after the accession; however the rates of overweight and unfavourable eating habits have not improved. The relationship between smoking and poverty and structure of the family have become stronger. Unhealthy lifestyle habits among Polish teenagers remain a major issue for public health in Poland.

P3672 | BEDSIDE

Dysfunctional heart discharge in an Italian cardiology department: causes and features of the phenomenon

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The phenomenon of Delayed Hospital Discharge (DHD) is well known, but studies so far were implemented in emergency departments, surgical or internal medicine ward. This phenomenon is a source of inefficiency of the hospital care system and increase health care spending. From 08/01/2012 to 12/01/2016 we conducted a prospective study. We detected all the DHD in ICCU and CW, comparing all hospitalizations; for all pts were evaluated several clinical variables and for pts with DHD also the number of days lost and the reason for the delay. For 3 weeks, from 24/3 to 13/04/14, we calculated the period prevalence (PP) of the phenomenon.

Results: The cumulative incidence (CI) of DHD is 12.6% with 290 DHD (233 ICCU and 57 CW) of 2306 total admissions. The (PP) was 7.4%. Because of DHD were lost 759 bed-days. The inappropriate bed occupation days (IBOD) due to the phenomenon of DHD are 8.3% of total hospitalization days. The phenomenon has different features in ICCU and CW. In ICCU the CI of DHD is 24.9% and the PP 15.5% and in CW is respectively 4.2% and 3.3%. However the bed-days lost are similar (ICCU 364 and CW 395), because the IBOD in ICCU is shorter (1.56 vs 2.10 days). An analysis of the causes of the phenomenon reflects the difference between ICCU and CW. In ICCU 100% of the DHD is explained by an inefficient operation system due to the lack of non-acute beds (LNA) to transfer the pt. In CW the LNA accounts for a 62.3%, not cardiological co-morbidities 8.8% and a high nursing burden with difficulties for an acceptable care of pts and care-givers 28.0%. Of pts with DHD hospitalized in CW, 37.5% live alone or do not have a family support and 31.5% had cognitive impairment. For pts in CW to univariate analysis are significantly associated with the DHD age-85 years old, heart failure, disorientation, anemia, recent stroke and/or surgery. At multivariate analysis (logistic regression) remain significant recent stroke and/or surgery, age -85 years, and heart failure with Odds Ratio, respectively, 20.5, 4.1, 5.3 and 1.9.

Conclusions: Even in our Cardiology Dept. (hub center with Cath Lab) the phenomenon of DHD is relevant and cause the loss of more than one bed per day throughout the year both in ICCU and in CW. In ICCU it is more evident with an IBOD 11% and is due to organizational reasons (LNA), while in CW is largely attributable to clinical and social pieces, which make it difficult to discharge
P3674 | BEDSIDE
Cost effectiveness analysis of oral anticoagulant therapy with rivaroxaban for nonvalvular atrial fibrillation in a secondary hospital in Spain
R. Andion Ogando1, J. M. Martín Antoranz2, E. M. Arias Valdés3, E. Laherrera Rodríguez4, J. M. Asín Guillén1, J. A. San Roman Calvar1,2,3, Complejo Asistencial Universitario, Cardiology, Palencia, Spain;3 Complejo Asistencial Universitario, Haematology, Palencia, Spain;4 Medena del Campo Hospital, Medina del Campo, Spain;4 University Hospital Clinic (HCU), Valladolid, Spain

Background: Atrial fibrillation (AF) is the most prevalent arrhythmia. Prevalence in Spain is estimated in 4.4% of total population. It is widely associated with increased risk of stroke, cardiac failure and quality of life loss. Classic preventive treatment was dose-adjusted vitamin K antagonist (VKA) therapy (warfarin or acenocoumarol, International Normalized Ratio (INR) 2.0–3.0). ROCKET AF study (2011) showed that Rivaroxaban is an effective treatment for preventing stroke in AF patients.

Purpose: To assess a cost effectiveness analysis of anticoagulant treatment with Rivaroxaban vs VKA in nonvalvular AF patients in a Secondary Hospital in Spain.

Methods: Retrospective analysis of all patients treated with Rivaroxaban or acenocoumarol with diagnosis of nonvalvular AF discharged from a secondary hospital during 2012 and 2013. Demographic and clinical variables as well as main costs of treatment, hospitalization, rehabilitation, INR determinations were included in an Excel database for analysis.

Results: 336 p were included in the study; 292 p were treated with acenocoumarol and 44p with Rivaroxaban. Mean age was 79±8.6 years, 53% women (150p) with a CHA2DS2-VASC score of 3.7±1.3. There were no statistical differences between groups in age, gender, hypertension, diabetes, ejection fraction, CHA2DS2-VASC score or mortality. Treatment with Rivaroxaban was dominated by standard therapy with VKA. We analysed a subgroup of patients treated with VKA with suboptimal mean time in therapeutic range (TRT) (<60%). For this patients Rivaroxaban proved to be cost effective but at an Incremental Cost Effectiveness Ratio (ICER) of 105300€ for avoided ischemic stroke and 288017€ for haemorrhagic stroke. Rivaroxaban therapy did not showed gain of QALYs versus standard anticoagulant therapy.

Cost effectiveness analysis

<table>
<thead>
<tr>
<th>Group</th>
<th>Annual cost</th>
<th>Incremental ICER/stroke ICER/major ICER/death</th>
<th>p</th>
<th>cost bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acenocoumarol</td>
<td>196030</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>367469</td>
<td>1714.39 Dominated Dominated Dominated</td>
<td>&lt;0.001†</td>
<td></td>
</tr>
<tr>
<td>Acenocoumarol (TRT &lt;60%)</td>
<td>262169</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>167489</td>
<td>1053 1053000 Dominated Dominated Dominated</td>
<td>&lt;0.001†</td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: In our population novel oral antiagulant therapy with Rivaroxaban did not seem to be cost effective. Further and wider studies are needed to take on the best therapeutic options at an optimal cost.

DELETERIOUS EFFECTS OF OBESITY AND DIABETES

P3675 | BEDSIDE
Impact of low serum levels of 1,5-anhydroglucitol on cardiovascular events in patients after first-time elective percutaneous coronary intervention

Background: Postprandial hyperglycemia plays an important role in the pathogenesis of coronary artery disease and cardiovascular events. Serum 1,5-anhydroglucitol (1,5-AG) levels are known to be a clinical marker of postprandial hyperglycemia. We examined whether serum 1,5-AG levels can predict cardiovascular events in patients after the first-time elective percutaneous coronary intervention (PCI).

Methods: We enrolled 278 consecutive patients after first-time elective PCI with drug-eluting stents. We excluded the patients with a history of acute coronary syndrome, advanced chronic kidney disease (eGFR <30 mL/min/1.73 m²), or a protocol violation. Serum 1,5-AG at the follow-up angiography. We assessed the relationship between glycemic markers and cardiovascular events in patients after the first-time elective PCI.

Results: No significant differences in baseline clinical characteristics, including FBS, HbA1c, and 1,5-AG, were observed between the two groups. At follow-up, serum levels of 1,5-AG (14.2±6.9 μg/mL vs 16.5±7.3 μg/mL, P=0.05), but not HbA1c (6.10±0.7% vs 6.1±0.7%, P=0.86) at the follow-up were significantly lower in the EV group than in the NEV group. After adjusting for confounding factors including age, gender, creatinine, and C-reactive protein, 1,5-AG level was an independent risk factor for cardiovascular events (OR 0.95, P<0.04)

Conclusion: Low 1,5-AG levels were associated with cardiovascular events after first-time elective PCI. These data suggest that postprandial hyperglycemia and lower 1,5-AG are important risk factors for adverse clinical events after first-time elective PCI.

P3676 | BEDSIDE
Exercise intolerance in elderly asymptomatic type 2 diabetes: left ventricular dysfunction, diabetes control, therapy or insulin resistance?
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Background: LV dysfunction is associated with impaired exercise capacity adverse outcome in type 2 diabetes mellitus (T2DM). We hypothesized that the mechanism of this was through insulin resistance (IR), which is linked to waist circumference (WC). We tested the hypothesis that WC is associated with 6-minute walk distance (6MWD) independently and incrementally to clinical, biochemical, therapeutic and echo variables in T2DM without overt heart failure.
Methods: From a community-based population, we enrolled 284 asymptomatic T2DM pts (71±4y, 55% men). Associations were sought between 6MWD and WC, diabetes duration, HbA1c, health questionnaire (EQ5D) and echo results including global longitudinal strain (GLS). Nested multivariable linear regression models were created to assess increment value of 6MWD.

Results: Tertiles of increasing WC were associated with worsening 6MWD (1st:54±7595m; 2nd:470±796m; 3rd:404±117m; p<0.001), and worsening GLS (1st:−18.1±2.5; 2nd:−17.4±2.7; 3rd:−16.7±2.9; p=0.01). Reduced exercise capacity was significantly associated with age (r=−0.30, p<0.001), gender (r=−0.14, p<0.001), BMI (r=−0.42, p<0.001), diabetes duration (r=−0.29, p<0.001), insulin use (r=−0.27, p<0.001), WC (r=−0.38, p<0.001), WC was independently associated with 6MWD after adjusting for other variables including BMI (model R2=0.45). The association of clinical variables (age, sex, EQ5D and BMI) was not improved by adding GLS (p=0.45), diabetes duration (p=0.90), insulin use (p=0.72), or HbA1c (p=0.03), but significantly increased by adding WC (p=0.05).

Conclusions: Clinical, biochemical, therapeutic and echo information appear inferior to simple measurement of WC as a predictor of exercise capacity in asymptomatic T2DM.

P3677 | BEDSIDE

Effects of renin-angiotensin-aldosterone system blockers on contrast-induced nephropathy and its association with NGAL levels in diabetic patients undergoing coronary angiography


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Introduction: Contrast-induced nephropathy (CIN) is a common cause of hospital-acquired acute kidney injury (AKI). NGAL represents non-invasive, troponin-like biomarker for the early prediction of AKI in various clinical settings. In this study, the aim was to investigate effects of renin-angiotensin system blockers (RASB) on the development of CIN in diabetic patients after coronary angiography.

Methods and results: We prospectively enrolled consecutive 80 patients undergoing elective coronary angiography. Serum creatinine (SCr) and plasma NGAL levels were measured at baseline and after intervention (SCR at 72. hour and NGAL at 4. hour). CIN was defined as an increase in SCr of ≥0.25 or 0.5 mg/dl from baseline within 48–72 h after angiography.

Patients were divided into two arms based on the use of RASB: RASB+ (patients 4839±3374 pg/ml versus 4304±1814 pg/ml, p=0.68) (see table).

Comparison of NGAL and serum creatinine levels in contrast induced nephropathy (+) and (-) patients.

Variables CIN(+), n=12 CIN(−), n=68 P value

SCr baseline (mg/dl) mean±SD 0.96±0.24 0.89±0.25 0.35
SCr (72. Hour) (mg/dl) 0.25±0.30 0.19±0.26 0.03
NGAL baseline (pg/ml) mean±SD 6734±6031 4251±3417 0.05
NGAL (4. Hour) (pg/ml) mean±SD 4839±3374 4304±1814 0.68

Conclusion: In diabetic patients undergoing coronary procedure, chronic usage of RAASB doesn’t increase the risk of CIN significantly. Plasma NGAL appears to be a powerful early biomarker of AKI, however, in our study NGAL levels did not increase in contrast-induced nephropathy.

P3678 | BEDSIDE

Concordance of glucose based and of HbA1c based diagnoses of diabetes in patients with established coronary atherosclerosis: a comparison between men and women

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Background and introduction: Concordance between glucose based and HbA1c based diagnoses of diabetes was a matter of controversy in recent years.

Purpose: The purpose of our study was to investigate their concordance in men and in women with stable coronary artery disease (CAD).

Methods: We measured fasting glucose as well as HbA1c and performed standard oral glucose ingestion tests in a consecutive series of 711 patients, 513 men and 198 women, who had angiographically proven coronary artery disease (CAD) but not previously diagnosed diabetes. Based on glucose values, diabetes was diagnosed with a fasting plasma glucose (FPG) ≥126 mg/dl or a postchallenged glucose >200 mg/dl 2 hours after the oral glucose load; based on HbA1c values diabetes was diagnosed with an HbA1c ≥6.5%.

Results: Among men, 33 had diabetes based on fasting or postchallenge glucose values, of whom 26 also had diabetes according to the HbA1c criteria. Of the 480 men who did not have diabetes based on glucose values, 446 also did not have diabetes according to HbA1c criteria; among women, 3 had diabetes based on glucose values, of whom 2 also had diabetes according to the HbA1c criterion.

Conclusion: Concordance of glucose and HbA1c criteria in patients with stable CAD is high and is similar in men and women with CAD. However, for both sexes the specificity of the HbA1c criterion is poor in this patient population.

P3679 | BEDSIDE

Divergent association of obesity with aortic stiffness and wave reflections in patients with metabolic syndrome: the obesity paradox

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Introduction: Metabolic syndrome (MS) is associated with increased cardiovascular (CV) risk values, and beyond its clustering risk factors, has been questioned. Aortic stiffness is an independent predictor of cardiovascular events, whereas wave reflections determine part of the left ventricular afterload. The relationship of obesity with aortic stiffness and central hemodynamics has shown inconsistent results. The aim of the present study was to investigate the association of total and central obesity with aortic stiffness and wave reflections in patients with MS.

Methods: We studied 526 never treated hypertensive patients with MS defined by the ATP III criteria. Aortic stiffness was assessed by measuring carotid-femoral pulse wave velocity (PWV) using the Complior device. Wave reflections were evaluated by measuring heart rate-corrected augmentation index (AIx75) with the Sphygmacor device. Body mass index (BMI) and waist (W) circumference were used as indices of total and central obesity, respectively. High-sensitivity C-reactive protein was measured as an inflammatory marker.

Results: In the whole population, PWV was associated with age, mean arterial pressure (MAP), heart rate (HR), fasting glucose, W, BMI, and hsCRP, whereas AIx75 was associated with the Sphygmacor device. Body mass index (BMI) and waist (W) circumference were used as indices of total and central obesity, respectively. High-sensitivity C-reactive protein was measured as an inflammatory marker.

Conclusions: Obesity has a differential effect on aortic stiffness and wave reflections in hypertensive patients with MS. The significant inverse association of central obesity with wave reflections can be attributed to decreased wave reflection resistance and might have important implications for the prognosis of patients with MS. Future studies need to confirm the present findings and establish definite pathophysiological relationships.

P3680 | BEDSIDE

Role of interleukin-6 in the visual impairment of diabetic patients

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1 University of Athens Medical School, 1st Cardiology Department, “Hippokration” Hospital, Athens, Greece; 2 University of Athens Medical School, Department of Ophthalmology, Athens, Greece

Background: Diabetic Retinopathy (DR) is a complication of diabetes mellitus leading to deterioration of vision. Inflammatory cytokines are key players in the pathophysiology of atherosclerotic disease.

Purpose: To investigate the association of inflammatory status with visual acuity in subjects with diabetes mellitus.

Methods: We enrolled 100 consecutive subjects with diabetes mellitus. Patients were divided in those with DR (53 subjects, mean age 68±9) and those with no evidence of DR (NDR) (mean age 64±6). The diagnosis of DR was made by ophthalmoscopy and best-corrected visual acuity (BCVA) was measured in both eyes. A BCVA less than 0.8 was considered as severely impaired. C reactive protein (CRP) and Interleukin-6 (IL-6) were measured as well established inflammatory markers of progression.

Results: Although there were no significant differences in baseline characteristics, patients with DR compared to NDR patients had increased levels of IL-6 [2.24 (1.33–3.99)pg/ml vs. 1.51 (0.96–3.05)pg/ml, p=0.03] and worse BCVA [0.8 (0.92–
1) vs. 0.8 (0.5–1.0; p = 0.001), while there was no significant difference in CRP levels [2.85 (0.91–4.41) mg/L vs. 1.25 (0.56–4.29) mg/L; p = 0.12]. Moreover, in diabetics mellitus subjects, BCVA was inversely correlated with IL-6 levels (r = 0.25, p = 0.03), CRP levels (r = 0.26, p = 0.16) glycosylated hemoglobin levels (r = 0.38, p = 0.001), age (r = 0.34, p = 0.001) and with duration of diabetes mellitus (r = 0.41, p = 0.001) and positively correlated with creatinine clearance (r = 0.21, p = 0.04). Interestingly, after adjustment for age, gender, body mass index, smoking habits, CRP levels, insulin treatment and the aforementioned confounders, IL-6 was independently associated with BCVA [b = −0.034 95% CI (−0.056, −0.012), p = 0.004] while CRP was not a significant factor in the multivariate model. Moreover, ROC curve analysis revealed that IL-6 levels (AUC=0.70, p =0.01) have a significant diagnostical ability in detecting diabetic subjects with severely impaired BCVA. More precisely, IL-6 levels more than 1.85pg/ml has a sensitivity of 78% and a specificity of 87%, for the diagnosis of severely impaired BCVA.

Conclusion: Patients with DR have significantly impaired visual acuity which is associated with systemic inflammatory status. These findings highlight the significant role of inflammation in the progression of diabetic complications and provide therapeutic implications which merit further study.

P3681 | BEDSIDE
Metabolic syndrome and the contributory predictive role of inflammatory and renal markers on cardiovascular disease: 10 year (2001-2011) follow-up of the ATTICA Study
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Background and purpose: To evaluate the influence of metabolic syndrome (MS) and the contributory predictive role of inflammatory or renal markers on cardiovascular disease (CVD) incidence.

Methods: 2001–2002, 1514 men and 1528 women (>18y) without any clinical evidence of CVD or any other chronic disease, at baseline, living in Greece, were enrolled. In 2011–2012, the 10-year follow-up was performed in 2583 participants (15% of the participants were lost to follow-up). Incidence of fatal or non-fatal CVD was defined according to WHO-ICD-10 criteria. MS was defined using three definitions, provided by the National Cholesterol Education Program Adult Treatment Panel III (revised NCEP ATP III definition), the Internation Diabetes Federation (IDF) or the Harmonized definition. Furthermore, the contributory predictive role of C-reactive protein (CRP), inteleukin-6 (IL-6), uric acid and estimated glomerular filtration rate, in addition to MS presence, regarding CVD incidence, was evaluated.

Results: History of MS according to the revised NCEP ATP III definition was positively associated with CVD, after adjusting for potential confounding factors; age, sex, physical activity, smoking and eating habits, using the MedDietScore (OR: 1.83, 95% CI: 1.24-2.72). CRP and IL-6, and to a lesser extent uric acid, mediated the influence of MS on cardiovascular events; when examining the associations based on the NCEP ATP III definition, the CRPs for MS tended to decrease while the IL-6 levels were increased in the models (ORs: 1.13; (1.72, 2.61) and 1.78 (1.18–2.68), respectively). Further analyses were performed in order to better clarify these relationships, evaluating the C-statistic. The values for the models including potential confounding factors and the inflammatory or renal markers and the MS definitions exceeded 0.78, indicating fair to good predictive probability. Furthermore, the C-statistic for the models including CRP or IL-6 exceeded 0.80 for all three MS definitions.

Conclusion: Results of the present work better clarify the mediating role of inflammatory and renal parameters in the MS and CVD association.

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P3682 | BEDSIDE
Decreased insulin sensitivity and abdominal obesity promote coronary atherosclerosis' extent and severity in non-diabetic patients
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Objective: To study mobilization of endothelial progenitor cells (EPC) in patients with type 2 diabetes mellitus (T2DM), with high cardiac and vascular risk, was associated with altered mortality. Design: Population based cohort study Setting: The pseudonymised records of 9596 men (mean follow-up of 6.9 years) aged 40–89 years diagnosed with AMD before January 2007 were identified from 42 GP practices in Cheshire, UK.

Main outcome measures: We used hazard ratios (HR) from Cox regression models to describe the association between PDE5i use and all cause mortality.

Results: A lower percentage of deaths (18% versus 25%) and mortality rates (26.7 (22.7–30.7) vs. 37.0 (35.0–39.2) per 1000 person-years; P < 0.001) as well as a significantly reduced risk of all-cause mortality from unadjusted Cox regressions [hazard ratio (HR) = 0.69 (95% confidence interval: 0.60, 0.79); P < 0.0001], was observed amongst the 1,359 (22.8%) men prescribed a PDE5i, compared to those without such a prescription. This reduction in risk remained after adjusting for age, eGFR, smoking status, history of myocardial infarction, systolic blood pressure (per 5 mmHg), use of a statin, metformin, aspirin and beta-blockers (HR=0.83 (0.70–0.98); p = 0.038) equaling to a 17% reduction in risk of death.

The pattern of lower mortality (unadjusted HR=0.69. P = 0.009) was similar in those with a history of acute MI (25.7%, (49/191) versus 40.1% (337/840) deaths prior to 2007. The reported incidence of an acute myocardial infarction during 7 years follow-up was greater in those who were never prescribed PDE5is treatment (8.9%) compared to those with a history of PDE5i use (5.2%; P = 0.0001). In this sub-group, reduced risk of mortality remained after adjusting for age, smoking status and use of a statin (HR 0.62 (0.47–0.83), p = 0.001).

Conclusion: In a population of men with T2DM, on-demand use of PDE5is was associated with decreased risk of both overall mortality and mortality in those with a history of AMI.

P3684 | BEDSIDE
Mobilization of endothelial progenitor cells after endovascular interventions in patients with type 2 diabetes mellitus
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AIM: To study mobilization of endothelial progenitor cells (EPC) in patients with type 2 diabetes mellitus (T2DM) after endovascular interventions on coronary and peripheral arteries.

Methods: We observed 50 patients (22 women), admitted for elective percutaneous coronary intervention (PCI) or endovascular revascularization of lower extremity, 27 patients with T2DM were included in group 1 (14 women, mean age 65±10.9 years), who received PCI within 24 hours before and 27 patients fixed in group 2 (8 women, mean age 65±10.0 years). PCI was done for stable angina. Endovascular revascularization of lower extremity was done for critical limb ischemia (CLI). In group 1 PCI was performed in 15 patients, endovascular limb revascularization in 12.
Conclusion: Appropriate measurement of HbA1c is considered as a useful
respectively; p<0.001). Levels of CD34 + CD45- cells in increased in 27.7% (0.01±0.01%) and 0.023±0.007% before and after procedure, respectively; p=0.048). Levels of EPC in the peripheral blood of patients with T2DM before and after endovascular interventions did not significantly differ. We divided patients with T2DM into 2 subgroups: the 1st subgroup included 14 patients with HbA1c≦7.5%; the 2nd subgroup included 13 patients with HbA1c≈7.5%. In the 1st subgroup the increase of CD34 + VEGFR2 + CD45- cells in 46.6% (p<0.01), and CD34 + CD133 + CD45- in 40.3% (p<0.006) were observed after endovascular intervention.

Conclusions: The study has shown that patients with T2DM had the alteration of EPC mobilization after endovascular interventions. In addition, the dynamics of EPC levels depended on the glycemic control. Thus, in the subgroup of patients with T2DM with good glycemic control (HbA1c<7.5%) the EPC levels were significantly higher after endovascular interventions.

P3685 | BEDSIDE
The optimal interval of screening to detect type2 diabetes for pre-diabetic patients with coronary artery disease
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Background: It has been recommended to adopt hemoglobin A1c (HbA1c) testing as one basis for identifying diabetes and pre-diabetes. We assessed the optimal interval of measuring HbA1c to detect new onset of type2 diabetes for pre-diabetic patients with coronary heart disease (CHD).

Methods: We retrospectively assessed a trend of HbA1c of 1049 Japanese pre-diabetic patients (5.7≦HbA1c<6.4%, age 65.9±10.9, male 860) who had undergone percutaneous coronary intervention or coronary artery bypass graft surgery from April 2001 to December 2013. Two groups were defined as the lower group (5.7<HbA1c≦6.4%) and the higher group (6.0≦HbA1c<6.4%). We analyzed the number needed to diagnose (NND) by annual measuring of HbA1c for 632 patients as the lower group and 417 patients as the higher group. The optimal interval of screening was defined the estimated time for 10% of patients whose HbA1c rose up to 6.5% and over.

Results: The NND was 70.2 in the lower group and 5.63 in the higher group. The estimated optimal screening interval of HbA1c was 6 years in the lower group, whereas 6 months in the higher group.

Conclusion: Appropriate measurement of HbA1c is considered as a useful adjunct to prevent coronary disease in this challenging population. Metabolic follow-up is desirable in a potential high risk group (HbA1c 6.0≦HbA1c<6.4%), whereas unnecessary investigation should be reconsidered in a relatively low risk group (5.7≦HbA1c<6.4%) from the point of clinical benefits and cost-effectiveness.
Methods:

Between October 2005 and December 2008, 641 consecutive patients with 711 CTO lesions underwent percutaneous coronary intervention (PCI) at our institution. Creatine kinase-myocardial band (CK-MB) fraction was measured before PCI and from 12 to 24 hours after PCI in all patients. PMI was defined as CK-MB increase >3 times the upper limit of normal. Cardiac death during 5-year follow up was evaluated.

Results:

The procedural success rate was 88.5%. PMI occurred in 30 patients (4.7%). PMI was significantly more common in the retrograde approach than in the antegrade approach alone (7.7% vs. 3.0%, P < 0.01). Clinical follow-up was completed in 85.8% of patients at 5 years. The cumulative incidence of cardiac death at 5 years was similar between PMI and no-PMI (12.0% vs. 5.6%, P=0.157). A multivariate analysis revealed that procedural failure was an independent predictor of cardiac death (hazard ratio [HR] 3.48, 95% confidence interval [CI] 1.65 to 7.32, P < 0.01), but the retrograde approach was not (HR 0.86, 95% CI 0.42 to 1.77, P=0.68). Kaplan–Meier curves of cardiac death event rate at 5 years are shown in the Figure.

Conclusions:

PMI was more common with the retrograde approach, but was not associated with cardiac death during long-term follow-up. When procedural failure which causes PMI occurs, though relatively rare, target vessel revascularization may be required.

P3689 | BEDSIDE

Long-term clinical outcome of periprocedural myocardial injury in patients undergoing percutaneous coronary intervention for chronic total occlusion lesions

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Purpose:

to evaluate the incidence and clinical implications of periprocedural myocardial injury (PMI) during percutaneous coronary intervention (PCI) for chronic total occlusion (CTO) lesions.

Methods:

From January 2011 to January 2015, we performed re-PCI to consecutively 709 ISR lesions. Lesions of ISR were divided into two groups (PCB angioplasty). We compared the patients who underwent successful desk implantation. Patients were recruited between January 2010 and October 2013, and were followed up over 3 years. The primary outcome was major adverse cardiac and cerebrovascular events (MACCE) defined as cardiovascular death and hospitalization due to acute coronary syndrome (ACS), stroke, and coronary vascularization. The median follow-up was 617 (interquartile range, 320–937) days. Pre-procedural serum levels of high-sensitivity C-reactive protein (hsCRP), VEGF-A, and VEGF-C were measured. During the follow-up period, MACCE developed in a total of 88 patients (19.9%). At baseline, there was no significant difference in the age, rate of male gender, and prevalence of risk factors, chronic kidney disease, and previous myocardial infarction and stroke between MACCE and non-MACCE groups. Serum levels of hsCRP and VEGF-A did not differ between the two groups. In contrast, those of VEGF-C were significantly lower in non-MACCE compared with non-MACCE group. Then, we performed Kaplan-Meier analyses. Patients were divided into two groups based on the median of each biomarker. Notably, low-VGF-C (P=0.01 by log-rank test), but not high-hsCRP (P=0.6) or high-VEGF-A (P=0.5), was significantly associated with an increased risk of MACCE. Furthermore, multivariate Cox proportional hazards regression analysis showed that VEGF-C was independently associated with the risk of MACCE and stroke between MACCE and non-MACCE groups. Serum levels of hsCRP and VEGF-C levels, revealed that the VEGF-C level (hazard ratio [HR], 0.79 per 1 SD increase; 95% confidence interval [CI], 0.62–0.99; P=0.04) was an inverse and independent predictor of MACCE.

Conclusions:

A low VEGF-C value may serve as a predictive marker of atherosclerotic cardiovascular events after DES implantation.

P3690 | BEDSIDE

Independent predictors of the recurrent restenosis after paclitaxel-coated balloon angioplasty for in-stent restenosis; importance of initial ballooning and balloon positioning during procedure

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Background:

Recently, the efficacy and the safety of paclitaxel-coated balloon (PCB) angioplasty for in-stent restenotic lesions has been reported. However, some cases still repeat the in-stent restenosis (ISR) after PCB angioplasty. Purpose: At the aim of this study was to evaluate the predictors of the recurrent restenosis in patients who underwent PCB angioplasty for ISR.

Methods:

From January 2011 to January 2015, we performed re-PCI to consecutive 156 ISR lesions. Lesions were divided into two groups (PCB angioplasty and conventional angioplasty group) for the retrospective analysis of the angiographic data. Follow-up angiography was performed 6 months after the procedure.

Results:

Incidence of the binary restenosis (≥50%) after repeat-PCI was significantly lower in PCB angioplasty group compared with conventional balloon angioplasty group [15.0% vs. 38.2%, P < 0.01], and target lesion revascularization was performed in 5.0% and 29.1% in each group, respectively (P < 0.01). Then, we investigated the predictor of recurrent ISR after PCB angioplasty. Multivariate analysis showed that diameter stenosis at initial ballooning for ISR and geographic mismatch between PCB position and target re-PCI site during PCB angioplasty were independent predictors of recurrent ISR after PCB angioplasty.

Conclusions:

Recurrent ISR occurred in 15.0% of patients who underwent PCB angioplasty. Careful positioning of the PCB to avoid the geographic mismatch and optimal expansion at the initial ballooning should be important to prevent recurrent restenosis after PCB angioplasty for ISR.
P3692 | BEDSIDE
Improvement of left ventricular function assessment by global longitudinal strain after successful percutaneous coronary intervention for chronic total occlusions
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Background: Little is known of the potential effects of successful revascularization of chronic total occlusions (CTO) on left ventricular (LV) function. LV global longitudinal strain (GLS) is a more sensitive measure of LV mechanics than LV ejection fraction (EF). GLS can be assessed with two-dimensional speckle-tracking echocardiography (2DSTE) and is significantly related to long-term clinical outcome in patients with chronic ischemic heart disease.

Objective: This study was conducted to investigate the impact of revascularization of CTO on LV function using LV GLS.

Methods: A total of 70 patients (65±8.9 years, 59 males, LVEF 52±12%) with CTO who underwent percutaneous coronary intervention (PCI) were included in this study. Echocardiography was performed before the procedure and 9 month after the procedure with conventional assessment including LV end-diastolic and end-systolic volume (LVEDV, LVESV), LVEF, ratio of early transmitral flow to atrial contraction (E/A ratio), deceleration time (DcT), and with 2DSTE analysis of GLS.

Results: Successful PCI (TIMI 3 flow) was obtained in 60 patients (86%). There were no stent thromboses during follow-up. All patients showed relaxation abnormal pattern assessed by E/A ratio and DcT. GLS showed a significant improvement for 9 months after successful PCI (Δ=−2.0±2.8%; p<0.01), whereas in failed PCI group did not change significantly (Δ=−0.9±4.0%; p=0.48). ΔGLS is greater in successful PCI group than failed group (p<0.05). LVEF, LVEDV and LVESV did not change during follow-up in both successful and failed groups.

Conclusion: Successful PCI for CTO improves left ventricular function assessed by LV GLS. This improvement may be associated with the long-term beneficial effect of PCI for CTO lesions.

P3693 | BEDSIDE
Timing, patterns and long term prognosis of recurrent myocardial infarction and coronary angioplasty: stent thrombosis versus non-stent-related reinfarction
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Background: In patients recovering from a ST-segment elevation myocardial infarction (STEMI), it is not clear if the negative impact of stent thrombosis (ST) is different from a non-stent-related recurrent myocardial infarction (NSRMI). This study sought to assess the long term incidence and prognostic impact of recurrent myocardial infarction (MI) after percutaneous coronary intervention (PCI) for STEMI by comparing outcomes of ST versus NSRMI.

Methods and results: From 2001 to 2007, 1025 consecutive patients undergoing PCI for STEMI were prospectively followed for at least 5 years. Patients with STE, NSRMI and those free from recurrent MI were compared regarding mortality and occurrence of subsequent major adverse cardiovascular events (MACCE). Definite or probable ST occurred in 54 patients (5.7%) and NSRMI occurred in 135 patients (13.2%). Occurrence of subsequent MACCE at end of follow up were not significantly different for patients with ST or NSRMI (HR 0.843 CI 95% [0.538–1.320] but were significantly lower for patients free from any recurrent MI (both log-rank p<0.001). However, all-cause death did not differ between the three groups (27.8 vs 26.7 vs 23.0%). Compared to NSRMI occurring in the first 30 days after PCI for STEMI, early ST was associated with increased risk for all-cause death (HR 5.128 CI 95% [1.40–18.51], p=0.013) but this association did not persist for recurrent MIs occurring in the late (HR 0.50 CI 95% [0.17–1.49]) or very late (HR 0.14 CI 95% [0.01–1.88], p=0.058) periods.

Conclusion: Long term incidence of recurrent MI after PCI for SYMETI was 18.4%, one third of which due to stent thrombosis. Although in the early recovery period ST was associated with a significant increase in adverse events, MACCE and all-cause mortality rates at long term were comparable to non-stent-related recurrent MI.

P3694 | BEDSIDE
Influence of side branch predilation on long-term follow-up in patients with bifurcation lesions treated by provisional stenting
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Introduction: Predilation of the side branch before main vessel stent implantation has been in the context of provisional stenting has generated many controversies.

Objective: The aim of our study was to compare the long-term follow-up of patients with and without side branch predilation before provisional stenting.

Methods: From February 2009 to November 2012, 372 patients with true coro- nary bifurcation lesions (side branch involvement) were randomised to either predilation of side branch (n=187) or no predilation (n=185) before main vessel stent implantation. Patients were monitored by telephone calls and scheduled visits in the outpatient clinic yearly during five years. Major cardiac events (MACE) were defined as cardiac death, myocardial infarction, and target lesion revascularisation.

Results: There were no significant differences between the patient groups regarding the baseline clinical, angiographic or procedural characteristics. After main vessel stent implantation the TIMI flow of the side branch was significantly higher in the patients with side branch predilation. Sixty patients (32%) from the side branch predilation group presented mild side branch residual stenosis and did not require any additional treatment. The side branch stenting rate was 4% in the predilation group and 3% in the no predilation group patients. In hospital and 1-month follow-up MACE were similar between groups (2.1% vs 3.7%, p=ns). The overall MACE rate at 42.1 years-followup was 9%. Mortality from cardiac causes occurred in 4 patients (2%) from the predilation group and in 4 patients (2%) from the no predilation group. Target lesion revascularisation was required in 16 patients (4%) from the predilation group (4%) and 9 from the no predilation group (5%). At 4-year follow-up, there were no significant differences in the Kaplan Meier event-free probability between groups (91% in the predilation group vs 86% in the no predilation group, p=ns).

Conclusions: Predilation of the side branch improved the immediate results and simplified the procedure of the provisional T stenting. However, this strategy had no influence on the long term clinical follow-up of these patients.

P3695 | BENCH
Drug eluting stent versus bare metal stent in saphenous vein graft lesions: a comprehensive meta-analysis of 14,000 patients
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Introduction: Drug eluting stents (DES) have been shown to significantly reduce the rate of target lesion revascularization in native coronary arteries compared to bare metal stents (BMS). However, there have been conflicting results use of DES in saphenous vein graft (SVG) lesions. Therefore, we aimed to investigate the risk of death, re-infraction (re-MI), target lesion revascularization (TLR) and/or target vessel revascularization (TVR), stent thrombosis (ST) and MACE compared to BMS in SVG lesions.

Methods: We searched PubMed and Cochran Library from January 2003 to December 2014. We extracted outcomes such as all-cause mortality, re-MI, TVR/TLR, ST and MACE. Because majority of trials were non-RCT, we pooled all trials data to analyze end-points. Additionally, independent analyses were separately conducted in randomized studies.

Results: We included 4 RCTs and 35 non-RCTs (a total 13958 patients, 6436 pa- tients in DES arm and 7522 patients in BMS arm). In the pooled population, use of DES were significantly associated with lower risk of death (11% vs 14%, RR=1.282 (1.103–1.489) and p=0.001), re-MI (10.2% vs 11.7%, RR=1.135 (0.999–1.290) and p<0.051), TVR/TLR (15.1% vs 18.8%, RR=1.165 (1.023–1.326), p=0.021 and 8.7% vs 13.4%, RR=1.535 (1.213–1.944), p<0.001, respectively), and MACE (23.8% vs 30.3%, RR=1.272 (1.153–1.404) and p<0.001). The risk of ST was similar between DES and BMS (1.3% vs 1.9%, RR=1.254 (0.819–1.919) and p=0.298). Specifically, in RCTs, the risk of death (RR=0.660 (0.179–2.436) and p=0.533), re-MI (RR=1.149 (0.520–2.534) and p=0.732), ST (RR=1.346 (0.825–2.194) and p=0.234) and MACE (RR=1.346 (0.825–2.194) and p=0.234) were similar. However, use of DES were significantly associated with TLR (RR for TVR/TLR = 0.452 (2.048–1.012) and p=0.025 and for TLR = 1.139 (1.053–3.572) and p=0.034).

Conclusion: Our meta-analysis results showed that use of DES might improve cardiovascular outcomes compared to BMS in SVG lesions.
Acknowledgement/Funding:

STEMI after PCI.

Conclusion:

bleeding risk factors.

independent predictor of major bleedings after adjustment of traditional clinical regression analysis identified log GDF-15 (OR 3.77, p=0.004) was a significant HR: 1.67, 95% CI: 1.07–2.55, p=0.02) were independent predictors of TLR.

None

Acknowledgement/Funding:

acceptable.

but did not increase ST, while long DES implantation up to 50 mm was safe and

Methods:

(DES).

ST) or target lesion revascularization (TLR) in first-generation drug-eluting stents DES (UL-2nd DES) implantation in real-world practice.

Objectives: This study investigated the safety and prognosis of ultra-long second DES (UL-2nd DES) implantation in real-world practice.

Background: Long stenting is a widely known predictor of stent thrombosis (ST) or target lesion revascularization (TLR) in first-generation drug-eluting stents (DES).

Methods: Participants were 1,669 patients (2,763 lesions) who had undergone successful 2nd DES implantation; they were assigned to one of three groups: ultra-long 2nd DES (UL-2nd DES: >50 mm, 166 patients, 259 lesions), long 2nd DES (L-DES: >20–50 mm, 758 patients, 1,212 lesions), or short 2nd DES (S-DES: <20 mm, 745 patients, 1,292 lesions). The primary endpoint was TLR, and secondary endpoints were ST, cardiac death, and major adverse cardiac events (MACE).

Results: Patient characteristics, including dual antiplatelet therapy (DAPT) duration, were similar across groups. Target lesion characteristics in the UL-DES group showed higher right coronary artery (49.0% in UL-DES, 27.9% in L-DES, 31.7% in S-DES, p<0.001) and chronic total occlusion lesion (39.7% in UL-DES, 9.4% in L-DES, 2.9% in S-DES, p<0.001) rates. TLR rates (23.1±13.2 months) were significantly higher in ST in the UL-DES group relative to other groups during follow up (UL-DES 19.5% vs L-DES 12.4% vs S-DES 10.3%, p<0.001). TLR rate was similar between S-DES and L-DES. The incidence of ST was similar across groups. MACE was significantly higher in the UL-DES group relative to other groups due to higher TLR rates (UL-DES 41.5% vs L-DES 27% vs S-DES 26.4%, p=0.01). In a Cox proportional hazard model, hemodialysis (adjusted HR: 2.53, 95% CI: 1.70–3.67, p<0.001) and total stent length of >50 mm (adjusted HR: 1.67, 95% CI: 1.07–2.55, p=0.02) were independent predictors of TLR.

Conclusions: Ultra-long DES implantation was associated with higher TLR rates but did not increase ST, while long DES implantation up to 50 mm was safe and acceptable.

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P3697 | BEDSIDE

Growth differentiation factor-15 predicts bleedings in patients with STEMI after PCI

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Background: Growth differentiation factor 15 (GDF-15), a stress-responsive member of the transforming growth factor beta cytokine superfamily, has emerged as a biomarker of recurrent cardiovascular events in coronary heart disease.

Purpose: The aim of this study was to determine the predictive value of GDF-15 on major adverse cardiac events (MACE) in patients with STEMI after percutaneous coronary intervention (PCI).

Methods: Between January 2013 and October 2013, a total of 332 consecutive patients with STEMI who received an uneventful PCI and were exposed to standard dual antiplatelet therapy, were enrolled in the single-center registry. All the enrolled patients received measurement of GDF-15 level on day 2 of PCI. The primary clinical safety end point was the incidence of major bleedings including type 3 and 5 in the analysis. The follow-up period was 12 months.

Results: Overall, 7 (2.1%) ischemic events occurred and 10 (3.0%) major bleedings occurred. Plasma GDF-15 level was significantly higher in patients with major bleedings compared to patients with ischemic events or no events (2563.4 vs. 1822.8 vs 1007.2 ng/L, p < 0.001). By receiver operating characteristic curve analysis, plasma GDF-15 ≥ 2068.1 ng/L had a predictive value of major bleedings with an area under the curve = 0.827 (95% CI 0.744–0.865, p < 0.001). Binary logistic regression analysis identified log GDF-15 (OR 3.77, p = 0.004) was a significant independent predictor of major bleedings after adjustment of traditional clinical bleeding risk factors.

Conclusions: GDF-15 is a strong predictor of major bleedings in patients with STEMI after PCI.

Acknowledgement/Funding: This study was supported by the National Natural Science Foundation of China (81170194, 81470486).

Conclusions: LVEF changes following elective PCI are common. Long term outcomes are associated with both pre and post procedural LVEF.

P3699 | BEDSIDE

Prognostic significance of whole blood viscosity in patients with ST elevation myocardial infarction undergoing primary coronary intervention

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Introduction: Whole blood viscosity (WBV), as the major determinant of endothelial shear stress (ESS), has a strong relationship between cardiovascular (CV) diseases and risk factors. We aimed to investigate the association of WBV with in-hospital and long-term outcomes in STEMI patient population undergoing primary PCI.

Methods: 2663 consecutive patients admitted to hospital with acute STEMI and underwent PCI between 2010 and 2015 were prospectively screened. The mean follow-up were 34.6 months.

Results: During the in-hospital period, MACE, the prevalence of stent thrombosis, impact of LVEF rise or fall following PCI upon patients with coronary artery disease.

Methods: We included consecutive patients who underwent elective PCI in our institution between 2004 and 2013 who were evaluated with echocardiography before and after the procedure. Patients were grouped in respect to baseline LVEF (preserved (>50%), moderately impaired (30–50%), and poor (<30%), 1-year and 5-year hazard ratio (HR) for all-cause mortality and myocardial infarction (MI) were calculated for baseline LVEF groups and in respect to LVEF variation between baseline and repeat examinations.

Results: A total of 974 patients were included, of whom 571 (58.7%) with preserved LVEF, 320 (32.9%) with moderately reduced LVEF, and 83 (8.5%) with poor LVEF. A repeat echocardiogram was performed at a median interval of 168 days following PCI. Decline to impaired LVEF following PCI occurred in 13% of patients with baseline preserved LVEF and was associated with an increased 1-year risk for death (HR: 2.63; 95% CI: 1.18–5.90; p = 0.001) and MI (HR: 4.91; 95% CI: 2.01–11.98; p = 0.001) and an increased 5-year risk for death (HR: 2.91; 95% CI: 1.75–4.83; p = 0.001) and MI (HR: 2.73; 95% CI: 1.29–5.80; p = 0.001). Recovery to preserved LVEF occurred in 22% of patients with baseline impaired LVEF and was associated with a decreased 5-year risk for death (HR: 0.47; 95% CI: 0.23–0.95; p = 0.036).

P3698 | BEDSIDE

The prognostic impact of variation in left ventricular ejection fraction following elective percutaneous coronary intervention


Introduction: There is paucity of data about the impact of elective percutaneous coronary intervention (PCI) on left ventricular function (LVEF) and the prognostic implications of changes in LVEF on cardiac prognosis.

Purpose: To explore the effect of elective PCI on LVEF and to estimate the prognostic impact of LVEF rise or fall following PCI upon patients with coronary artery disease.
P3701 | BEDSIDE
Impact of successful revascularization of chronic total occlusion on long-term clinical outcome: comparison of clinical factors between successful and failed procedures
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Background: The epoch-making techniques for percutaneous coronary intervention (PCI) of chronic total occlusions (CTO) have contributed to the improved initial success of PCI of CTO lesions (CTO-PCI); however, there have been sporadic reports regarding the benefit of the successful revascularization of CTO on long-term mortality.

Purpose: The purpose of this study was to speculate the effect of CTO-PCI on the long-term mortality of CTO patients.

Methods: Of all cases of PCI performed in our hospital between 2006 and 2013, CTO-PCIs were extracted and classified into two groups: PCI success (n=656 patients) and PCI failure (n=89 patients). Succeeded on 2nd attempt in the failure group and CTO-PCIs to any branches in both groups were excluded. Survival was retraceable by a telephone interview or consultation history in the outpatient clinic. Moreover, the clinical factors affecting the long-term clinical outcome were collected retrospectively and compared between the two groups.

Results: Overall initial success rate of CTO-PCI was 88.1%. Kaplan Meier plot with log rank analysis shows cumulative death was significantly lower in the success group than in the failure group (p=0.06; average follow-up duration; success group vs. failed group = 1531±33.5 vs. 1565±397.5 days, p=0.7). Moreover, successful revascularization of CTO significantly decreased evident cardiac death [25% (95% CI: 18.9%–34.2%) vs. 15% (9.6%–22.6%), P=0.001], ensuing need for CABG [15/656 (2.3%) vs. 9/89 (10.1%), P<0.001], and presentation of congestive heart failure was numerically lower in the success group [21/656 (3.2%) vs. 6/89 (6.7%), P=0.09].

Conclusions: This study suggests that the successful revascularization of CTO improves not only long-term mortality, but also quality of life of CTO patients.

P3702 | BEDSIDE
Very long-term clinical outcomes after sirolimus-eluting stent implantation
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Aims: Late adverse events such as very late stent thrombosis (VLST) or late target lesion revascularization (TLR) after sirolimus-eluting stents (SES) implantation remain an important concern. However, there is little data regarding clinical outcome beyond 5 years after SES implantation. We sought to assess very long-term clinical outcome after SES implantation.

Methods: Between April 2004 and December 2006, a total of 794 patients with 978 lesions underwent percutaneous coronary intervention only with SES. We assessed the major adverse cardiac events, defined as all-cause death, myocardial infarction (MI), target-lesion revascularization (TLR), and stent thrombosis (ST).

Results: During the median follow-up (8.2 years [IQR; 6.2–8.9 years]), cumulative incidence of MACCE, all-cause death and MI were 44.7%, 28.5%, and 9.8%, respectively. Cumulative incidence of TLR was 25.3% (7.4% at 1 year, 14.6% at 5 years, and 22.9% at 8 years, respectively). Cumulative incidence of ST was 7.2% (0.3% at 30 days, 0.7% at 1 year, 2.1% at 5 years, and 3.8% at 8 years, respectively). The predictors of MACCE were hemoablation (hazard ratio [HR] 3.12, 95% confidence intervals [CI]:1.97–4.73, p<0.001) and multivessel disease (HR 2.07, 95% CI: 1.38–3.24, p<0.001).

Conclusions: Late catch-up phenomenon regarding ST and TLR continued up to 8 years without attenuation. Careful clinical follow-up is required in patients treated with SES beyond 5 years.

P3703 | BEDSIDE
Are there different outcomes following diffuse long lesion intervention between chronic total occlusion and non-chronic total occlusion lesions?
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Background: The aim of the study is to investigate whether there are different clinical outcomes in diffuse long lesion of CTO patients (pts) versus non-CTO pts following successful percutaneous coronary intervention (PCI).

Methods: A total of 1081 consecutive pts underwent PCI who had diffuse long disease (>30mm) were divided into two groups; CTO group: n=118 pts, Non-CTO group: n=963 pts. Six-month angiographic and clinical outcomes were compared between the two groups.

Results: The baseline clinical characteristics were similar between the two groups except prior MI, PTCA was more frequent, whereas female gender was less common in the CTO group. The baseline lesion characteristics were similar between the two groups except small vessel (<2.5mm diameter) and calcification were more frequent in the CTO group whereas bifurcation lesion was more frequent in the Non-CTO group. At six months angiographic outcomes, the CTO group showed higher incidence of binary restenosis, higher mean diameter stenosis (DS) and lower minimal luminal diameter (MLD). This result translated into higher incidence of repeat PCI including higher target lesion revascularization (TLR) and higher trend of target vessel revascularization (TVR) up to 3 years despite of similar individual hard endpoints (table). In multivariate analysis, diffuse long lesion in CTO was not an independent predictor for repeat PCI and TLR. However,
small vessel stenting (\(\leq 2.25\) mm) was a predictor for repeat PCI (OR=1.81, CI: 1.0-3.93, p=0.05).

Conclusion: The safety profile, and major clinical outcomes in diffuse long lesion of CTO vs. Non-CTO were similar, following successful PCI except higher rate of repeat PCI and TLR in the CTO group. Long-term randomized clinical trials with larger study population will be necessary to elucidate the final conclusion.

P3704 | BEDSIDE
Bioreorbable vascular scaffolding for the percutaneous treatment of long diffuse coronary lesions
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Purpose: Diffuse coronary lesions (length \(\geq 2\) mm) are still considered at high risk for restenosis after percutaneous intervention, even in the current drug-eluting stent era. Everolimus eluting bioreorbable vascular scaffolding (BVS) may avoid the disadvantages of long permanent metallic stents. From a total of 556 patients (680 lesions) treated with BVS, we selected for analysis 206 patients with 236 long diffuse coronary lesions (35%).

Methods and results: The mean age was 57±9 years. The clinical presentation was stable in 56 patients (24%) and acute coronary syndrome in 180 (76%); 56 patients were diabetics (24%). The mean length of the lesion was 32±12 mm and 42 were considered for BVS implantation after recanalization of a chronic total occlusion. The mean proximal reference diameter was 2.99±0.36 mm; 149 lesions received once single BVS (26 mm), 62 lesions were treated by overlapped multiple BVS and 25 by multiple non-overlapped BVS. The scaffolded length was 34±14 mm. In all cases the BVS was successfully implanted with (n=150; 63%) or without (n=86; 37%) lesion predilation. Balloon postdilation was performed in 88 lesions (37%) with non compliant balloons (diameter 3.2±0.4 mm). After BVS implantation all the side branches \(\geq 2\) mm remained patent. All patients were discharged free of symptoms under dual antiplatelet therapy for at least one year. Clinical follow-up was obtained in all patients. After a mean follow up of 13±7 months the cumulative MACE was 4%; there were 2 subacute stent thrombosis (0.9%), and one of them died (0.5%). During the follow-up, one patient died (0.5%) due to late thrombosis (11 months after the procedure). A balloon coronary computed tomography scanner (CT) was performed in 88 patients evaluating 103 lesions scaffolded with BVS. Six restenosis were detected and target lesion revascularization was performed in all of them (3%). According to CT findings, all intermediate or large side branches (\(\leq 1\) mm in diameter) along the scaffolded segment remained patent at follow up.

Conclusions: Percutaneous treatment with BVS for long diffuse coronary lesions seems to be a promising strategy. The incidence of major cardiac events during the hospitalization time and at mid-term follow-up is low and comparable with the second generation metallic drug-eluting stents.

P3705 | BEDSIDE
Long term prognostic value of risk scores after drug-eluting stent implantation for unprotected left main coronary artery disease - a pooled analysis of the ISAR LEFT MAIN and ISAR LEFT MAIN 2 trials
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Background: Besides Syntax score (SxScore), risk scores incorporating anatomical and clinical data have been recently introduced, to further refine the selection of the most appropriate revascularization strategy. However, data regarding the prognostic value of these newer risk scores in the specific subset of PCI for unprotected left main coronary artery (uLMCA) disease are relatively limited.

Purpose: to evaluate the long-term prognostic value of risk scores in the setting of drug-eluting stent (DES) implantation for uLMCA disease.

Methods: The present report represents a patient-level pooled analysis of the ISAR LEFT MAIN and the ISAR LEFT MAIN 2 randomized clinical trials (1257 patients undergoing DES implantation for uLMCA disease). The predictive accuracy of the occurrence of mortality at 3 years was evaluated with the SxScore, the Syntax Score II (SS-II), the EuroSCORE and the Global Risk Classification (GRC).

Results: At a mean follow-up of 3 years there were 160 deaths (12.7%). In the multivariable Cox regression analysis, EuroSCORE showed a strong independent predictive value (HR (95% CI): 1.99 (1.32–2.97), p=0.001) while SxScore (HR (95% CI): 1.06 (0.84–1.35) p=0.62), SS-II (HR (95% CI): 1.19 (0.80–1.79) p=0.39) and GRC (HR (95% CI): 1.19 (0.91–1.56) p=0.21) didn’t result to be independent predictors of mortality. The predictivity of a multivariable model was significantly improved after inclusion of the EuroSCORE but not after inclusion of the remaining risk scores (Table).

Conclusions: In this large population of patients undergoing DES implantation for uLMCA disease, among evaluated risk scores, EuroSCORE resulted to be the only independent predictor of mortality at three years follow-up.
bleeding events were observed in 48 (2.8%) and 35 (2.2%) patients during follow-up duration (23.1±16.3 months). Bleeding events related with stent implantation were observed only in early bleeding events and other cause of bleeding events were similar between early and late bleeding events (p=0.67). The incidence of fatal bleeding defined as type 5 bleeding was similar between early and late bleeding events (3.9% vs 20%, p=0.12). Warfarin use, past history of GI were independent predictors of early bleeding events (adjusted HR: 3.93, 3.6, p=0.001, 0.005). All patients who used warfarin and suffered from early bleeding events kept dual antiplatelet therapy. Age >80, severe renal dysfunction, hypertension were independent predictors of late bleeding events (adjusted HR: 3.2, 5.1, 3.6, p=0.01, 0.001, 0.04).

**Conclusion:** Predictors of bleeding events after DES implantation differ depending on the time period. Triple antithrombotic therapy included highly risk of early bleeding events.

**Acknowledgement/Funding:** None

### P3708 | BEDSIDE

**Long-term clinical results after first generation drug-eluting stent implantation**


**Background:** There are limited data about very long-term clinical outcomes after first generation drug-eluting stent implantation.

**Purpose:** The aim of this study is to compare the long-term clinical outcomes between sirolimus-eluting stent (SES) and Paclitaxel-eluting stent (PES).

**Methods:** A total of 3577 patients with 5955 lesions (SES: 4366 lesions vs. PES: 1589 lesions) were analyzed retrospectively to compare long-term (>5 years) clinical outcomes.

**Results:** The baseline characteristics were similar between the 2 groups. Although the incidence of target lesion revascularization (TLR) in SES group within 2 years was significantly lower, however, that after 2 years was significantly higher than PES group (figure). Finally, seven-year Kaplan-Meier curves of TLR demonstrated in PES group within 2 years was significantly lower, however, that after 2 years was significantly higher though the incidence of target lesion revascularization (TLR) in SES group within 1589 lesions) were analyzed retrospectively to compare long-term (>5 years) clinical outcomes.

**Conclusion:** Late TLR and ST after SES implantation should be considered during long-term follow-up period.

### P3709 | BEDSIDE

**Clinical predictors of mortality following rotational atherectomy and stent implantation in high risk patients**

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**Background:** Contemporary rotational atherectomy (RA) is mainly used to facilitate stenting in complex lesions. Outcomes involving RA and stenting have been investigated, yet high risk patients have not been adequately described.

**Purpose:** Our aim was to assess procedural success and determine clinical predictors of post-procedure mortality, following RA and stenting in high risk patients.

**Methods:** Data of 218 consecutive patients who underwent RA were evaluated in a prospective database. The primary end-point was the composite of angiographic success of the procedure and long term mortality. Secondary end-points were procedural success, consumption of the angioplasty equipment and peri-procedural major adverse events (MACE). The impact of the relevant angiographic and clinical characteristics on long term mortality were analyzed using uni- and multivariate Cox regression analysis.

**Results:** Mean age was 70±8.2 years, diabetes was present in 44%, chronic renal failure in 29%, Prior myocardial infarction and three vessel disease amounted to 42.2% and 32.6%, respectively. Altogether, 52.8% of patients underwent RA after a failed, non-RA intervention attempt and 35.7% of cases presented as acute coronary syndromes. Angiographic success was 100% and all patients received stents after RA. Periprocedural MACE occurred in five patients (2.3%). Post-procedural death was investigated, with a mean follow-up of 36 months. Mortality amounted to 37.2%. Multivariate analysis revealed that left ventricular ejection fraction <50%, glomerular filtration rate <60 ml/min, cardiogenic shock and diabetes were the only independent mortality predictors.

**Conclusions:** We have found that RA and stenting is a feasible and viable option in elderly high-risk population, with exceptional procedural success and acceptable long term results.

### P3710 | BEDSIDE

**Impact of angiographically visible stent malaposition (Peri-stent contrast staining: PSS) and stent fracture on five-year clinical outcome after drug-eluting stent implantation**

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**Background:** While per-stent contrast staining (PSS) is thought to represent angiographically-visible incomplete stent apposition, IVUS/CCT studies revealed that incomplete stent apposition plays a role in thrombus formation. However, previous studies have provided conflicting circumstantial evidence concerning the role of PSS in very late stent thrombosis (VLST). We investigated the prognostic significance of PSS in patients with sirolimus-eluting stents (SES).

**Methods and results:** Consecutive patients undergoing stent implantation with follow-up angiography (n=807, 644 male, mean age 66.0 years) were studied. Stent fracture was defined as the significant disappearance of stent struts in the stent at follow-up angiography in comparison with the presence of stent struts immediately after stent implantation. The primary endpoint was major adverse cardiac events (MACE) defined as a composite of death, myocardial infarction, stent thrombosis, and target lesion revascularization. Twenty patients (2.48%) exhibited PSS at follow-up angiography. After a median of 5 years/3744 patient-years follow-up, 7 (35.0%) in the PSS group reached the primary endpoint versus 117 (14.9%) in the non-PSS group (P=0.013). Together with diabetes, renal failure, unstable angina, saphenous vein graft and longer total stent length, PSS independently predicted the primary endpoint (HR: 2.94, 95% confidence interval 1.36 to 6.35, P=0.006). Although stent fracture was more frequently found in PSS group than non-PSS group (20% vs 5.7%, P=0.008), stent fracture was not an independent predictor of MACE by multivariate analysis. PSS was also significantly associated with VLST, which occurred in 3 (15.0%) patients with PSS versus 13 (1.7%) in those without PSS (P=0.006).

**Conclusion:** While PSS is an uncommon but significant angiographic finding in patients treated with SES implantation that independently predicts MACE, stent fracture was not an independent predictor of MACE by multivariate analysis. Whilst PSS was also significantly associated with VLST, PSS should be recognised as a potential risk-marker for very late drug-eluting stent failure.

### P3711 | BEDSIDE

**Implications of pre-procedural TIMI flow in patients with acute coronary syndromes: undergoing percutaneous coronary intervention:**

A study of 21,024 patients from the London Heart Attack group


**Introduction:** Although the negative prognostic impact of reduced Thrombolysis in Myocardial Infarction (TIMI) flow before percutaneous coronary intervention (PCI) in ST-segment elevation myocardial infarction (STEMI) has been relatively well described, whether this relationship holds in patients with acute coronary syndromes (ACS; unstable angina and non-STEMI) is not well established.

**Methods:** We undertook an observational cohort study of 21,024 patients with ACS admitted with PCI between 2004 and 2011 at 8 tertiary cardiac centres across London, UK. Patient’s details at the time of the procedure were recorded at the time of the procedure and were included in the local clinical databases using the British Cardiac Intervention Society (BCIS) PCI dataset.

**Results:** From the 8 centres were merged for analysis. Outcome was assessed by in hospital major adverse cardiac events (MACE) and all-cause mortality. The primary end-point was the all-cause mortality at a median follow-up of 3.0 years (GR range: 1.2–4.6 years).

**Conclusions:** 10,929 Patients presenting with STEMI and 10,095 patients with NSTEMI/UA were treated by PCI. These patients were divided in 3 groups according to pre-procedural culprit vessel TIMI flow (TIMI 0/1, TIMI 2 and TIMI 3 flows). Patients undergoing PCIPI had higher rates of TIMI 0/1 flow compared to NSTEMI/UA patients (77.4% vs 12.6%, p<0.0001) with corresponding lower rates of TIMI 3 flow (9.6% vs 76.5%, p<0.0001). Post-PCI TIMI 3 flow was achieved more often in patients with the TIMI 3 group compared to the other groups in both PCIPI and NSTEMI/UA patients.

Kaplan-Meier analysis demonstrated in PCIPI patients that there was a statistically significant difference in mortality rates between the TIMI groups (26.3% TIMI 0/1
as the population ages, we are undertaking revascularisation pro-
cedures on older patients with more co-morbidities, the benefits of which are often
debated. We examine temporal trends in clinical outcomes and procedural safety
following PCI in a large unselected “real world” population.

Methods: Data from the BC cardiac registry from June 1999 to May 2013 on methods:
all PCI cases undertaken on elderly patients (age ≥ 80yrs) was linked to the Vital Statistics
registry for all-cause mortality and Central Transfusion Registry for red
cardiac use transfusions in the given days following 10 PCI cases. Staged PCI and CABG
within 10 days were excluded.

Results: From a total of 83,659 PCI cases performed, 9,613 were undertaken on elderly
patients. Of these, there was a significant rise in the proportion of the PCI cohort
being elderly across the study period (6.8% to 15.6% of total from 1999 to 2013;
< 0.0001). Further more, even within the cohort of older patients, there was a
shift towards higher prevalence of patients aged 85 or older. 20.7% (n=1,988) of
elderly patients presented with stable angina and 79.3% (n=7,625) presented with
acute coronary syndrome of which 19% (n=1,454) were emergent ST-elevation
myocardial infarction (STEMI).

In the elderly cohort undergoing PCI for stable angina, both 30 day (0.7%) mortal-
ity and 1 year (6.2%) mortality remained stable across the 14 year study period.
However, clinical outcomes for the elderly emergent STEMI cohort improved in the
first four years (1999-2002) with a reduction in 30-day mortality from 27.7% to
15.4%, followed by a gradual rise to 17.1% in 2010-2012. Similarly, 1-year mor-
ality declined from 37.8% in 1999-2002 to 22.6% in 2003-2006, then gradually
increased to 27.6% in 2010-2012. Overall, transfusion rates following PCI in the elderly cohort were approximately
double that of those patients under 80 (5.6% vs 2.6%; p<0.0001) and was much
higher in the elderly STEMI cohort throughout the study period (11.1% vs 6.8%;
p<0.0001). In the setting of stable angina, transfusion rates decreased from 3.5%
in 1999-2002 to 0.5% in 2010-2012 (p=0.0032).

Conclusions: Using more than a decade of clinical data, we report a substan-
tial initial fall in mortality for elderly patients presenting with STEMI who undergo
emergency PCI, but with increased uptake there has been a gradual rise in mortal-
ity. Although these findings do not oppose the performance of PCI in the elderly,
more work needs to be undertaken to ensure that the increasing mortality in emerg-
ent STEMI represents an appropriate increased application of PCI in this more
complex population.

P3713 | BEDSIDE
Long-term angiographic outcomes of recurrent restenosis in patients with
drug-eluting stent implantation for in-sent restenosis of
drug-eluting stent
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Background: Long-term angiographic outcomes of recurrent restenosis in pa-
tients treated with drug-eluting (DES) implantation for in-sent restenosis of
the lesion are little known.

Methods: From January 2004 to January 2013, 459 consecutive patients with 619 lesions underwent DES implantation for DES of ISR, in which 8-month follow-
up angiography (fu CAG) was performed in 547 (88.3%) of the 619 lesions and
20-month fu CAG was performed in 378 (57.9%) of the 645 lesions which were without target lesion revascularization (TLR) at 8-month fu CAG.

Results: In the 547 lesions after 8-month fu CAG, recurrent restenosis was doc-
umented in 138 (25.2%) lesions and TLR was performed in 106 (19.5%) lesions
(acute gain, 1.79±0.68; late loss, 0.56±0.68). In the 378 lesions after 20-month fu CAG, recurrent restenosis was documented in 70 (18.5%) lesions and TLR was
performed in 33 (8.7%) lesions (acute gain, 1.77±0.64; late loss, 0.40±0.88).
By multivariate analysis, non-focal type restenosis (odds ratio 2.87, 95% confi-
dence interval, 1.67 to 4.90; p<0.001) was an independent predictor of recurrent restenosis.

Conclusion: Late recurrent restenosis can occur in patients treated with DES
implantation for ISR of DES. When a non-focal type restenosis is documented,
the lesion should be followed up long and carefully.

P3714 | BEDSIDE
Long-term outcomes with 3rd versus 2nd generation coronary drug
eluting stents - a meta-analysis
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Background: Durable polymer drug eluting stents (DES) technology has evol-
ved since its inception in regards to strut size, polymer platforms, and drug elution. The 3rd and 2nd generation coronary DES have favorable outcomes when com-
pared to 1st generation, however limited data exists on long-term outcomes be-
tween the 3rd and 2nd generation DES.

Methods: A systematic MEDLINE search included only direct comparison ran-
domized controlled clinical trials of 3rd and 2nd generation DES up to February
12, 2015. Clinical endpoint of interest include: Myocardial infarction (MI), target
vessel revascularization (TVR), target lesion failure (TLF), stent thrombosis (ST),
all cause death and combined endpoint of MI, TVR, TLF, ST, and death (MACE).
Six trials were included and odds ratio (OR) used to assessed effect size. A fixed
and random effect model was used for calculated summary odds ratio using com-
prehensive meta-analysis statistical software version 2.0.

Results: Among 6 trials, there were a total of 6,363 patients with mean follow
up of 26 months, mean stent length of 24.9±10.1 mm and a cumulative 1,863
combined events of MI, TVR, TLF, ST and death. There were no significant dif-
fences observed in the individual endpoints between 3rd and 2nd generation DES.
The OR for the combined endpoint is depicted in figure 1.

Conclusion: Similar rates of MI, TVR, TLF, ST, and death were observed be-
tween 3rd and 2nd generation DES. Numerically lower rates of combined MACE
favoured 3rd generation DES, but did not reach statistical significance.
D. Moliterno4, T. Henry5, G. Steg6, R. Mehran1 on behalf of PARIS study group.

We followed 353 consecutive patients aged ≥70 years with ACS.

Methods and results: Evidence for improved survival after use of percutaneous coronary intervention (PCI) in elderly patients with acute coronary syndrome (ACS) is limited. SS-II accurately predicts very long-term mortality in STEMI patients (AUC = 0.88).

Background: Evidence for improved survival after use of percutaneous coronary intervention (PCI) in elderly patients with acute coronary syndrome (ACS) is limited. SS-II accurately predicts very long-term mortality in STEMI patients (AUC = 0.88).

Purpose: To assess the association between PCI and long-term mortality in octogenarians with ACS.

Methods and results: We followed 353 consecutive patients aged ≥70 years hospitalized with ACS, 182 treated with PCI, 171 were not. In overall cohort (n=353) five-year all-cause mortality was 46.2% and 89.5% in the PCI and non-PCI subgroups respectively. In propensity matched cohort (n=71+71) adjusted for 20 baseline variables, Kaplan-Meier survival curves and log rank test showed significantly improved survival (P=0.001). Cox regression analysis showed that PCI was associated with reduced long-term mortality in matched and overall cohort, (HR 0.5, 95% CI 0.2–0.9, P<0.020) and HR 0.4, 95% CI 0.2–0.5, P=0.020 respectively.

Table 1. Univariable and multivariable Cox analyses for relationship between PCI and long-term all-cause mortality

<table>
<thead>
<tr>
<th>P value</th>
<th>Multivariable HR (95% CI)</th>
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<tbody>
<tr>
<td>In overall cohort:</td>
<td>Adjusted for the confounders</td>
<td>0.4 (0.2–0.5)</td>
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<tr>
<td>In matched cohort:</td>
<td>Adjusted for propensity score (PS)</td>
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<td>Adjusted for PS and the confounders</td>
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Kaplan-Meier curves, matched groups

Conclusions: In octogenarians with ACS, PCI was associated with improved survival from all-cause death over five years of follow up.

P3716 | BEDSIDE
Acute coronary syndrome in octogenarians, association between percutaneous coronary intervention and long-term mortality

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Background: Evidence for improved survival after use of percutaneous coronary intervention (PCI) in elderly patients with acute coronary syndrome (ACS) is limited.

Methods and results: We followed 353 consecutive patients aged ≥70 years hospitalized with ACS, 182 treated with PCI, 171 were not. In overall cohort (n=353) five-year all-cause mortality was 46.2% and 89.5% in the PCI and non-PCI subgroups respectively. In propensity matched cohort (n=71+71) adjusted for 20 baseline variables, Kaplan-Meier survival curves and log rank test showed significantly improved survival (P=0.001). Cox regression analysis showed that PCI was associated with reduced long-term mortality in matched and overall cohort, (HR 0.5, 95% CI 0.2–0.9, P<0.020) and HR 0.4, 95% CI 0.2–0.5, P=0.020 respectively.

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P3717 | BEDSIDE
Patterns of dual anti platelet therapy cessation in left main and proximal left anterior descending artery PCI: Results from the PARIS registry

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1Mount Sinai School of Medicine, New York, United States of America; 2London School of Hygiene and Tropical Medicine, London, United Kingdom; 3St. Luke’s Mid America Heart Institute, Kansas City, United States of America; 4University of Kentucky, Lexington, United States of America; 5Minneapolis Heart Institute Foundation, Minneapolis, United States of America; 6Hospital Bichat-Claude Bernard, Paris, France

Background: Stenting of the left main (LM) and proximal left anterior descending artery (pLAD) are considered high risk procedures as these coronary segments subtend a substantial proportion of left ventricular myocardium. Heightened attention is deserved to avoid peri-procedural abrupt closure and post-procedural stent thrombosis.

Purpose: We aimed to assess patterns of dual antiplatelet therapy (DAPT) cessation, and clinical outcomes in patients undergoing LM/pLAD PCI, from the prospective all-comer PARIS registry (n=5018).

Methods: We undertook a post-hoc analysis comparing patients undergoing LM/pLAD PCI, versus those undergoing PCI to other coronary segments. DAPT cessation was classified as physician-guided discontinuation, brief interruption, or discontinuation due non-compliance or bleeding. The primary efficacy endpoint was 2-year major adverse cardiovascular events (MACE; composite of cardiac death, myocardial infarction (MI) or definite/probable stent thrombosis). The primary safety endpoint was major bleeding as per the bleeding academic research consortium (BARC) definitions, BARC bleeding 3 or 5.

Results: Of the study population, 25.0% (n=1252) underwent LM/pLAD PCI, and 75.0%, (n=3766) underwent non-LM/pLAD PCI. While the groups were similar for age (mean, 63.9 years) and female gender (25.4%), patients undergoing LM/pLAD PCI had fewer comorbidities including current smoking, diabetes, prior MI or peripheral arterial disease compared to those undergoing non-LM/pLAD PCI. In contrast, multivessel disease and bifurcational disease was more common in the LM/pLAD group, as was use of 2nd generation drug eluting stents and implantation of multiple stents or longer stents (≥20mm). Patients in the LM/pLAD group also presented more often with stable angina rather than acute coronary syndrome. At 2 years, the rate of discontinuation was higher (43.3% vs. 39.4%, p=0.01) in the LM/pLAD group while rates of disruption (12.7% vs. 14.8%, p=0.06) and interuption (9.7% vs. 10.7%; p=0.30) were not significantly different. Two-year Kaplan Meier estimates of MACE (6.4% vs. 6.6%; p=0.82) and BARC major bleeding (4.1% vs. 4.1%; p=0.98) were similar between these groups.

Conclusions: In the PARIS registry, patients with LM/pLAD PCI presented with fewer clinical comorbidities but anatomically more complex disease. Despite implantation of more stents and longer stent lengths, DAPT discontinuation was higher in such patients without an increased risk of adverse outcomes at 2 years.

P3718 | BEDSIDE
Results of percutaneous coronary intervention of de novo lesions with sesquiplease paclitaxel eluting balloon catheter at a very long-term follow-up

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Introduction: Drug eluting balloons currently constitute one of the therapeutic tools used in percutaneous coronary intervention (PCI) in de novo coronary lesions, mainly in bifurcations and small vessels. Nowadays, their results at a very long-term follow-up are unclear.

Purpose: The main objective of this study was to evaluate the efficacy and safety of second-generation Sequent Please® paclitaxel eluting balloon (PEB) in de novo coronary lesions at 6 years.

Methods: We prospectively included 81 consecutive patients (69±12 years, 64.2% male) with 81 de novo lesions treated with PEB between March 2009 and March 2014. Additional bare metal stent (BMS) or drug-eluting stent (DES) was implanted before PEB if the result was not satisfactory because of dissection, recoil or significant residual stenosis. We evaluated the presence of major cardiac events (MACE) after a prolonged clinical follow-up (median 49 months): death, nonfamilial myocardial infarction, target lesion revascularization (TLR) and thrombosis.

Results: 32.1% of patients had stable coronary artery disease and 67.9% acute coronary syndromes (48.1% Non-STEMI and 19.8% STEMI). 48.1% of patients were diabetic. 46.9% of lesions were bifurcations, 17.3% diffuse and 53.1% type B2/C. Mean vessel diameter and length were 2.43±0.35 mm and 16.2±5.7 mm, respectively. 75.3% of the lesions were treated with PEB, 21% with PEB and BMS and 3.7% with PEB and DES. There were no significant differences regarding baseline characteristics of these three groups neither in the MACE rate after a long-term follow-up (p=0.5). During follow-up, 6 patients died (1 cardiovascular and 5 non-cardiovascular deaths) and a TLR rate of 2.5% was observed. Two cases of non-fatal myocardial infarction (2.5%) and no cases of thrombosis were observed, immediately after the procedure nor during follow-up. 17.3% of patients had angiographic follow-up.

We did not observe a higher need for additional stent after PEB in complex lesions such as diffuse lesions (p=0.7) and bifurcations (p=0.7).

Conclusions: Percutaneous interventions of “De Novo” coronary lesions with Sequent Please® PEB offers very favorable results at a very long-term follow up. There was not a higher need for additional stent in cases of diffuse and bifurcated lesions.

P3719 | BEDSIDE
Long-term clinical outcomes after combined drug-coated balloon/bare metal stent angioplasty compared with everolimus-eluting stents


Background: In the randomized OCTOPUS trial (NCT01056744) elective PCI of de novo stenoses using bare metal stents (BMS) postulated with drug-coated balloons (DCB) proved safe with discontinuation (DAPT) at 6 months, without significant differences in stent coverage at optical coherence tomography (OCT) between BMS+DCB and everolimus-eluting stents (EES). However, 6-month OCT revealed significantly more in-stent proliferation.
Methods: The new Syntax-II score was superior to the anatomical SYNTAX score (HR 1.02, 95%-CI: 1.00–1.04, p=0.011).

Conclusion: The combined BMS+DCB treatment with 6-month DAPT showed long-term cardiovascular outcomes comparable to EES.

P3721 | BEDSIDE
Gender differences in 5-year clinical outcomes following percutaneous coronary intervention

Background: Several studies have reported that clinical outcome after percutaneous coronary intervention (PCI) was worse in female compared with male. However, many of these studies evaluated short-term clinical outcomes. To date, gender difference in long-term clinical outcomes after PCI has not been elucidated.

Methods: We analyzed data of patients following PCI in Juntendo University (Tokyo, Japan) from 1984 to 2008. The patients were divided into two groups according to gender. Primary endpoint was a composite of 5-year all-cause mortality and acute coronary syndrome.

Results: A total of 3531 patients were examined (Female; 605 and Male; 2926). Mean age, a prevalence of hypertension, dyslipidemia and a percentage of ACS at presentation were higher in the female group. Lipid profiles were worse and LVEF was reduced in the male group. Kaplan-Meier estimation for 5-year all-cause death and acute coronary syndrome was superior to the male group (Figure 1). Univariable Cox regression analysis for cardiovascular events in the whole population revealed that male gender was associated with reduction in the long-term clinical outcomes (HR 0.79, 95% CI 0.65–0.97, P=0.03). After controlling confounding factors, gender was not associated with the long-term clinical outcomes. Multivariable Cox regression analysis showed that higher age and MVD was associated with worse clinical outcomes, while BMI, Hb, eGFR and LVEF were inversely associated with the incidence of the long-term clinical outcomes.

Figure 1. Kaplan-Meier curves for 5-year all-cause death and ACS

Conclusions: Gender difference in 5-year all-cause mortality and ACS was not observed in our study population following PCI.

P3722 | BEDSIDE
Impact of first generation drug-eluting stents on the long-term clinical results compared with bare-metal stent

Background: Short-term clinical outcomes after first generation drug-eluting stent (DES) implantation were dramatically improved compared with those after bare-metal stent (BMS) implantation. However, very long-term clinical outcomes have not been fully estimated.

Purpose: The aim of this study is to compare the long-term clinical outcomes between first generation DES and BMS.

Methods: A total of 6007 patients with 9566 lesions (DES: 5955 lesions vs. BMS: 3611 lesions) were analyzed retrospectively to compare long-term (≥5 years) clinical outcomes.

Results: Ten-year Kaplan-Meier curves demonstrated that target lesion revascularization (TLR) rate was significantly lower in DES group (DES: 11.4% vs. BMS: 19.4%, p<0.01). On the other hand, although TLR rate in DES group within 2 years was significantly lower, that after 2 years was significantly higher than BMS group (Figure). The rate of stent thrombosis (ST) in DES group continued to increase after 2 years follow-up and demonstrated a higher rate compared with BMS group during 10 years follow-up period (0.76% vs. 0.22%, p<0.01).

Figure 2. Kaplan-Meier curve for 10-year TLR rate after first generation DES and BMS

Conclusions: Gender difference in 5-year all-cause mortality and ACS was not observed in our study population following PCI.

Figure 2. Kaplan-Meier curve for 10-year TLR rate after first generation DES and BMS
Conclusion: Late TLR and ST after DES implantation should be considered during long-term follow-up period.

P372 | B ED SIDE

The influence of aortic root calcium volume and distribution on the risk of paravalvular regurgitation after transcatheter aortic valve replacement

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Introduction: Paravalvular regurgitation (PAR) after transcather aortic valve replacement (TAVR) is associated with increased mortality. Further data on the influence of aortic root calcium on the risk of PAR is warranted.

Purpose: We sought to determine the impact of aortic root calcium volume and distribution on the risk of PAR in a multicenter setting.

Methods: 288 patients from 3 centers underwent multidetector computer tomodraphy (MDCT) prior to TAVR with the Edwards Sapien XT valve. Balloon post-dilatation (PD) for treatment of PAR- mild was performed at the discretion of the treating operator. PAR was assessed using predischARGE TTE. Quantitative calcium analysis incorporating a detailed 3-dimensional regional analysis on contrast-enhanced pre-TAVR MDCT scans was performed. Aortic root calcium was quantified volumetrically in three anatomical regions: 1) the Aortic Valve Region (from the aortic annulus plane to the left coronary ostia), 2) the Overall Left Ventricle (OLV; from the aortic annulus plane and 10 mm into the left ventricle) and 3) the Upper LVOT (from the aortic annulus plane and 2 mm into the left ventricle). A combined endpoint of predischarge PAR- mild or PAR (as a surrogate for PAR- mild) was defined (PD/PAR patients).

Results: Mean age 81±6 years, mean STS risk score was 6.3±3.9 and 50% (144) were female. PD was performed in 7% (21/288) of the patients. Post-procedural PAR- mild was present in 10% (29/288) of the patients. The combined endpoint of PAR- mild or PD occurred in 15% (44/288) (PD/PAR patients). Medial interceptant range. Upper LVOT and Overall LVOT calcium volumes were higher in PD/PAR patients compared to non-PAD/PAR patients, 25 [5–66] mm³ vs. 0 [0–8] mm³ (p<0.0001) and 44.9 [112] mm³ vs. 3 [0–59] mm³ (p=0.03), respectively. Aortic Valve Region calcium volume did not differ between PD/PAR patients and non-PD/PAR patients, 496 [347–732] mm³ vs. 565 [245–1004] mm³ (p=0.49). Upper LVOT calcium volume was more predictive of PD than PAR- Overall LVOT calcium volume, area under receiver operating curve (AUC) (95% CI): 0.70 (0.59–0.79) vs. 0.60 (0.51–0.70) (p=0.001). In patients with prosthesis valve oversizing, >15% relative to annular area, Upper LVOT calcium volume was more predictive of PD than PAR: Overall LVOT calcium volume was area under receiver operating curve (AUC) (95% CI): 0.83 (0.72–0.93) vs. 0.53 (0.38–0.67) (p<0.0001).

Conclusion: PAR- mild and need for PD is best predicted by calcium volume in the Upper LVOT. Pre-TAVR planning and prosthesis valve selection may be further refined by assessing aortic root calcium distribution.

P373 | BEDSIDE

Clodipogrel not indicated before TAVI, after TAVI with caution and under platelet reactivity assessment

K. Czerwinska, A. Witkowski, M. Dabrowski, J. Stepinska. Institute of Cardiology, Warsaw, Poland

Dual antiplatelet therapy (DAPT): aspirin (ASA) + clopidogrel (CLOP) after TAVI is recommended. Safety of DAPT has not been defined. While in ACS pts the under platelet reactivity assessment is recommended, Clopidogrel not indicated before TAVI, after TAVI with caution and under platelet reactivity assessment.

Methods: A total of 286 patients from 3 centers underwent multidetector computer tomography (MDCT) prior to TAVR with the Edwards Sapien XT valve. Balloon post-dilatation (PD) for treatment of PAR- mild was performed at the discretion of the treating operator. PAR was assessed using predischARGE TTE. Quantitative calcium analysis incorporating a detailed 3-dimensional regional analysis on contrast-enhanced pre-TAVR MDCT scans was performed. Aortic root calcium was quantified volumetrically in three anatomical regions: 1) the Aortic Valve Region (from the aortic annulus plane to the left coronary ostia), 2) the Overall Left Ventricle (OLV; from the aortic annulus plane and 10 mm into the left ventricle) and 3) the Upper LVOT (from the aortic annulus plane and 2 mm into the left ventricle). A combined endpoint of predischarge PAR- mild or PD (as a surrogate for PAR- mild) was defined (PD/PAR patients).

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Conclusion: PAR- mild and need for PD is best predicted by calcium volume in the Upper LVOT. Pre-TAVR planning and prosthesis valve selection may be further refined by assessing aortic root calcium distribution.

P375 | BEDSIDE

Pressure half-time by echocardiography in comparison with cardiac magnetic resonance for quantification of paravalvular regurgitation after transcatheter aortic valve implantation

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Background: Aortic regurgitation is common after transcatheter aortic valve implantation (TAVI) and is associated with negative impact on patient outcome. Assessment of paravalvular regurgitation severity is limited by most methods of continuous-wave Doppler echocardiography (PHT) and color TAVI. Pressure half-time (PHT) is a parameter easy to assess by echocardiography in these patients but it is affected in case of left ventricular hypertrophy (LVH).

Purpose: This study sought to evaluate the accuracy of PHT with distinct cut-off values in differentiating patients with and without LVH for grading of paravalvular aortic regurgitation after TAVI in comparison with cardiac magnetic resonance (CMR) as the reference method.

Methods: In 71 patients (age 81±6 years) with severe aortic stenosis transthoracic echocardiography and CMR were performed after TAVI. Paravalvular regurgitation was assessed using continuous-wave Doppler echocardiography of aortic regurgitation velocity curve. In 18 of 71 patients (25%) with at most trace regurgitation PHT could not be obtained due to no or very faint signal. CMR imaging of the ascending aorta was used for calculation of regurgitant fraction by division of aortic backward flow by aortic forward flow. According to CMR guidelines paravalvular regurgitation severity was graded more than mild when regurgitant fraction was >15%.

Results: In 13 of 53 patients (25%) paravalvular regurgitation after TAVI was more than mild as graded by CMR analysis. LVH was present in 29 of 53 patients (55%). PHT correlated less to regurgitant fraction by CMR analysis in patients without LVH (r=−0.1474; p=0.4919) than in patients with LVH (r=−0.5431; p<0.0001). In patients without LVH accuracy of PHT to predict more than mild paravalvular regurgitation using a cut-off value of 347 ml (AUC=0.738, sensitivity 66.7%, specificity 90.5%) was comparable to analysis in patients with LVH using a cut-off value of 340 ml (AUC=0.800, sensitivity 80.0%, specificity 84.2%).

Conclusion: Analysis of PHT with distinct cut-off values differentiating patients without and with LVH allows accurate identification of more than mild paravalvular regurgitation after TAVI as defined by CMR.

Acknowledgement/Funding: This study was supported by a research grant from GE Ultrasound, Horton, Norway.

P376 | BEDSIDE

3-D Echocardiographic measurement of aortic annulus using area or circumference for TAVI. Does it make a difference?

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Introduction: The use of Transcatheter Aortic Valve Implantation (TAVI) to treat aortic stenosis is increasing worldwide. Accurate sizing of the AV prosthesis is paramount. We present our 7-year experience using 3-D TOE and investigate if different sizing methods of the aortic annulus (AA) lead to different results.

Methods: We investigated 193 patients who underwent TAVI in our Hospital and had 3D TOE datasets of the AA. We derived the AA diameter by two different methods: a) Diameter by annulus area; DA = 2 × (area –) and b) diameter by circumference; DC = circumference/π. Using the Edwards Sapien 3 Valve 3D Sizing

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Abstract P3727


Percutaneous left atrial appendage (LAA) closure is a relatively new procedure in interventional cardiology for stroke prevention in the patients with atrial fibrillation. Continued access registry of the PROTECT AF study reported learning curve in multiple center registries. Until now, single center report of learning curve in this procedure is rare. Therefore the aim of the present study was to evaluate procedure learning curve in clinical routine.

Methods: A total of 372 patients (145 males, 72.6±8.5 years, CHADs score: 3.3±1.4) with atrial fibrillation receiving LAA closure at a single center from August 2009 to June 2014 were investigated. The patients were divided into five groups according to the procedure date. The fluoroscopy time, radiation exposure, procedure duration, amount of contrast agents were analysed.

Results: Overall successful implantation rate was 99.2% (369 of 372 patients). The radiation exposure showed significantly forward less (p<0.001), and the amount of contrast agent showed also significantly forward smaller quantity (p<0.001). Total number of the device showed a trend forward less but statically not significant. The procedure duration and fluoroscopy time were not significantly different among the groups.

Conclusion: Our data show a clear reduction in the radiation exposure and the amount of contrast agent use with a strong trend forward. Interestingly, we added in future physiciens during the study. We conclude there was a clear learning curve in LAA closure in clinical routine at a high volume center.

P3729 | BEDSIDE

Ruptured sinus of Valsalva aneurysm closure with new types PDA devices

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Introduction: Ruptured sinus of Valsalva aneurysm (RSOVA) is a rare shunt lesion frequently treated percutaneously. Lately for this purposes have been also Chinese PDA nitinol wire mesh devices very similar to Amplatzer Duct Occluder (ADO). Experience with this occluders is scant.

Aim: To present results of transcatheter closure of RSOVA with PDA occluders taking in consideration short and midterm results.

Methods: From September 2010 to August 2014, 8 patients (pts) from 17 to 72 years old (mean age 40 y) have closed their RSOVA with nitinol wire mesh PDA occluders (produced by 3 different companies). All but two pts had congenital sinus of Valsalva aneurysm. Two pts had acquired RSOVA after previous cardiac surgery (one after aortic valve replacement, another after surgery of tight subaortic stenosis – LVOT). In all pts arterio-venous loop was created and PDA devices were implanted transvenously. There were used devices 2–6 mm bigger than orifice of RSOVA. There were 7 connection between right coronary or noncoronary sinus with right atrium and 1 between noncoronary sinus and right ventricle.

Results: All PDA devices (sizes from 12/10 to 18/16) were successfully implanted in RSOVA. In one pt with istiocographic RSOVA (after LVOT operation) device have been retrieved because of massive aortic regurgitation after implantation provoked by the device. In 72 y old woman, after aortic valve replacement, duct occluder was applied in proximal entrance to the RSOVA. Because of the presence of important residual leak on the edge of the implant the procedure had to be supplemented by closing of the distal RF orifice of RSOVA with 10 mm Muscular VSD Occluder. In one pt after embolization of ADO to pulmonary artery and its transcatheter retrieval, bigger device were applied. In another pt after ADO implantation 2–3 years later during pregnancy recanalization of SVA occurred treated successfully by PDA occluder after delivery. In follow-up (ranged from 0,5 till 4 years) no complications were observed in any pt.

Conclusions: Transcatheter closure of ruptured sinus of Valsalva aneurysm with new nitinol mesh occluders are safe and effective procedures.

P3730 | BEDSIDE

Impact of complex septal anatomy on clinical events in long term follow up after percutaneous closure of patent foramen ovale

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Purpose: In patients with cryptogenic stroke, certain anatomical features of a patent foramen ovale (PFO), as atrial septal aneurysm (ASA) or a large right-to-left shunt (RLS) have been associated with stroke recurrence in follow up. Our aim was to investigate the impact of the complex septal anatomy in the long term risk of stroke after percutaneous effective closure of the PFO.

Methods: From January 2000 to November 2014, a total of 172 patients (mean age 46±12 years, 60% male) underwent percutaneous PFO closure after suffers of
ing a cryptogenic stroke associated to PFO and the presence of at least one of the following risk factors for recurrence: deep vein thrombosis, hypercoagulability status, extensive right-to-left shunt volume of contrast bubbles through the PFO at rest, atrialseptal aneurism, recurrent stroke despite anticoagulant treatment or anticoagulant intolerance. We performed a comparative study of baseline clinical variables and follow up outcomes among patients with a complex septal anatomy defined as atrial septal aneurysm or large right-to-left shunt volume of contrast bubbles through the PFO versus the rest of the series.

**Results:** A complex septal anatomy was present in 111 patients (65%): an ASA was present in 75 patients (44%) and a large shunt in 70 patients (41%). Baseline clinical features were similar in patients with and without a complex anatomy, except that the first group was older (48±13 versus 43±9 years, p=0.01). Most patients received an Amplatzer device in both groups (85% versus 83%, p=0.84) but the complex anatomy received a >25 mm device more frequently (76% versus 36%, p=0.0005). Primary success rate was 100% in both groups. Only in one case there was a periprocedural minor complication (a groin hematoma). After 5±4 years of follow up, we observed 6 deaths (with only one of cardiovascular cause, an acute myocardial infarction) and 8 non-fatal cerebrovascular ischemic events (4 strokes and 4 transient ischemic attacks). The percentage of patients free of antithrombotic treatment at last follow up was similar in both groups: 44% versus 49%, p=0.54. Probability of recurrent cerebrovascular ischemic events at follow-up was low and similar in the study group than in the rest of series (1.08 versus 0.33/100 patient-years, p=0.24), even after adjusting by age and device size (HR 2.52, 95% CI 0.28–22.75, p=0.41).

**Conclusion:** In this real-life series, we have not found a significant adverse impact of a complex septal anatomy in recurrent cerebrovascular events, after the effective closure of the PFO.

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**P3731 | BEDSIDE**

**Transmural tricuspid valve-in-valve and valve-in-ring implantation using the Edwards SAPIEN XT valve: one-year follow-up**

C. Boulet1, D. Himbert1, E. Brochet1, P. Ou2, B. Iung1, M. Urena1, G. Ghodbane3, A.A. Fassa1, P. Nataf3, A. Vahanian1.

**Background:** Redo tricuspid surgery may be high risk or even contraindicated due to comorbidity. Transcatheter valve implantation (TVI) has been recently reported in this setting.

**Purpose:** The aim of this study was to evaluate the feasibility of transmural implantation of Edwards SAPIEN XT prostheses in failed tricuspid bioprostheses (BP) and ring annuloplasty (RA).

**Methods:** Between 2011 and 2013, TVI was performed in 6 patients for failed tricuspid surgical valves (3 BP, 3 RA) in our institution. Median age was 58 years and patients were in NYHA class II. All patients had a history of cardiac surgery and had previously undergone at least 2 interventions.

**Results:** The procedure was successful in 100% for BP and 67% for RA. One patient had indeed a moderate residual paravalvular leak at the level of the open portion of a rigid incomplete ring. In-hospital complications included: 1 major bleeding related to esophageal ulceration and 1 severe vascular complication. The transvalvar gradient decreased from 8.0 mmHg at baseline to 4.1 mmHg at day 7. Residual regurgitation was absent in 3 cases, trace in 1 case, mild in 1 case and moderate in 1 case. All patients had a >1 year clinical and echocardiographic follow-up (Figure). Survival was 100% 1 year after the procedure. For only 1 patient, the tricuspid gradient remained stable. Only 1 patient was in NYHA class II, 3 in NYHA class III and 2 in NYHA class I.

**Conclusions:** Transmural implantation of SAPIEN XT valves in failed tricuspid BP are feasible in selected high-risk patients, with good early and 1 year hemodynamic and clinical results. However, RA may raise issues due to their oval shape and open configuration.

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**P3732 | BEDSIDE**

Clinical outcomes of the intra-aortic balloon pump for resuscitated patients with acute myocardial infarction complicated by cardiac arrest

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**Background:** The aim of this study was to investigate the clinical effects of intra-aortic balloon pump (IABP) in patients who received cardiopulmonary resuscitation (CPR) before procedure.

**Methods and results:** Between November 2005 and April 2014, 49,542 patients were enrolled in a prospective cohort study for AMI in Korea (KAMIR). Cardiopulmonary resuscitation (CPR) was performed in 1,700 patients with cardiac arrest. Patients were excluded from the study if they had not underwent a coronary angiogram, if extracorporeal membrane oxygenation (ECMO) or thrombolyis was performed, and if mechanical complications presented. The primary end point was 1-month all-cause mortality. A total of 883 patients in the IABP group and 476 in the control group were included. During the 1-month follow-up, all-cause mortality was 12.3% in the IABP group versus 17.1% in the control group (HR 0.71, 95% CI 0.51–0.98, p=0.037). The proportion of recurrent cerebrovascular events was 4.5% in the IABP group and 7.5% in the control group (HR 2.52, 95% CI 0.28–22.75, p=0.41).

**Conclusion:** IABP used in subjects with especially high risk of death. The use of IABP did not show clinical benefits in patients with AMI complicated by severe cardiogenic shock after propensity matching analysis.

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**P3733 | BEDSIDE**

A multi-modality intra-arterial imaging comparison of renal artery trauma induced by balloon-based and non-balloon-based renal denervation devices

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**Background:** Renal denervation has been associated with acute vascular trauma. Potential differences in the pattern or incidence of acute renal artery injury according to the denervation method have not been investigated.

**Purpose:** To investigate by quantitative angiography, intravascular ultrasound (IVUS) and optical coherence tomography (OCT), the acute repercussion of renal denervation on the treated and non-treated vessels in patients with coronary-based denervation (BD) and non-balloon-based denervation (nBD) devices.

**Methods:** Twenty-five patients underwent bilateral renal denervation in two centers with 5 different systems, 2 nBD [Symplity™ (n=6), EnliHTM™ (n=3)] and 3 BD [Oneshot™ (n=6), Paradigm™ (n=4) and Vessix V2™ (n=5)]. Analysis included quantitative angiography pre- and post-procedure, morphometric measurements by IVUS pre- and post-procedure, and assessment of vascular trauma (dissection, edema, or thrombus) by OCT after denervation.

**Results:** In nBD-treated vessels, there was a significant reduction of minimal lumen diameter by 0.52±0.86mm (p<0.05) by angiography, while by IVUS the minimal lumen area decreased by 3.11±4.38mm (p<0.05) and the percent intima & media volume increased by 4.0±3.9% (p<0.01). Conversely, in BD-treated vessels, these differences were not significant.

By post-denervation OCT, dissection was seen in 2 vessels treated with nBD devices (13.3%) vs. 12 nBD-treated vessels (42.9%; p=0.09). Thrombus was observed in 12 nBD-treated vessels (80.0%) vs. 23 BD-treated vessels (82.1%; p=0.76). Edema was detected in 13 nBD-treated vessels (88.7%) vs. 6 BD-treated vessels (67.9%; p=0.28). Percent frames with dissection was lower in nBD-treated vessels vs. BD-treated vessels [0.1% (0–1.4%) vs. 2.8% (0.6–11.2%); p<0.05], whereas there was no difference for percent frames with thrombus [6.1% (2.9–12.6%) vs. 7.5% (4.3–12.6%); p=0.68] and percent frames with edema [14.6% (2.3–35.2%) vs. 5.2% (2.4–12.7%); p=0.18].

In BD-treated vessels, balloon-to-artery ratio had a good discriminative ability for predicting dissection by OCT [ROC: 0.81 (0.65–0.97); p<0.01], with a value >1.18 predicting dissection with 56.3% sensitivity and 87% specificity.

**Conclusion:** A varying extent of vascular injury was observed after renal denervation. nBD systems were associated with a “spasm-like” response with reduction of lumen dimensions and increase of intimal-medial volume. BD systems were associated with higher extent of dissection, which was observed in ≤40% of the cases. The occurrence of dissection in these vessels was associated with a higher balloon-to-artery ratio.
One-shot circumferential renal artery denervation with relative sparing of the arterial wall may be possible using a novel microwave catheter

**P3734 | BENCH**

**Purpose:** To show that a microwave catheter may induce deep circumferential heating while sparing the luminal surface of the vessel wall and nearby viscera even with reduced renal artery flow.

**Methods:** A microwave catheter was constructed and tested in a renal artery model. This consisted of transparentphantom materials for renal artery, perinephric fat and nearby viscera embedded with a thermochromic liquid crystal sheet that changes colour with temperatures between 50–78°C. 0.9% saline was perfused through the renal artery at 37°C. 25,200J ablations were performed at 140W for 180s and 120W for 210s with saline flow at 0.5L/min and 0.1L/min. The 53°C isotherm was taken as the lesion boundary and dimensions were assessed using serial digitalphotograph and analysed with in-house built software.

**Results:** At maximal lesion growth, ablations at 140W at 0.5L/min flowed perforated the luminal 1.0mm (95% CI 0.8–1.1mm) of the vessel wall, extended 5.9mm (95% CI 5.6–6.1mm) deep from the vessel lumen and was 19.2mm in length (95% CI 17.7–20.7mm). Reductions in renal artery flow to 0.1L/min had minimal impact on lesion dimensions. Delivering ablation energy at 120W produced significantly smaller lesions with more vessel sparing compared with 140W. No heating peripheral to the10mm thick perinephric fat phantom layer was observed.

**P3735 | BEDSIDE**

**Effects of renal denervation on cardiac sympathetic activity and innervation**

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**Background:** Renal denervation (RDN) demonstrated its efficacy not only in reducing blood pressure (BP), but also in reducing heart rate (HR), cardiac hypertrophy and arrhythmia in certain patients. These pleiotropic effects are partly independent from the BP reduction. A direct effect of RDN on the heart could explain previously described findings, but data in this respect are lacking.

**Purpose:** To investigate if RDN has a direct effect on cardiac sympathetic activity and innervation density.

**Methods:** Sixteen patients with resistant hypertension (mean office systolic BP 175±18 mmHg, mean ambulatory systolic BP 141±19 mmHg, mean antihypertensive medications 5.9±1.4) underwent I-123-mIBG scintigraphy to measure cardiac sympathetic innervation and activity before and 6 months after RDN. Cardiac sympathetic innervation was assessed by heart to mediastinum ratio and cardiac sympathetic activity by wash out ratio. RDN was performed with a single electrode catheter. Effects on office BP, ambulatory 24-hours BP monitoring, office HR and 24-hours HR monitoring were also measured.

**Results:**Despite antihypertensive treatment, baseline SBP and DBP in this group of patients were –179, 41±29, 19 and –105,23±17,95 respectively. Office BP decreased by –23,08/10.08 (p<0.05) and –22, 01±11, 23 mmHg (p<0.05) at 6 and 12 month respectively. No significant changes of GFR and renal blood flow were found, however, RENI decreased significantly in segmental RA: from 0.72±0.1, initially till 0.67±0.04 and 0.67±0.03 respectively, at follow-up points. Postprocedural renal duplex ultrasound was performed without detecting abnormalities (eg, significant renal artery stenosis or aneurysm) of the renal arteries through the study period.

**Conclusions:** In the control points of patients with RH after RDN there was observed a significant and sustained reduction in office blood pressure. Also RDN had no adverse effect on either renal function or blood flow trunk and segmental branches of the RA according to GFR and renal duplex ultrasound. On the contrary, the decrease of resistive index in segmental RA after the intervention indicates improvement of renal blood flow.
P3738 | BEDSIDE
Effects of renal sympathetic denervation on cardiac sympathetic activity and function in patients with therapy resistant hypertension
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Background: Renal sympathetic denervation (RSD) is currently being investigated in multiple studies of sympathetically driven cardiovascular diseases such as heart failure and arrhythmias. In the present study, our aim was to assess systemic and cardiac sympathetic effects of RSD by measurement of cardiac sympathetic activity and cardiovascular parameters.

Methods: A total of 21 consecutive patients with refractory hypertension (daytime ambulatory blood pressure (BP) ≥ 150/100 mmHg despite the use of 3 or more antihypertensive drugs), no evidence for secondary hypertension and normal renovascular anatomy were included. RSD was performed with the Medtronic Symplicity renal denervation catheter with an average of 4.2 (range 3–6) ablation lesions per renal artery. 123I-mIBG cardiac scintigraphy was performed before and after 6 weeks after RSD to assess cardiac sympathetic activity. In addition, the effect of RSD on peripheral BP and cardiac hemodynamics were assessed non-invasively in supine position and after standing.

Results: 123I-mIBG uptake before and after RSD was 1.7±0.4% vs. 1.7±0.5% at urea clearance at baseline and 8.5±1.7% after RSD. In the group treated with RSD, there was a significant drop in heart rate (p=0.04) was detected. However, no changes were seen in stroke volume.

Conclusions: This study highlights the differences between first- and new-generation RDN devices. ABPM at 1 and 6 months showed a trend, although not statistically significant (due to the small sample size) towards a larger BP reduction in the Symplicity group. In conclusion, the Symplicity renal denervation system delivers a predictable pattern of simultaneous multiple ablations and allows for a more effective RDN compared with the Symplicity single-electrode system. Moreover, the different mechanism of Venusix RDN system with low power radiofrequency delivery by a low pressure balloon in a short time does not probably cause any local tissue injury at the ablation sites, as confirmed by the absence of RAS observed at 6 months with CT scan.

P3739 | BEDSIDE
Left atrial appendage closure followed by a single anti platelet therapy: a single center experience
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Introduction: The purpose of the present study was to assess the safety and efficacy of LAAC for stroke patients with NVAF and contraindication for anticoagulation.

Methods: Consecutive patients with a previous ischaemic or hemorrhagic stroke, NVAF and contraindication for anticoagulation underwent LAAC with the Amplatzer Cardiac Plug device between July 2010 and July 2013 in a French university hospital. Follow-up included clinical evaluation at 3 and 12 months, and a control cardiac CT demonstrated complete LAA exclusion.

Results: 26 patients (age 73±8 years) were included. The mean CHA2DS2-VASc score was 4±1.5 and HAS-BLED scores were 4±0.8, respectively. The main contraindications for anticoagulation were: intracerebral hemorrhage while receiving anti-coagulation (62%), ischemic stroke with large hemodynamic transition (15%) and probable cerebral amyloid angiopathy (8%). The procedure was successful in 100%. Procedure-related complications were serious pericardial effusion (3.8%) and femoral bleeding (7.7%). During a mean follow-up of 8.6 (3–16) months, ischemic stroke occurred in 2 patients (7.7%), after antiplatelet therapy was stopped for one of them. One patient died of an intracranial hemorrhage.

Conclusions: LAAC followed by a single antiplatelet therapy could be a reasonable alternative for stroke patients with NVAF and contraindication for anticoagulation. Lifelong rather than short-term single antiplatelet therapy should be considered after the procedure for patients at high cardio-vascular risk.

P3740 | BEDSIDE
Multi-centre European experience of left atrial appendage closure using a new generation percutaneous epicardial suture device in non-valvular atrial fibrillation
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Introduction: The safety and efficacy of a modified new generation transcatheter epicardial left atrial appendage (LAA) suture-mediated closure device to prevent thrombo-embolic stroke in patients with non-valvular AF has not been studied before. We present the collective multi-centre European experience with the LARIAT+ percutaneous epicardial suture device.

Purpose: To define the safety and efficacy of the LARIAT+ device

Methods: 86 consecutive patients (pts) with AF underwent LAA ligation using the LARIAT+ device. In 84 pts percutaneous access was achieved with a novel micropuncture telescopic two-piece-needle; in the remaining 2 pts a conventional 18 guage
Tuohy needle was used. Acute LAO closure was assessed with angiography and transseptal echocardiography (TEE). All patients were scheduled for a 1–3 month post-procedure TEE to assess LAO closure. Patients with residual leaks from first follow-up TEE will have a repeat TEE after 3–6 months.

Results: The LARIAT+ procedure was successfully completed in all 86 pts. There were no device related complications. Complete LAO closure was achieved in 84/86 (97.7%) pts with a ≤1 mm residual communication in the remaining 2/86 (2.3%) pts, as assessed by TEE. Periprocedural complications occurred in 2/86 (2.3%) pts: early superficial subcutaneous bleeding at the site of subxiphoid needle entry treated with a surgically figure-of-8 stitch occurred in 1 pt and haemateme- sis, 12 hours later related to transseptal echocardiography and managed with upper GI endoscopy, occurred in 1 other patient. No patients required blood transfusion (2.3%) pts: early superficial subcutaneous bleeding at the site of subxiphoid needle entry treated with a surgically figure-of-8 stitch occurred in 1 pt and haematemesis, 12 hours later related to transseptal echocardiography and managed with upper GI endoscopy, occurred in 1 other patient. No patients required blood transfusion.

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A significant improvement of NYHA Class was recorded in CoQ10 treated patients (p=0.003). CoQ10 treated patients had significantly lower cardiovascular mortality (p=0.020) and lower occurrence of hospitalizations for heart failure (p=0.001). All cause mortality was significantly lower in the CoQ10 group, 10 patients (9%) vs. 24 patients (19%) in the placebo-group (Hazard Ratio: 0.37 (95% CI: 0.16–0.82; p=0.014).

Conclusions: The therapeutic efficacy of CoQ10 demonstrated in the Q-SYMBO study is confirmed in a European subgroup analysis. The treatment is safe and effective with improvement of symptoms and survival and with a significantly lower rate of hospitalization due to worsening HF.

Acknowledgement/Funding: The Q-SYMBO trial received partial support from the International Coenzyme Q10 Association, Pharma Nord ApS, Denmark and Kaneka Corp., Japan.

P3745 | BENCH
UM206, a peptide fragment of wnt5a, attenuates post-infarct remodeling

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Introduction: Following myocardial infarction (MI), left ventricular (LV) remodeling aims to maintain cardiac function. Nevertheless, adverse remodeling results in thinning of the infarct and LV dilation which may subsequently lead to the development of heart failure with poor prognosis. Wnt/Frizzled signaling plays a key role in cardiac remodeling following MI. We have shown previously that blockade of Wnt/β-catenin signaling in UM206 (peptide fragment of Wnt5a) reduced infarct expansion and prevented heart failure development in mice. This was accompanied by increased myofibroblast presence in the infarct region in treated mice. The aim of the present work was to investigate the effects of UM206 in a porcine model of repaired myocardial infarction.

Methods: Twelve Yorkshire x Landrace swine were subjected to 2 hours of myocardial ischemia by ligation of the proximal left circumflex artery, followed by reperfusion. Starting 24 hours post-MI, 6 animals were treated with continuous infusion of UM206 (0.6 μg/kg/day i.v.) for 5 weeks using a balloon pump. The 6 control swine were treated with vehicle. Another 8 swine were sham-operated.

Cardiac dimensions and infarct mass (IM) were determined by echocardiography and dedicated markers, respectively. At follow-up, infarct tissue was stained for alpha-smooth muscle actin to quantify myofibroblast content of the infarct region. In addition, components of Wnt/Frizzled and TGF-β signaling were measured at follow-up with qPCR.

Results: Treatment with UM206 for 5 weeks resulted in a significant decrease in IM compared to baseline (~41±10%), whereas IM remained stable in the control group (3±17%). This was accompanied by progressive dilatation of the LV in the control group between 3 and 5 weeks after MI while adverse remodeling was halted in the UM206 treated group. Myofibroblast presence was significantly lower in the UM206 treated animals (1.53±0.34% vs 3.38±0.61%). Fzd-4 mRNA was increased in the infarct area of UM206 treated swine but not of control swine with MI. Fzd-2 mRNA as well as mRNAs expression of the inflammatory mediators TGF-β1, TGF-β3 and the ECM protein tenasin-c were increased in remote non-infarcted myocardium as compared to sham, and their expression increased even more in the control group but was not influenced in the UM206 treated group.

Conclusion: UM206 treatment in a clinically relevant swine model of repaired myocardial infarction attenuates adverse remodeling, but is not accompanied by an increased myofibroblast presence in the infarcted area 5 weeks after MI.

P3746 | BEDSIDE
The adoption and application of ivabradine treatment along with beta blocker therapy in real life clinical practice: Results from REALITY HF Study

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Purpose: Although heart rate (HR) modulation therapy has been shown to improve outcomes in patients with heart failure (HF) both in pivotal trials and in registries of patients with heart failure (HF) treated with medication or device, their clinical application in clinical practice is less than optimal. REALITY HF (Resting Heart Rate and Real Life Treatment Modality in Outpatients with Left Ventricular Systolic Dysfunction) study data were analyzed to evaluate the adoption and application of ivabradine treatment along with beta blocker (BB) therapy 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 the effects of current real world care on patients with HF. The extent of adherence to ivabradine and beta blocker (BB) therapy in real life routine clinical care in patients with chronic HF.

Results: In patients with sinus rhythm, mean resting HR was found to be 76.7±14 bpm and 69.1% of the patients had a resting HR <70 bpm. Mean HR was significantly lower in patients receiving BB therapy than those not receiving BB (75.8±13 bpm vs 80.4±15 bpm respectively, p=0.001). However, 65.8% patients using BB therapy and 75% patients not receiving BB therapy still had a resting HR >70 bpm (p=0.028), and also no significant difference was found in mean HR between patients on target doses and those not on target doses of BB therapy (75.1±12 and 75.7±13 bpm; p=0.999). 33.5% patients (n=277) in sinus rhythm was met the HF guidelines recommendation on ivabradine use. However, the percentage of patients eligible for and treated with ivabradine was only 6.9% (n=19) and those eligible but untreated with ivabradine was 26.6% (n=258). Moreover, additional 15.6% of patients not receiving BB, in sinus rhythm and with a HR >70 bpm were still a candidate for ivabradine treatment.

Conclusions: These results show, despite the significant reduction in resting HR by BB, most patients still have a resting HR >70 bpm and almost one-fourth of patients in sinus rhythm and receiving BB therapy were eligible but untreated with ivabradine treatment in real life clinical practice.

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P3747 | BENCH
High use of statins in heart failure patients also after trials that failed to show a benefit: a Danish nationwide study

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Introduction: Although the role of statins in primary and secondary prevention of cardiovascular events is well-established, their role in tertiary prevention after development of heart failure (HF) is still unresolved.

Purpose: The aim of this study was to compare temporal trends in initiation and persistence with statin treatment after establishment of HF diagnosis in Denmark, before and after the publication of two large randomized trials that failed to demonstrate a benefit of rosuvastatin in patients with HF.

Methods and results: The study period (1995–2009) was divided into 5 intervals of 3 years each. All patients hospitalized with first-time HF (n=184,044) were identified in national registers. Incidence rate of HF decreased over time regardless aetiology. A total of 23,027 HF patients with no previous statin therapy initiated statins. Initiation increased significantly after publication of abovementioned trials that failed to show a benefit of initiation of statin therapy (log-rank test p=0.0001). Multivariate Cox logistic regression showed a significant effect of age, sex, diabetes and previous myocardial infarction on initiation during the study-period. However, persistence on statin therapy was unchanged after publication of the abovementioned studies (log-rank test p=0.2567). Age was the only factor with significant positive effect on persistence throughout the study-periods.

Conclusion: Despite lack of evidence for the benefit of statin treatment in HF patients, initiation of statins in HF patients increased during the study period.

P3748 | BENCH
STAT3 is indispensable for cardioprotective effects of DPP-4 inhibitor on heart failure after myocardial infarction


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Background: Dipeptidyl peptidase-4 (DPP-4) inhibitors are a new class of antidiabetic drugs that block DPP-4 enzyme activity. Many basic researches reported that DPP-4 inhibitors have protective effects on various organs including pancreas, kidney, and heart. There are several papers that demonstrate the cardioprotective activities and decreased the infarct size. DPP-4 inhibitor increased the ratio of endothelial nitric oxide synthase (eNOS) expression and improved cardiac function after myocardial infarction (MI).

Methods and results: We investigated the effects of DPP-4 inhibitor only on myocardium after MI. Male rats were then treated with vehicle or DPP-4 inhibitor. Left ventricular function, infarct size, α-smooth muscle actin, STAT3 expression and phosphorylation were measured. The extent of α-smooth muscle actin expression was increased in the infarcted area after MI, but was not influenced by DPP-4 inhibitor. The extent of STAT3 phosphorylation and of STAT3 expression was increased in the infarcted area in DPP-4 inhibitor treated group. However, there is no significant difference in the phosphorylation of STAT3 between vehicle and DPP-4 inhibitor treated group. Blocking of STAT3 with neutralizing anti-STAT3 antibody reduced the cardioprotective effects of DPP-4 inhibitor. STAT3 is indispensable for cardioprotective effects of DPP-4 inhibitor.

Conclusion: DPP-4 inhibitor increased the ratio of eNOS expression and improved cardiac function after MI. STAT3 is indispensable for cardioprotective effects of DPP-4 inhibitor.
increased by DPP-4 inhibitor. Those cardioprotective effects after MI were abolished by cardiomyocyte-specific deletion of STAT3.

Conclusions: DPP-4 inhibition prevented LV remodeling and heart failure after MI through SDF-1α/CXCR4/STAT3 signaling pathways in cardiomyocytes. DPP-4 inhibition augmented cardiomyocyte apoptosis of cardiomyocytes and a decrease in vessel number. Our study suggests the potential clinical efficacy of the DPP-4 inhibitors for prevention of heart failure after MI.

P3750 | BENCH
The angiotensin receptor neprilysin inhibitor LCZ696 improves systolic cardiac function compared to angiotensin converting enzyme inhibition in experimental myocardial infarction

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Introduction: PARADIGM-HF recently reported the superiority of LCZ696 (LCZ) compared to valsartan (Veh) in reducing cardiac fibrosis and improves its function in the heart failure model of diabetes mellitus in mice.

Methods: LCZ696 group was lighter than that in the control group (valsartan, p < 0.05; LCZ696, p < 0.01). Treatment with LCZ696 more improved left ventricular EF (43±12%) and cardiac output (2.6±1.2 ml/min) than the control group (29±12%, p < 0.01; 1.7±0.9 ml/min, p < 0.05). Genotype of TGF-beta was significantly suppressed in the LCZ696 group than the control group (33% reduction, p < 0.05). Gene expressions of atrial NP and brain NP and fibrosis were also suppressed in the LCZ696 group.

Conclusions: The ARNi LCZ696 improved cardiac function in HFrEF model of diabetes mellitus.

P3751 | BENCH
Exogenous extracellular heat shock protein HSC70 protects against experimental septic cardiomyopathy

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Introduction: Recent studies suggest that heat shock protein, a previously recognized intracellular protein, can also be released to extracellular space and protect myocardium from ischemia-reperfusion injury. The purpose of this study was to determine if exogenous heat shock cognate protein 70 (HSC70) can protect against ischemic cardiomyopathy induced by LPS.

Methods: In an animal model of septic cardiomyopathy, we anesthesitized the S-D rats and injected E. coli endotoxin LPS (10 mg/kg, iv) with or without pretreatment of HSC70 (20 μg/kg, iv). Hemodynamic changes were monitored during the 4-hour study period. Parameters including heart rate, MAP left ventricular systolic pressure, Max dP/dt and Min dP/dt were continuously recorded. Plasma levels of TNF-α, NOx, GPT/GOT, glucose, LDH were also measured serially. In addition, activation of pro-inflammatory mediators including INOS, COX-2, and the nuclear factor-κB (NF-κB) pathway in heart tissue were also examined.

Results: Pretreatment with recombinant HSC70 attenuated LPS-induced hypotension and tachycardia by 21% and 23%, respectively (P < 0.05), improved myocardial dysfunction (left ventricular systolic pressure: 33%; max dP/dt: 20%; heart rate: 33%, P < 0.05). There were also improvement of biochemical parameters including GPT, GOT, LDH and glucose at 4h. Furthermore, HSC70 inhibited the elevation of plasma TNF-α and NOx, and decreased myocardial levels of INOS and COX-2 in response to LPS challenge. Finally, HSC70 attenuated increased nuclear translocation of NF-κB by blocking phosphorylation of IκB. Conclusion: Our results indicate that extracellular HSC70 has a promising role in the treatment of septic cardiomyopathy through anti-inflammatory pathways.

P3770 | BEDSIDE
RELAX-AHF-EU: a prospective, multicenter, randomised, open-label study assessing the efficacy and safety of serelaxin in patients hospitalised for acute heart failure in Europe

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Background: Approximately 10–30% of patients hospitalised for acute heart failure (AHF) develop in-hospital worsening heart failure (WHF), a condition that is associated with increased length of stay of the index hospitalisation, a 2- to 3-fold increased risk for re-hospitalisation, morbidity, and mortality. In a randomized Phase III clinical trial (RELAX-AHF), serelaxin was found to improve dyspnoea and reduce risk of in-hospital WHF through Day 5.

Methods and results: RELAX-AHF-EU is an open-label study planned in ~400 cardiology, internal medicine, emergency, and intensive care departments in 26 countries across Europe. The study will enroll ~2,700 patients with AHF and systolic blood pressure ≥125 mmHg, heart rate ≤125 bpm, and renal function ≤0.5. Patients (randomized 2:1 to receive intravenous infusion of 30 g/kg/day serelaxin for 48 hours added to standard of care (SOC) versus SOC alone. The primary endpoint is incidence of in-hospital WHF or all-cause death through Day 5. Cases of AHF are initially identified by need for intensification of therapy for AHF and subsequently confirmed by a central adjudication committee of experts blinded to treatment allocation. Secondary endpoints include incidence of (a) in-hospital WHF, all-cause death, or re-hospitalisation for AHF through Day 14, (b) failure to achieve heart failure improvement through Day 5, (c) renal worsening, patients are defined as ≥0.3 mg/dL increase in serum creatinine) through Day 5, (d) index length of hospital stay, (e) health-related quality of life, and (f) economic burden of disease. Safety and tolerability assessment is performed through Day 30. The study is on-
Methods: Maintenance HD patients receiving 300mg EPA thrice daily in conjunction with standard therapy (n=106, EPA group) and those without (n=353, control group) were enrolled in this study. Serum EPA and arachidonic acid (AA) levels were measured at baseline and administration start and after 6 months in the EPA group. They were followed-up for 3 years. To reduce the difference of baseline characteristics, a propensity score analysis using multivariate logistic model with all baseline characteristics, a propensity score analysis using multivariate logistic model with all baseline characteristics was performed. The median of EPA/AA ratio significantly increased from 0.48 to 1.49 at 6 months after EPA administration (p < 0.057, respectively). The median of EPA/AA ratio significantly increased from 0.48 to 1.49 at 6 months after EPA administration (p < 0.057, respectively). The median of EPA/AA ratio significantly increased from 0.48 to 1.49 at 6 months after EPA administration (p < 0.057, respectively).

Results: Diabetes and peripheral arterial disease were more prevalent in the EPA group than in the control group (58.5% vs. 41.1%, p=0.016 and 24.8% vs. 13.7%, p=0.016, respectively). The median of EPA/AA ratio significantly increased from 0.48 to 1.49 at 6 months after EPA administration (p < 0.0001). During follow-up period (34 months), 109 patients died (22.9%) including 61 CVD cause. After adjustment for the propensity score, the EPA group had better survival for all-cause mortality (adjusted hazard ratio (HR) 0.53, 95% confidence interval (CI) 0.31–0.92, p=0.023) and for CVD mortality (adjusted HR 0.41 (95% CI 0.18–0.91, p=0.029) compared to the control group, respectively. Furthermore, in 93 propensity score-matched patients in each groups, 3-year Kaplan-Meier survival rate was still higher in the EPA group than in the control group for all-cause mortality (83.5% vs. 68.8%, HR 0.48, 95% CI 0.26–0.89, p=0.022) and for CVD mortality (91.8% vs. 80.4%, HR 0.38, 95% CI 0.16–0.92, p=0.032, respectively).

Conclusion: Administration of EPA reduced CVD- and all-cause mortality in chronic HD patients who are consistently at highest risk of CVD.

HEART FAILURE THERAPY, VARIOUS II

P3753 | BENCH
Angiotensin II Receptor-Nephrin Inhibitor, LCZ696 Blocked Aldosterone Synthesis in Human Adrenocortical Cell Line
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Background: Recent clinical study indicated that the angiotensin II (Ang II) receptor-nephrin inhibitor (sacubitril valsartan sodium complex, known as LCZ696) was superior to enalapril in reducing the risks of death and hospitalization for heart failure.

Purpose: We investigated whether nephrin inhibition enhances an atrial natriuretic peptide or brain natriuretic peptide (ANP or BNP)-evoked signals which can block Ang II/Ang II type 1 (AT1) receptor-induced aldosterone (Ald) synthesis in human adrenocortical cells.

Methods and results: Binding affinity of valsartan + LBO-657 (the active form of nephrin inhibitor pro-drug sacubitril) was better than that of valsartan alone in an AT1 receptor expressing HEK cell-based living assay, although there was no difference in the dissociation from AT1 receptor between valsartan + LBO-657 and valsartan alone. In Ang II-sensitized human adrenocortical cells, ANP or BNP alone, but not LBO-657 or valsartan alone, significantly decreased Ald synthesis. Most important finding was that valsartan + LBO-657 with ANP or BNP transiently suppressed Ald synthesis in Ang II-sensitized cells, the suppression levels were comparable to basal levels of Ang II-nonsensitized cells. The suppression of ANP was blocked by inhibitors of regulator of G protein signaling protein and cyclic GMP-dependent protein kinase. In addition, the suppression levels of Ald synthesis in valsartan+LBO-657 with ANP were stronger than those in valsartan with ANP. Finally, nephrin inhibition did not change the mRNA levels of AT1 receptor, NP receptor and regulator of G protein signaling protein.

Conclusion: The complementary effects of LCZ696, a dual blockade of AT1 and nephrin receptor, may be partly due to the reduction of Ald synthesis by its nephrin inhibition.
Results: DSC occurred in 260 of 1767 (14.7%; 5.4 per 100 p-yr) in the Americas compared with 35 of 1678 (2.1%; 0.6 per 100 p-yr) in R/G. In the Americas, but not in R/G, treatment with spironolactone increased the incidence of DSC (6.8 vs. 4.2 per 100 p-yr, HR 1.60, 95% CI 1.25–2.05, p < 0.001). (Figure) In multi-variable models, assignment to spironolactone, diabetes, NYHA class, smoking, lower potassium and lower hemoglobin were important predictors of DSC. In contrast to hyperkalemia, neither age nor baseline renal function was a statistically important determinant of DSC.

Conclusions: DSC is common in HF-PEF and risk is independent of age and baseline renal function. Because spironolactone enhances the risk for DSC, use in this population requires careful laboratory surveillance.

P3757 | BENCH
Pharmacological inhibition of galectin-3 and aldosterone pathways prevents isoproterenol-induced left ventricular dysfunction and fibrosis in mice
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Background: Galectin-3 (Gal-3) is involved in cardiac inflammation, fibrogenesis and remodeling. Previous evidences show that Gal-3 interacts with aldosterone in promoting macrophage infiltration and vascular fibrosis, and that genetic and pharmacological inhibition of Gal-3 prevents cardiac remodeling in a pressure overload animal model of heart failure (HF).

Purpose: We aimed to test the effect of selective inhibitors of either Gal-3 (modified citrus pectin, MCP) or aldosterone (potassium canrenoate) on left ventricular (LV) function in a murine model of HF.

Methods: Forty-one 3 to 5-month old male mice with cardiac specific hyper-aldosteronism (AS mice) underwent isoproterenol subcutaneous injections, and were then randomized to receive placebo (n=12), MCP (n=10), canrenoate (n=9), and MCP+canrenoate (n=10) for 14 days.

Results: Isoproterenol induced a rapid and persistent decrease in left ventricular fractional shortening in placebo-treated mice (−20% at day 14), that was markedly improved by treatment with either MCP or canrenoate (both p < 0.001 vs placebo). MCP, and canrenoate also reduced the extent of cardiac hypertrophy and fibrosis, as well as the expression of genes involved in fibrogenesis (Col-I and Col-III) and macrophage infiltration (CD-68 and MCP-1). Gal-3 gene expression (p < 0.05 vs placebo) and protein level (−61% and −69% vs placebo) were decreased by both MCP and canrenoate. Combined use of antagonists of Gal-3 and aldosterone resulted in additive effects, compared to MCP or canrenoate alone, on cardiac hypertrophy, inflammation and fibrosis.

Conclusions: Inhibitors to the mechanisms of aldosterone-mediated myocardial damage in a HF murine model with cardiac hyperaldosteronism. Inhibition of Gal-3 and aldosterone can reverse isoproterenol-induced LV dysfunction, by reducing myocardial inflammation and fibrogenesis. Gal-3 inhibition may represent a new promising therapeutic option in HF.

P3759 | BENCH
The influence of metformin on mortality and hospitalization in patients with heart failure and type 2 diabetes
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Background: Heart failure (HF) is often associated with diabetes mellitus (DM), either as cause or comorbidity. It has been proven that hyperglycemia increases the risk of hospitalization and mortality in patients with HF, worsens its course among other through proteins glycation and oxidative stress, leading to myocardial fibrosis followed by diastolic dysfunction. The position of metformin as first-line therapy in type 2 diabetes (T2DM) is generally accepted. Although, it seems that metformin is the only hypoglycemic drug that may decrease the risk of major cardiovascular events and mortality in T2DM subjects, the use of this medication is contraindicated in diabetics with HF.

Purpose: The aim of this post-hoc analysis was to assess whether metformin administration in patients with heart failure and type 2 diabetes affects the risk of all causes mortality and hospitalization rates during a 12-months follow-up.

Methods: The study included 1030 of 1126 patients with HF representing Polish population of the Heart Failure Long Term Registry. Three hundred and forty-two patients of the study population with history of DM were identified (111 women, mean age 69±10.9 years; BMI 30±5.6 kg/m²; LVEF 37.6±15.5%) and divided into two groups: 1. patients receiving metformin monotherapy or metformin plus other hypoglycemic agent and 2. diabetic subjects not treated with metformin.

Results: At 1-year follow-up death occurred in 128 HF patients of the whole population (12.4%), in 53 patients with diabetes (15.5%) compared with 75 patients without diabetes (10.9%) (HR 1.42; 95% CI: 1.40 to 1.44; p < 0.0001). 118 of 342 patients (34.5%) were treated with metformin. Metformin treatment was associated with lower mortality rates compared with not-metformin treated group (11.0% vs. 17.9%) (HR 0.62; 95% CI: 0.58 to 0.66, p = 0.003). All-cause hospitalization rates including HF hospitalisation, was similar in both groups with diabetes (HR 0.96; 95% CI: 0.83 to 1.08).

Conclusion: The results of this study suggest, in agreement with previous observations, that metformin treatment is associated with a reduction in mortality in diabetics with heart failure. Therefore, we support the other authors suggestion that indications for metformin should be reconsidered.
P3760 | BENCH
Negative effect of right ventricular systolic failure on time in therapeutic range (TTR) of patients with warfarin treatment
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Background: Patients on warfarin therapy need to achieve and maintain anticoagulation control for effective treatment while minimizing bleeding risk. However, warfarin is a challenging therapy from various causes. Aim of this study was to investigate the effect of left and right systolic heart failure (sys-HF) on TTR.
Methods: This study used longitudinal patient-level anticoagulation management records collected from five medical centers. We enrolled 775 consecutive patients with a mean age 66.3±5.7 years, with CHF classes II to III (New York Heart Association) combined with chronic obstructive pulmonary disease. The groups were similar in some clinical and demographic variables (age, gender, BMI, obesity, diabetes mellitus, hypertension, smoking, coronary artery disease, renal disease, HAS-BLED bleeding score, ATRIA bleeding score, creatinine level, duration of warfarin use and total INR value/week) except for CHADS2-VASC score which was lower in patients in left or right sys-HF (p<0.001). Mean TTR values of patients without left or right sys-HF and isolated left sys-HF were higher than patients with isolated right sys-HF and combined sys-HF (p<0.001) (Table 1). But, mean TTR values were similar in patients isolated right sys-HF and combined sys-HF (p=0.215). Similarly proportion of the effective TTR was higher in patients without left or right sys-HF and isolated left sys-HF as compared with right or combined sys-HF groups.

Table 1

<table>
<thead>
<tr>
<th>Patients without left or right sys-HF</th>
<th>Patients with isolated left sys-HF</th>
<th>Patients with isolated right sys-HF</th>
<th>Patients with combined sys-HF</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean TTR 65.4±22.5</td>
<td>61.6±22.7</td>
<td>44.1±26.1</td>
<td>39.5±25.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TTR &gt;65% (%)</td>
<td>57.7</td>
<td>54.6</td>
<td>24.1</td>
<td>&lt;0.001</td>
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</tbody>
</table>

Conclusion: Right ventricular sys-HF has negative effect on TTR and effective warfarine treatment which should be taken into consideration while planning warfarine monitoring.

P3761 | BEDSIDE
Clinical efficacy and safety of tiotropium and indacaterol administration in patient with chronic heart failure due to coronary artery disease combined with chronic obstructive pulmonary disease
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Purpose: To compare clinical efficacy and safety of indacaterol and tiotropium administration in patient with chronic heart failure due to coronary artery disease combined with chronic obstructive pulmonary disease.
Methods: After enrolment in this trial 143 patients (96 men and 47 women), aged 66.3±5.7 years, with CHF classes II to III (New York Heart Association) combined with moderate to severe COPD (GOLD) and with initial ejection fraction of the left ventricle (LVEF) less than 45%, were randomized into three groups - tiotropium (18 μg daily, n=50), indacaterol (150 μg daily, n=45) and tiotropium+indacaterol (18 μg tiotropium, n=48). Patients of all groups received the complex CHF treatment comprising diuretics, nebivolol, losartan, cardiac glycosides (if necessary) and basic COPD therapy (inhaled corticosteroids). Echocardiography, exercise tolerance (6-min walk distance), 24-hour electrocardiography and blood pressure monitoring were assessed at baseline and after 6 months of treatment, respectively. Mortality was tested at assessment of baseline, after 1 month and after 6 months. The quality of life was evaluated by MYHQF, SGRQ and mHRC.
Results: After 6 months of therapy the improvement of clinical condition and quality of life were marked in all groups. In 1st, 2nd and 3rd group LVEF was increased by 6.5, 6.4% and 11.2%, pulmonary hypertension decreased by 7.0, 8.4% and 15.1%, episodes of silent myocardial ischemia decreased by 14%, 17.4% and 20.8%, respectively. Towards the end of the observation period, in all groups there was a confident and authentic increase of forced expiratory volume during 1st second (FEV1) which made 5.8, 7.4%, and 10.2% accordingly. 6-min walk distance increased by 18.0%, 23.5% and 26.2% accordingly. Patients showed statistically significant and clinically meaningful reduction of SGRQ score (14.1, 18.5, 24.5%) and MYHQF score (25.6, 27.4, 32.0%), significant improvements in mHRC dyspnea grade (20.5, 23.2%, 24.6% respectively). All treatments were well tolerated and side effects of therapy and the number of deaths in comparison to all groups was comparable.

Conclusions: The tiotropium and indacaterol inclusion in the structure of complex therapy in patients with CHF combined with COPD raises efficiency of treatment, improves quality of life, basic parameters of central hemodynamics and pulmonary function. Efficacy and safety of tiotropium and indacaterol in patient with CHF due to CAD combined with COPD are similar. Combination of these drugs significantly enhances the positive effects of the therapy.

P3762 | BEDSIDE
Comparative temporal effects of nitrate-centred and diuretic-centred treatment of acute decompensated heart failure on congestion and renal function injury as well as tubular damage biomarkers
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Background: Our purpose was to assess and compare “early” (at day 4–6) and “late” (discharge – Dsc) effects of prolonged optimal-dosed nitrate continuous infusion plus low doses of i.v. diuretics (“nitric centered strategy” - NC) and moderate-dosed diuretics plus short intermittent nitrate infusion (“diuretic-centered strategy” - DC) on congestion markers (CVP and NT-pro-BNP) and renal function (eGFR and tubular damage biomarkers) in pts with acute decompensated heart failure (ADHF).
Methods: In single-blind parallel-group phase patients with “wet–wet” ADHF were randomized 1:2 to 2 groups. NC group (n=27) received optimal-dosed NTG continuous infusion ≥72 hrs plus low doses of i.v. diuretics (<80 mg pd for furosemide), while DC group (n=51) moderate doses of i.v. diuretic (41–120 mg pd for furosemide) plus short intermittent (<10hrs pd, <3 days) NTG. Congestion endpoints were CVP at D4–6 and plasma NT-pro-BNP (ELISA) at D4–6 and Dsc. Renal endpoints included acute kidney injury with AKIN criteria as well as eGFR (MDRD) and serum Cystatin C as functional injury biomarkers and plasma NGAL as tubular damage biomarker, both at D4–6 and Dsc.
Results: Furosemide total 1st week dose in NC group was 191±2,3mg, in DC group – 398±18,7mg, duration of NTG infusion – 3,5±0,4 days vs 0,77±0,08 days (p<0.001), Dsc – in 9,4±1,3 and 11,4±1,5 days (all p<0.05). CVP lowering from D1 (NC group – 166±15,8, DC – 189±12,1 mmHg2, p<0.05) to D4–6 (both p<0.01) was more pronounced in NC group (81±7,4 vs 88±2,4 mmHg2 p<0.05). AKIN rate was correspondingly 17,3% and 22,8% (p<0.05). Other endpoints see in table.

Conclusion: In ADHF patients “nitrate centered” strategy compared to moderate “diuretic centered” one provides more pronounced progressive decongestion assessed by CVP and NT-pro-BNP lowering. It is associated with less marked early transient worsening of renal function (Cystatin C) and tubular damage (NGAL) followed by more pronounced improvement of both from baseline in “nitric centered” group.
up-titration of a beta-blocker, 19.0% of patients in the full dataset (158/830) met the indication for ivabradine at the last visit. Of these ‘ivabradine-suitable’ patients, 101/158 (63.9%) received bisoprolol “at any time” during the study period; 20/158 (12.7%) achieved the target dose (10 mg daily); 52/158 (32.9%) received 5 mg or 7.5 mg daily; and 93/158 (58.9%) received < 5 mg daily.

**Conclusions:** This group of Scottish cardiology patients previously hospitalised with ADHF and under the care of a protocol-driven clinic, 19% met the indication for ivabradine, and may benefit from the increased control of CHF that ivabradine can provide. Among these ‘ivabradine-suitable’ patients, –15% achieved the target dose of beta-blockers, illustrating the substantial clinical need for a well-tolerated and effective therapy such as ivabradine.

**Acknowledgement/Funding:** Servier UK

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**P3764 | BEDSIDE**

Early administration of tolvaptan can improve in-hospital clinical outcomes in patients with acute heart failure: a dual center experience

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**Background:** Patients with acute heart failure (AHF) are often in volume overload state. Conventionally, loop diuretics are the first-line drug to treat for AHF patients. Previous studies reported that tolvaptan, a nonpeptide V2 receptor antagonist, can improve pulmonary edema by reducing the insufficient effect of conventional diuretics. Furthermore, the best timing of administering tolvaptan to patients with AHF has remained unclear.

**Methods:** Between November 2013 and November 2014, we retrospectively enrolled 159 patients with AHF at 2 medical centers who comprised 2 different strategies: tolvaptan group (tolvaptan + diuretics, n=66), and conventional group (diuretics, n=73). Tolvaptan was administered within 24 hours after admission. The primary endpoints were discharge within 14 days, and worsening of renal function (WRF; defined as a > 0.5mg/dl increase in serum creatinine at 1 week after admission).

**Results:** Patient characteristics were as follows 97 males with a mean age 77±13 years and mean LVEF 26% and 74%, respectively. The duration of hospitalization due to pulmonary edema was significantly shorter in tolvaptan group compared with conventional group (16.1±8.5 vs 19.7±11.7 days, P=0.03). WRF was no significant difference after admission.

**Conclusion:** Tolvaptan was administered within 24 hours after admission. In patients with AHF of ischemic etiology, tight heart rate control with bisoprolol + ivabradine combination was characterized by an increase in Tr from 21.1 [11.7; 28.9] to 29.1 [15.9; 31.1] ms, p<0.01, but not in patients with a combination of bisoprolol and ivabradine from 20.1 [11.7; 25.2] to 21.1 [11.7; 28.9]. Moreover, up-titration of bisoprolol resulted in a reduction of time to return reflected wave (Tr) from 140.4±26.2 ms to 134.7±3.1 ms, while bisoprolol + ivabradine combination was characterized by an increase in Tr from 140.4±26.2 ms to 134.7±3.1 ms.

**Conclusions:** In pts with HF of ischemic etiology, tight heart rate control with bisoprolol up-titration, but not with a bisoprolol and ivabradine combination, can cause a deterioration of pulsatile hemodynamics parameters. Further studies are needed to investigate long-term effects of HR lowering therapy on the pulsatile hemodynamics in pts with HF of ischemic etiology.
recorded at baseline and after 12 months were analysed by a physiologist blinded to allocation and date. Changes in echocardiographic variables between the groups were compared using unpaired t-tests.

Results: 54 patients (44 men), mean age 72, SE (1.3) years were recruited; due to death (3) and withdrawal (3), 48 completed the study (25 in intervention group and 23 in placebo group). Baseline clinical variables were comparable between the groups. After 12 months, vitamin D levels in the intervention group increased significantly compared to the placebo group (96.19 ng/mL versus 1.01 ng/mL; p = <0.001), with no adverse effect on any biochemical marker including calcium.

Conclusion: Twelve months of vitamin D supplementation improved LV systolic and diastolic volumes in patients with HF and vitamin D deficiency.

Conclusion: In Korean patients with atrial fibrillation and heart failure, use of digoxin during hospitalization was related to decreased mortality up to 1000 days follow-up. This finding could have an impact on the management of patients with atrial fibrillation and heart failure.
results were significantly greater K+-decline than pts with milder HK, suggesting ZS-9 may be a potential option in management of severe HK.

Conclusion/Funding: Supported by ZS Pharma, Inc., Coppel TX, USA.

P3774 | BEDSIDE
Safety and efficacy of G-CSF and autologous bone marrow-derived cells in ischaemic cardiomyopathy: Results of the REGENERATE-HD Phase II trial
Aims: The effect of combined cytokine and cell therapy in ischaemic cardiomyopathy is unknown. Meta-analyses suggest improved cardiac function with cell therapy. The optimal cell delivery route remains unclear. We investigated whether granulocyte-colony stimulating factor (G-CSF) alone or in combination with intramyocardial (IC) or intramyocardial (IM) injection of autologous bone marrow-derived cells (BMC) improves cardiac function.
Methods and results: 90 patients with symptomatic ischaemic cardiomyopathy and no further treatment options were enrolled in the randomised, placebo-

Comparisons: 20.5%; P < 0.0001, all comparisons).

Results: Across studies, 337 pts received ZS-9 10g TID in the acute phase: 50% had mild, 37% moderate, and 13% severe HK. In pts with severe HK, significant K+ reduction occurred immediately (1 hr) after initial ZS-9 dose (Figure). After 48h of ZS-9 treatment, K+ reduction was greater in pts with severe HK (1.5 mmol/L: 23.2%) compared to mild (0.78 mmol/L: 14.7%) and moderate (1.2 mmol/L: 20.5%; P < 0.0001, all comparisons).

Conclusions: ZS-9 rapidly reduced serum K+ in pts with severe HK, who had significantly greater K+ decline than pts with milder HK, suggesting ZS-9 may reduce K+ to a greater amount in highest risk pts. Pending further studies in the emergency setting, these findings suggest ZS-9 may be an attractive therapeutic option in management of severe HK.

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P3773 | BENCH
Does higher stimulation dosage in cardiac contractility modulation increase patient outcome? Data from the FIX HF 13 Trial
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Aims: Cardiac contractility modulation (CCM) signals are non-excitatory electrical signals delivered during the absolute refractory period intended to improve contraction and cardiac function. Clinical trials have shown that CCM treatment significantly improves exercise tolerance and quality of life in symptomatic heart failure patients.

Studies with CCM therapy typically include CCM delivery for 3, 5 or 7 hours per day, although other configurations are also commonly used. Each has been associated with improved outcomes in heart failure, but it is not clear whether different application durations are associated with different degrees of benefit. The purpose of the current study was to evaluate quality of life, exercise tolerance, and cardiac function, over a 6 month period when CCM was delivered for 5 hours/day vs. 12 hours/day.

Methods: This single center study involved 19 medically refractory symptomatic patients with heart failure and reduced LV function who underwent implantation of an Optimizer™ system. Patients were randomized into one of two treatment groups; 5 hours/day CCM treatment or 12 hours/day CCM treatment. Subjects returned to the hospital after 12 and 24 weeks for evaluations. Efficacy was measured in terms of changes in MLWHFQ, Peak VO2, NYHA, 6 min W, and EF.

Results: At the end of 24 weeks, clinical improvement was observed in the entire cohort in all efficacy measures (mean change from baseline of −17.1 in MLWHFQ, −0.86 in NYHA, and improvement trend of 1.48 ml O2/kg/min in Peak VO2, 23.25/min in 6 min W, and 2.25% in EF). There were no significant differences, either clinically or statistically, between the groups receiving CCM for 5 vs. 12 hours/day.

Conclusions: Together with previously reported experience with CCM, delivery of CCM therapy is safe and effective over the range of shorter (5 hours) to longer (12 hours) daily periods of application.

P3772 | BEDSIDE
Acute phase efficacy of sodium zirconium cyclosilicate (zs-9) in patients with severe hyperkalaemia: analysis from two phase 3 studies
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Background: Patients with type-2-diabetes (T2DM) and hypertension have an increased risk of heart failure (HF). We aimed to assess treatment strategies and outcomes in patients with or without HF.

Methods: DIALOGUE is a prospective, multi-center registry in patients with T2DM and hypertension followed for 12 months. HF was recorded at baseline (physician assessment) and patients grouped into those with or without HF.

Results: 13.4% out of 8392 patients were diagnosed with HF. Patients with HF achieved BP values after 6 month more closely match the individual target values, and patients grouped into those with or without HF.

Conclusions: HF is a frequent co-morbid disease in patients with T2DM and hypertension. Individualized treatment in patients with comorbid type-2 diabetes and hypertension is necessary. Further studies are needed to identify strategies to improve BP control in patients with HF.

Acknowledgement/Funding: Novartis

P3771 | BEDSIDE
Individualized treatment in patients with comorbid type-2-diabetes and heart failure: insights from the DIALOGUE registry
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Conclusions: HF is a frequent co-morbid disease in patients with T2DM and hypertension. Individualized treatment in patients with comorbid type-2 diabetes and hypertension is necessary. Further studies are needed to identify strategies to improve BP control in patients with HF.

Acknowledgement/Funding: Novartis
controlled, single-centre study. Randomisation was to 1 of 3 arms: peripheral, IC or IM. In each arm, patients were randomised to active treatment or placebo. All patients, apart from the peripheral placebo group (saline only) received G-CSF for 5 days. The IC and IM arms received either BMC or serum (placebo). The primary endpoint was change in left ventricular ejection fraction (LVEF) at 1 year assessed by cardiac MRI/C. Only the IM BMC group showed a significant improvement in LVEF 4.99% (95% CI 0.33–9.6; p=0.038) at 1 year. This group also showed a reduction in NYHA class at 1 year and a fall in NT pro-BNP at 6 months. None of the other groups showed a significant change in LVEF.

**Conclusion:** We have shown that G-CSF alone has no effect in patients with ischaemic cardiomyopathy. However G-CSF combined with autologous BMC, when delivered intramyocardially, had a beneficial effect on cardiac function and symptoms. Given the lack of treatment options for this patient group a clinically driven outcome study is warranted.

**P3775 | BEDSIDE**

Chronic vagus nerve stimulation reduces cardiac electrical instability assessed by quantitative T-wave alternans analysis and suppresses ventricular tachycardia in heart failure patients

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**Introduction:** Autonomic regulation therapy (ART) by way of chronic vagus nerve stimulation (VNS) improves ventricular function in heart failure (HF) patients, but its effects on cardiac electrical instability remain unknown.

**Purpose:** Effects of ART on T-wave alternans (TWA), a marker of cardiac electrical instability and risk for life-threatening arrhythmias, were studied in patients with chronic, symptomatic HF and reduced ejection fraction enrolled in the ANTHEM-HF study (NCT01823887).

**Methods:** TWA quantified using Modified Moving Average method and ventricular tachycardia (VT) incidence were assessed in 24-hour ambulatory ECG recordings. Measurements were made prior to ART system (Cyberonics, Inc., TX) implantation involving the left or right vagus nerve, and after 6 months of therapy (10 Hz, 250 μs pulse width, 16% duty cycle, maximum tolerable current amplitude after 10 weeks of titration). Effects of low (<2 mA, n=9) vs high-intensity (>2mA, n=11) stimulation levels were investigated.

**Results:** TWA levels were 68±5 μV at baseline (abnormal: >47 μV). After 6 months, TWA amplitude increased with low-intensity VNS and decreased with high-intensity VNS, and the change was significantly different between the two groups (29±17 vs. 14±8 μV, p=0.026). Figure shows typical QRS-aligned TWA template response to VNS. The occurrence of VT was also lower in the high-intensity group (2 patients vs. 4, p=0.039).

**Conclusion:** High-intensity chronic VNS in patients with symptomatic HF can decrease cardiac electrical instability, as reflected in reduced TWA levels and suppression of VT. These findings underscore the importance of appropriate VNS parameter selection to optimize the potential benefits of ART.

**Acknowledgement/Funding:** Cyberonics Inc., Houston USA

**P3776 | BEDSIDE**

Effects of beta blocker therapy on resting heart rate in real life clinical practice in patients with chronic heart failure and reduced ejection fraction: results from reality HF study

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**Purpose:** Heart rate (HR) reduction in chronic heart failure (HF) is associated with improved outcomes. Although, the achievement of target dose of beta-blocker (BB) treatment in systolic HF is strongly recommended by HF guidelines, recent meta-analysis showed that the magnitude of HR reduction may be more important than the recommended target doses. REALITY HF (Resting Heart Rate and Real Life Treatment Modality in Outpatients with Left Ventricular Systolic Dysfunction) study data were analyzed to evaluate the effects of BB treatment on resting HR in real life clinical practice in chronic HF patients.

**Methods:** REALITY HF was a multicenter, prospective, observational, national registry designed to evaluate HF patients’ clinical characteristics and the effects of current treatment modalities on resting heart rate (HR) and enrolled 1251 patients (mean age 61±12 years, 76% male) from 16 centers who were admitted to the outpatient clinic with the diagnosis of chronic HF, LVEF <40% and >18 years of age. 826 patients in sinus rhythm were included in this analysis, in whom 653 (79.1%) were receiving BB treatment and 173 (20.9%) were not. In patients receiving BB therapy, 6.3% of those were using bisoprolol, 42.4% -carvedilol, 49.1% -metoprolol succinate and 3.2% -nebivolol. The target doses of BB treatment had only been reached in 13.9% of patients.

**Results:** In patients with sinus rhythm, HR was found to be 76.7±14 bpm and 69.1% of patients had a resting HR ≥70 bpm. HR was significantly lower in patients receiving BB therapy than those not receiving BB (75.8±13 bpm vs 80.4±15 bpm respectively, p=0.001). Although patients receiving BB had lower resting HR, 65.8% patients receiving BB and 75% patients not receiving BB therapy had a resting HR >70 bpm (p=0.028). Mean HR were 71.5±10.7, 78.6±13, 74.5±13 and 73.8±12 bpm with bisoprolol, carvedilol, metoprolol succinate and nebivolol respectively (p<0.01). Patients with a resting HR >70 bpm were 59.4%, 72.7%, 60.4% and 67.4% in bisoprolol, carvedilol, metoprolol succinate and nebivolol groups, respectively (p<0.022). However, no significant difference was found in mean HR between patients on target doses and those not on target doses of BB therapy (75.1±12 and 75.7±13 bpm, p=0.999).

**Conclusions:** The results of this study show that despite the highly prevalent use of BB therapy in patients with systolic HF in real life clinical practice and despite the significant reduction in resting HR by BB, most patients still have a resting HR >70 bpm and there was no significant additional effect of target doses of BB treatment on resting HR.

**Acknowledgement/Funding:** This study is supported by Servier

**H E A R T  F A I L U R E  T H E R A P Y ,  V A R I O U S  I V**

**P3777 | BEDSIDE**

Tolvaptan in patients with acute decompensated heart failure, could reduce renal worsening from randomized controlled trial two

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**Background:** Prevention of worsening renal function (WRF) is very important in the treatment of acute decompensated heart failure (ADHF). Tolvaptan is known to induce the urinary excretion of fluid improving renal function. However, its clinical efficacy for patients with ADHF remains controversial. We evaluated the effects of tolvaptan on the renal function in ADHF patients with volume overload.

**Methods:** We enrolled 105 patients with ADHF. They were divided to three groups (A group: Conventional therapy only (including lupus, thiazide and carperidine), B group: Conventional therapy with 14 days of administration of tolvaptan 7.5mg/day, C group: Conventional therapy with 7 days of administration of tolvaptan 15mg/day.) We evaluated the rate of changes of serum creatinine, e-GFR, WRF, body weight, daily urine volume, serum sodium, serum potassium. We defined WRF as the serum creatinine increase ≥0.3 mg/dL between admission and 15th hospital day.

**Results:** Urine output in 48 hours after admission was significantly higher in the both tolvaptan groups than the conventional groups. Serum creatinine elevation was 0.17, 0.10, 0.03 in the group A, B, C, respectively. Incidence of WRF was significantly lower in the tolvaptan groups (B: 8%, B plus C: 12%) than in the conventional therapy group A; 33% (P=0.02 (A*B), P=0.03 (A*B+C)) by Paired T test.

**Conclusions:** Additional treatment with tolvaptan could prevent WRF in patients with ADHF.
P3778 | BEDSIDE
Effects of beta-blockers on heart failure with preserved ejection fraction; from the Korean Acute Heart Failure (KorAHF) registry
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Background: Beta-blockers are indicated in patients with heart failure with reduced ejection fraction. However, the efficacy of these drugs in patients with heart failure with preserved ejection fraction (HFpEF) is uncertain.

Purpose: To investigate the hypothesis that beta-blockers are associated with reduced adverse events in patients with HFpEF.

Methods: The KorAHF is a prospective observational multicentre cohort study. Patients hospitalized for acute heart failure syndrome in 10 tertiary university hospitals across the country have been consecutively enrolled 5,660 patients between March, 2011 and February, 2014. Of these patients, 2,152 patients with HFpEF (ejection fraction >40%) were investigated. We compared adverse outcomes (all-cause death, rehospitalization, a composite of all-cause death and rehospitalization) with the use of propensity-score matching and the inverse probability of treatment weighting (IPTW).

Results: Median follow-up in HFpEF was 139 days. In the overall HFpEF cohort, beta-blockers were not associated with all-cause death (hazard ratio [HR], 0.75; 95% confidence interval [CI], 0.59–0.94) and a composite outcome (HR, 0.74; 95% CI, 0.60–0.94). In the propensity-score matching cohort, beta-blockers were not associated with reduced all-cause death (HR, 0.76; 95% CI, 0.57–1.30) but significantly associated with reduced rehospitalization (HR, 0.75; 95% CI, 0.59–0.94) and a composite outcome (HR, 0.74; 95% CI, 0.60–0.94).

Conclusions: In Korean patients with HFpEF, use of beta-blockers was not associated with lower all-cause death but with lower rehospitalization.

Acknowledgement/Funding: The Korean National Institute of Health

P3779 | BEDSIDE
Long-term advantages of HR control with ivabradin-bisoprolol combination versus bisoprolol up titration on exercise capacity, chronotropic reserve and pulsatile arterial hemodynamics in CAD patients
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Purpose: To compare long-term effects of equivalent heart rate (HR) control at rest with ivabradin (IV) and bisoprolol (BS) combination and that of BS uptitration on exercise tolerance, its chronotropic support, LV function, pulsatile arterial hemodynamics assessed by pulse wave analysis (PWA) in CAD patients with mild LV dys fonction.

Materials and methods: In single-blind, parallel-group study 85 pts aged >60 years (53±7) in sinus rhythm >70 bpm with CAD (stable angina CCS class II), documented MI >3 months, mild hypertension and EF of 38–45%, treated with ACE inhibitors and BS 2,5 mg od or BB naive, were randomized into 2 groups. In Group 1 (n=40 per protocol, 9 women) BS was uptitrated to 5mg pd and IV was added (5mg bid uptitrated to 7,5 mg bid, 12,7±0,51 mg pd), in Group 2 (n=45 per protocol, 11 women) BS was uptitrated to 10 mg od (9,3±0,37 mg). At baseline (M0) and 6 months (M6), symptom-limited treadmill test (Bruce protocol) was performed, myocardial infarction in obese-insulin resistant rats

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Background: Adverse cardiac remodeling after myocardial infarction (MI) leads to progressive heart failure (HF). Obese-insulin resistance (IR) increases risks of MI and HF. Although dipetidyl peptidase-4 (DPP-4) inhibitor is known to exert cardioprotection, its effects on adverse remodeling after MI in obese-IR rats are unclear.

Results: Reaching HR was similar in both groups at M0 (78.6±3.59 vs 81.7±3.94 bpm) and M6 (67.2±2.98 vs 65.8±2.94 bpm) as well as brachial systolic BP (BSBP) (135.4±15.8 vs 133.6±5.9 and 120.4±4.8 vs 121.6±5.0 mmHg, all p>0.05).

Conclusions: In patients with CAD and mild EF lowering equivalent HR control at rest with long-term IV plus BS therapy, but not BS uptitration, produced exercise tolerance improvement, associated with major increase of chronotropic reserve, and to lesser extent - with resting mTR E/E’ reduction accompanied by arterial pulsatile unloading assessed by PWA.

P3780 | BEDSIDE
Clinical characteristics of responders to treatment with tolvaptan in patients with acute decompensated heart failure: importance of preserved kidney size
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Background: Recent clinical trials have demonstrated the efficacy of short-term treatment with tolvaptan, an oral vasopressin V2 receptor antagonist, in patients with heart failure. However, the response to tolvaptan varies among patients. The aim of this study was to determine factors associated with response to tolvaptan in patients with acute decompensated heart failure (ADHF).

Methods: We enrolled consecutive ADHF patients treated with tolvaptan and they were divided into two groups: responders and non-responders. Responders were defined as subjects who met all of the following three conditions: (1) increasing urine volume during a 24-hour period after the start of tolvaptan treatment, (2) improvement in NYHA functional class and (3) decrease in cardiothoracic ratio assessed by chest X-ray on day 3 of tolvaptan administration.

Results: Among the 114 patients, treatment with tolvaptan improved three conditions of heart failure (increase in urine volume, improvement in NYHA functional class and decrease in cardiothoracic ratio) in more than half of the patients with ADHF (number of responders versus non-responders: 71 (62%) versus 43 (38%). As for baseline characteristics, estimated glomerular filtration rate, urine osmolality, and kidney size were significantly greater in responders than in non-responders.

Multivariate logistic analysis revealed that kidney size was independently associated with responders.
Purpose: We tested the hypothesis that DPP-4 inhibitor reduces adverse cardiac remodeling and left-ventricular (LV) dysfunction in obese-IR rats with MI.

Methods: Rats were fed either normal-diet (ND) or high-fat diet for 12 weeks to induce obese-IR, followed by left anterior coronary artery ligation to induce MI. Then, rats in each dietary group were divided into 5 subgroups to receive vehicle, enalapril (E; 10 mg/kg/day), metformin (M; 30 mg/kg/day), DPP-4 inhibitor vildagliptin (Vl; 3 mg/kg/day), or combined metformin and vildagliptin (M+Vl) for 8 weeks. Heart rate variability (HRV), LV function, pathological and biochemical studies for LV remodeling, and myocyte apoptosis were determined.

Results: Obese-IR rats had severe insulin resistance, LV dysfunction, and had a higher mortality rate than the ND group. Although all drugs improved insulin sensitivity, HRV, LV ejection fraction as well as reduced cardiac hypertrophy and fibrosis, vildagliptin effectively reduced myocyte cross-sectional areas more than enalapril and metformin related to markedly decreased p-ERK1/2. In ND rats with MI, metformin neither improved UVEF nor reduced cardiac fibrosis. The infarct size and TGF-B expression were not different among groups.

Vildagliptin reduced crosssectional area

Conclusion: In obese-IR rats with chronic MI, DPP-4 inhibitor vildagliptin exerts better cardioprotection than enalapril in attenuating adverse LV remodeling.

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P3782 | BENCH
Resveratrol ameliorates dystrophic cardiomyopathy by activating FoxO transcription factors
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Purpose: We previously reported that resveratrol (RSV), an activator of the NAD--dependent protein deacetylase SIRT1, ameliorates cardiomyopathy in the dystrophic-deficient mdx mouse (MDX), a model of Duchenne muscular dystrophy. Here, we hypothesized that activation of FoxO transcription factors (FoxO), via gene transcription related to anti-oxidants and autophagy, contributes to protection afforded by RSV in the MDX heart.

Methods and results: First, we analyzed cardiac phenotypes in MDX. At 42-week-old, MDX showed cardiac hypertrophy evaluated by heart weight and echocardiography compared with those in age-matched C57BL10 mice. Left ventricular (LV) systolic function was preserved in MDX at this age. Dihydroethidium (DHE) staining for analysis of cardiac superoxide anion showed that fluorescence intensity was 4.5-fold higher in MDX than that in C57BL10. Although myocar dial mRNA levels of p62 and LC3b were unchanged between control and MDX, protein levels of p62 and LC3-II protein were rather higher in MDX than those in control. At 62-week-old, we examined the effect of RSV on cardiomyopathy in MDX. MDX were divided into untreated (RSVO) and RSV-treated (400 mg/kg chow, RSV400) groups. RSV administration was started at 8-week-old, and mice were sacrificed at 65-week-old. Echocardiography at 62-week-old demonstrated that LV fractional shortening was higher (38.2% vs. 34.1%, P < 0.05). IVS thickness was thinner, and end-diastolic LV dimension was smaller in RSV400 than those in RSVO. Compared with untreated MDX, RSV treatment significantly up-regulated cardiac mRNA levels of genes known as FoxO’s targets including anti-oxidant catalase (+2.0-fold), SOD1 (+2.8-fold) and autophagy-related LC3b (+2.5-fold), Bnip3 (+4.1-fold). This up-regulation of anti-oxidative genes was associated with a significant decrease (--45%) in DHE fluorescence in RSV400 compared with RSV0. Total cardiac LC3 level was rather decreased in RSV400, suggesting restoration of autophagic flux by RSV. Immunoblotting showed that FoxO1 and FoxO3a protein levels were elevated in RSV400 compared with RSV0. Importantly, nucleus-localized FoxO3a level assessed by immunostaining was increased by RSV, suggesting that RSV promotes translocation of FoxO3a via its nuclear localization.

Conclusion: RSV ameliorated cardiomyopathy in MDX probably by attenuating oxidative stress and restoring autophagy via FoxO activation.

P3783 | BENCH
Bendavia (MTP-131), a novel mitochondria-targeting peptide, improves mitochondrial respiration in isolated failing dog cardiomyocytes
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Background: Mitochondria of failed human hearts and hearts of dogs with experimental heart failure (HF) manifest structural and functional abnormalities characterized by hyperplasia and reduced organelle size and reduced respiration. These abnormalities lead to reduced rate of ATP synthesis that adversely impacts LV systolic and diastolic function. We previously showed that chronic therapy (3 months) with Bendavia (MTP-131), a novel mitochondria-targeting peptide, improves LV systolic and diastolic function in dogs with heart failure (HF). This improvement was associated with a reversal of mitochondrial abnormalities and normalization of mitochondrial rate of ATP synthesis in left ventricular (LV) myocardium of Bendavia-treated HF dogs. In the present study, we examined the direct effects of Bendavia on mitochondria ADP-stimulated state 3 respiration in freshly isolated cardiomyocytes from dogs with advanced chronic HF.

Methods: Cardiomyocytes were isolated from the LV free wall of untreated dogs with HF produced by intracoronary microembolizations (LV ejection fraction<30%). A standard collagenase-based enzymatic process was used for the isolation of mitochondria from freshly isolated cardiomyocytes that excluded trypan blue. Equal aliquots of cardiomyocytes were incubated in 0.0, 0.1, 1.0 and 10 μM concentration of Bendavia for one hour at 37°C. At the end of incubation, ADP-stimulated state-3 respiration was measured using a Strathkelvin respirometer system and qualified in nMol Oxygen/min/mg protein.

Results: State-3 respiration in the absence of Bendavia (Vehicle-Control) was 248±9 nMol Oxygen/min/mg protein. Compared to vehicle-control, incubation of failing cardiomyocytes with Bendavia significantly increased state-3 respiration to 303±33 nMol μM, p<0.05; 405±39 nMol μM, p<0.05; 371±28 at 1.0 μM, p<0.05; and 346±29 at 10 μM, p<0.05.

Conclusions: Results of this study indicate that the effects of Bendavia on mitochondrial respiration in cardiomyocytes is direct and not a consequence of improved global LV structure or function. Furthermore, the results indicate that the improvement in mitochondrial function with Bendavia treatment may occur early after initiation of therapy (within one hour) and is dose-dependent up to concentrations of 10 μM. These results support the in-vivo observations of improved mitochondrial function and rate of ATP synthesis in LV myocardium of dogs treated with Bendavia.

P3784 | BEDSIDE
Difference in efficacy of vasodilators for acute heart failure syndrome between female and male
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Introduction: Vasodilators play an important role in management of acute heart failure syndrome (AHFS). However, it remains to be elucidated which subgroups of patients should be treated with vasodilators.

Purpose: The aim of this study was to identify the characteristics of patients receiving benefit from vasodilators.

Methods and results: We retrospectively reviewed 763 patients (382 males, 77.6±12.9 years old) hospitalized due to AHFS. Vasodilators were used within 48 hours from admission in 329 (43.1%) patients. After propensity score matching, 546 well-balanced patients with or without vasodilators (273 patients in each group) were compared. The primary endpoint of this study was the composite of all cause death and re-hospitalization due to heart failure. During the follow-up period (median 228 days, interquartile range 55–1031 days), the primary endpoint was observed in 150 patients (28.6%). Cox regression analysis revealed that vasodilators did not significantly reduce the primary endpoint in all cohort (hazard ratio [HR] 0.79, 95% confidence interval [CI] 0.57–1.09, p=0.15). However, in subgroup analysis, the prognosis was significantly improved with vasodilators in female (HR 0.54, 95% CI: 0.34–0.85), but not in male gender (HR 1.23, 95% CI: 0.77–1.96). P value for interaction between male and female groups was significant (P=0.048).

Conclusions: The efficacy of vasodilators in AHFS differs between male and female. Vasodilator therapy may be preferred as initial treatment strategy for female patients with AHFS.

P3785 | BEDSIDE
Furosemide dose response curve after hypersaline in heart failure
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Aims: Loop diuretics remains a mainstay of heart failure (HF) therapy. The chief indicator to evaluate diuretic responsiveness is the urine production per unit dose of diuretic rather than the absolute urine output or diuretic dose. In many patients, sodium and water excretion plateau over time before adequate fluid elimination, leading to a phenomenon termed as diuretic resistance, which may be overcome by the administration of hypertonic saline solution (HSS) plus high dose furosemide (Furo).

Methods: Urine sample of 36 consecutive patients hospitalized for acute HF were collected at 30, 60, and 90 minutes and 3,4,5,6,8 and 24 hours after infusion of...
fur 125 mg (14 pts.), fur 250 mg (13 pts.) and fur 500 mg (9 pts.). Fur diluted in 150 ml of normal saline (initial) and hypertonic saline (after 24 hrs) was infused over 20 minutes. Diuresis, natriuresis, urinary osmolarity and fur urine delivery in all patients and at all detected times. No significant changes in serum sodium, BUN, serum creatinine and creatinine clearance estimated by MDRD formula were observed while body weight decrease significantly (p<0.0001). Furosemide concentration increases over time and was observed to rise into urine at all different doses when diluted in HSS. In 31 pts (86%), curves fit with sigmoid function (ALLFIT) confirming that HSS addition to fur have positive effects on diuresis and natriuresis.

Furosemide Dose response curves

Conclusion: This study demonstrates that addition of HSS to high dose fur, improves fur dose response curves, total diuresis, and natriuresis in acute HF. These results serve as pathophysiological basis of an innovative approach to manage acute HF.

P3786 | BENCH

Head to head comparison of therapeutic efficacy among three iron chelators on cardiac function in iron-overloaded rats

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Background: Iron overload cardiomyopathy is an important complication and responsible for high mortality rate in ß-thalassemia major and hereditary hemochromatosis patients. Currently, 3 available iron chelators for clinical use including parenteral iron chelator deferoxamine (DFO), and 2 oral iron chelators including deferoxiprone (DFP), and deferasirox (DFX) are used to prevent iron-overloaded complications. Despite their effective chelating effects, there are no reports on the head-to-head comparison regarding the efficacy of these 3 iron chelators on the heart in iron overload cardiomyopathy.

Purpose: To compare the therapeutic effects of DFO, DFP, and DFX on the iron accumulation and cardiac function in iron-overloaded rats.

Methods: Iron overload condition was induced in male Wistar rats by high iron (HFe) diet consumption for 4 months. At 2 months, iron-overloaded rats were determined.

Iron overload condition was induced in male Wistar rats by high iron (HFe) diet consumption for 4 months. At 2 months, iron-overloaded rats were determined. Iron-overloaded rats had increased cardiac iron deposit and decreased diuresis and natriuresis. Accumulation and cardiac function in iron-overloaded rats were evaluated for each collected urine sample.

Results: HSS addition to Fur significantly increased urine output, natriuresis, and was observed to rise into urine at all different doses when diluted in HSS. In 31 pts (86%), curves fit with sigmoid function (ALLFIT) confirming that HSS addition to fur have positive effects on diuresis and natriuresis.

Conclusion: This study demonstrates that addition of HSS to high dose fur, improves fur dose response curves, total diuresis, and natriuresis in acute HF. These results serve as pathophysiological basis of an innovative approach to manage acute HF.

P3787 | BEDSIDE

Different impacts of statin therapy on clinical outcomes in acute decompensated heart failure patients with or without ischemic etiology

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Background: It remains unclear whether statin treatment benefits the patients with heart failure (HF) in terms of clinical outcomes. The aim of this study was to evaluate the effectiveness of statin treatment on HF in patients with various comorbid conditions including ischemic cardiomyopathy and acute coronary syndrome.

Methods: A total of 4,183 patients (68.7±14.5 years, 2,252 males) from 10 regionally-representative tertiary university hospitals with acute heart failure (AHF) were consecutively enrolled in Korean AHF registry (KorAHF) between March 2011 and July 2013. They were divided into two groups according to use of statin; statin group (n=1,695, 70.4±12.4 years, 939 males) vs. non-statin group (n=2,488, 67.5±15.6 years, 1,313 males). Adverse clinical events including all cause death, and rehospitalization at short-term follow-up were compared between the groups.

Results: Adverse clinical events were developed in 1,045 patients (25.0%); 186 deaths (4.4%), 955 rehospitalizations (22.8%). The development of short-term adverse events were not different between the groups (28.1% vs. 29.1%, p=ns). In subgroup analysis between AHF patients with and without ischemic etiology, however, the use of statin reduced composite adverse events only in ischemic etiology (27.4% vs. 34.1%, p=0.033 by log-rank test), but did not in non-ischemic one (Fig 1).

HEART FAILURE THERAPY, VARIOUS V

Figure 1. Event-free survival between groups

Conclusion: Overall, the use of statin failed to show favorable effect on short-term clinical outcomes in Korean patients with AHF. However, the use of statin showed favorable effect in AHF patients with ischemic etiology. These results suggested that statin therapy may be useful in treatment of this category of patients.

Acknowledgement/Funding: This work was supported by a grant from Korea Centers for Disease Control and Prevention.

P3788 | BENCH

Growth hormone differentially modulates skeletal muscle proteins in rats with aortic stenosis-induced heart failure


Although chronic heart failure is usually associated with skeletal muscle atrophy, the physiopathological mechanisms involved in muscle mass loss are not completely established. Growth hormone (GH) has anabolic effects. It stimulates IGF-1, which activates the PI3K/Akt pathway to inhibit atrogin-1 and MuRF-1. GH can also modulate myogenic regulatory factors and myostatin and follistatin expression as well as satellite cell activation. However, the effects of GH on skeletal muscle preservation during catabolic diseases are not well understood. In this study we evaluated the effects of GH on trophicity and the intracellular signaling pathways involved in the atrophy process in peripheral skeletal muscles of rats with aortic stenosis (AS)-induced heart failure. After heart failure detection, GH was administered for 14 days (AS-GH group). Results were compared
with those from Sham and non-treated AS groups. Transthoracic echocardiogram was performed before and after treatment. Tropochemistry was analyzed in soleus and white part of gastrocnemius muscles. Protein expression was evaluated by western blot and satellite cell activation by immunofluorescence. Statistical analyses: ANOVA and Tukey or Kruskal-Wallis and Student-Newman-Keuls. Before treatment, AS groups presented similar echocardiographic parameters. GH attenuated systolic dysfunction. Gastrocnemius fiber cross-section areas did not differ between groups; soleus fiber cross-section areas were lower in both AS groups than Sham. In gastrocnemius, MRF-4 and atrion-1 were higher in AS and AS-GH groups. GH attenuated MyoD increase. Immunofluorescence showed that staining with anti-neural cell adhesion molecule (NCAM) and anti-neonatal myosin heavy chain isoform was statistically more intense in AS-GH than AS and Sham. In soleus, GH activated IGF-1 and PI3K proteins; NCAM immunofluorescence was increased in both AS groups. In conclusion, GH treatment attenuates left ventricular systolic dysfunction in rats with aortic stenosis-induced heart failure. GH administration for 14 days does not change skeletal muscle trophicity. However, GH differentially modulates expression of proteins involved in satellite cells activation and muscle atrophy. In preferentially glycolytic muscles (gastrocnemius), GH activates satellite cells and attenuates MyoD expression increase. In predominantly oxidative muscles (soleus), GH activates IGF-1 and PI3K protein expression.

P3789 | BEDSIDE
Clinical, biochemical and echocardiographic phenotyping of patients with cardiac dysfunction stratified according to prescription of loop diuretics
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Background: Congestion due to cardiac dysfunction is an important cause of symptoms and signs of heart failure. Diuretics are the mainstay of treatment for congestion. Patients treated with loop diuretics have a worse prognosis but whether this is because of their association with congestion or because they cause adverse neuroendocrine activation is uncertain.

Aim: To explore whether the relationship between loop diuretic use and outcome is explained by underlying evidence of congestion amongst patients referred for heart failure (HF) clinic.

Methods: A retrospective analysis of 1,190 patients admitted for AHF. Diuretics were categorized as intermittent (IVD, < 120 mg furosemide per day) and continuous (CIVD, > 120 mg furosemide per day). The primary endpoint was death at 30 days or during hospitalization. The secondary endpoint was death at 30 days. Logistic regression models were used to include variables that were associated with the outcome (p ≤ 0.20).

Results: Of 1,190 patients enrolled, 979 (82%) had cardiac dysfunction. A total of 51% of patients with cardiac dysfunction taking diuretics were older, had more evidence of congestion (more severe symptoms and signs, higher NTproBNP plasma levels), and were hospitalized for AHF within 12 hours of hospital admission compared to those without cardiac dysfunction, at admission. Although patients with low 24hDR were treated with significantly higher doses of furosemide and more frequently inotropes, they had higher levels of NT-proBNP at discharge (3139 ng/ml vs 2018 ng/ml, p=0.001). In a linear regression model the predictors of the 24hDR were SBP, renal function, and signs of congestion at admission. Low 24hDR was associated with higher in-hospital mortality and worsening renal function. The incidence of the primary endpoint was significantly higher in the low 24hDR group (p<0.001, Figure 1). In a multivariable model, 24hDR was an independent predictor of long-term events (HR 0.69 (0.57; 0.86), p=0.003) and resulted superior to 5DDR.

Conclusions: DR at 24 hours is a predictor of long-term events in patients with AHF. Further studies are needed to investigate the possible role of this parameter to optimize diuretic strategy.

P3790 | BEDSIDE
Impact of loop diuretic infusion modalities on congestion signs and clinical outcomes in patients with acute heart failure
A. Palazzuoli1, G. Ruocco1, M. Pellegrini1, B. Franci1, M.S. Campagna1, R. Nuti1, C. Ronco2, P. McCullough3, 1University of Siena, Cardiovascular Diseases Unit, Department of Internal Medicine, Siena, Italy; 2San Bortolo Hospital, Department of Nephrology Dialysis & Transplantation, Vicenza, Italy; 3Baylor University Medical Center, Baylor Heart and Vascular Institute, Dallas, United States of America

Background: Intravenous loop diuretics are the cornerstone of therapy in acute heart failure (AHF). However there are poor data regarding the relation between diuretic modality administration and the effects on decongestion as well the clinical impact.

Purpose: We sought to determine if there are any differences in decongestion signs and clinical outcomes between intravenous intermittent (IV) and continuous (CIV) of loop diuretics. Therefore we aim to evaluate the effects of two modalities administration on worsening renal function (WRF) and B-type Natriuretic Peptide (BNP) reduction.

Methods: Subjects with AHF within 12 hours of hospital admission were divided into two groups based on the median 24hDR. Univariate and multivariate analyses were performed to compare patients with the two different treatments with those from Sham and non-treated AS groups. Transthoracic echocardiogram was performed before and after treatment. Tropochemistry was analyzed in soleus and white part of gastrocnemius muscles. Protein expression was evaluated by western blot and satellite cell activation by immunofluorescence. Statistical analyses: ANOVA and Tukey or Kruskal-Wallis and Student-Newman-Keuls. Before treatment, AS groups presented similar echocardiographic parameters. GH attenuated systolic dysfunction and congestion signs despite an increased rate of WRF. In hospital WRF and continuous infusion (Civ) of loop diuretics. Therefore we aim to evaluate the effects of two modalities administration on worsening renal function (WRF) and B-type Natriuretic Peptide (BNP) reduction.

P3792 | BEDSIDE
Persistence of congestion 2.19 (1.09–4.38) 0.02 1.43 (0.70–2.92) N.S.

Impact of loop diuretic infusion modalities on congestion signs and clinical outcomes in patients with acute heart failure
A. Palazzuoli1, G. Ruocco1, M. Pellegrini1, B. Franci1, M.S. Campagna1, R. Nuti1, C. Ronco2, P. McCullough3, 1University of Siena, Cardiovascular Diseases Unit, Department of Internal Medicine, Siena, Italy; 2San Bortolo Hospital, Department of Nephrology Dialysis & Transplantation, Vicenza, Italy; 3Baylor University Medical Center, Baylor Heart and Vascular Institute, Dallas, United States of America

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P3790 | BEDSIDE
Early diuretic response is a long-term prognostic marker in patients hospitalized for acute heart failure
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Introduction: Response to diuretic therapy in acute heart failure (AHF) patients was associated with clinical outcome and events in several studies.

Purpose: The aim of our study was to evaluate the clinical and prognostic significance of early diuretic response (DR), as a prognostic predictor in patients admitted for AHF.

Methods: In a retrospective analysis we included 359 patients admitted for AHF. DR was defined as the overall diuresis amount per 40 mg of intravenous furosemide in the first 24 hours from admission (24hDR) and up to day 5 (5DDR). The primary endpoint was the composite of cardiovascular death, urgent heart transplantation and rehospitalization for HF at 1 year.

Results: The cohort was divided into two groups based on the median 24hDR value (320 ml/40 mg furosemide). Patients with low 24hDR had more signs of congestion, lower systolic blood pressure (SBP) and more comorbidities, namely renal dysfunction, at admission. Although patients with low 24hDR were treated with significantly higher doses of furosemide and more frequently inotropes, they had higher levels of NT-proBNP at discharge (3139 ng/ml vs 2018 ng/ml, p=0.001). In a linear regression model the predictors of the 24hDR were SBP, renal function, and signs of congestion at admission. Low 24hDR was associated with higher in-hospital mortality and worsening renal function. The incidence of the primary endpoint was significantly higher in the low 24hDR group (p<0.001, Figure 1). In a multivariable model, 24hDR was an independent predictor of long-term events (HR 0.69 (0.57; 0.86), p=0.003) and resulted superior to 5DDR.

Conclusions: DR at 24 hours is a predictor of long-term events in patients with AHF. Further studies are needed to investigate the possible role of this parameter to optimize diuretic strategy.

P3792 | BEDSIDE
Efficacy of addition of ibradipine to bisoprolol in patients with essential hypertension, coronary artery disease and reduced left ventricular systolic function
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Objective: Essential hypertension (EH) and coronary artery disease (CAD) contribute synergistically to high cardiovascular risk. The aim of this study was to
compare the efficacy of treatment with combined beta-blocker Bisoprolol (B) and If inhibitor Ivabradine (I) or beta-blocker B monotherapy in patients with EH, CAD and left ventricular (LV) systolic dysfunction.

Methods: Fifty two patients with mild EH, documented CAD and LV systolic dysfunction (<jection fraction-EF<35% or lower), who were in sinus rhythm and with a resting heart rate >70 beats/min., were treated with B at a constant dose (5 mg once a day) for 30 days or longer. 26 patients, aged 51–62 years (group A), were randomly assigned to receive 5 mg of I twice daily; 26 patients, aged 49–61 years (group B), were treated only with B until the end of the study. Echocardiography was performed at baseline and after 6 months of therapy. Parameters of LV systolic function [EF, endocardial and midwall fractional shortening (end FS and mid FS)] were calculated. Differences in the efficacy parameters were analysed using 2-tailed Student’s t test for quantitative parameters.

Results: At the end of the study blood pressure was lowered in both groups to less than 140/90 mm Hg. Mean number of anginal attacks per week decreased by 38.6% in group A (p<0.001) and by 23.1% in group B (p<0.01). EF increased in [51±2.1 vs 34±4.1, 1% in group A (p<0.001), 45±3.1 vs 34±7.1, 2% in group B (p<0.01)]. End FS and mid FS also increased at the end of the study in [41±8.1 vs 24±5.1, 2% and 25±1.5 vs 13±3.3, 3%, respectively in group A (p<0.001), 35±5.1 vs 24±8±1, 3% and 20±4.0 vs 13±6±5, 5%, respectively in group B (p<0.01)].

Conclusions: The combined therapy with B and I showed greater effects on clinical symptoms of CAD and LV function compared to monotherapy with B in patients with EH and CAD. Treatment with I is associated with significant improvement in all parameters of LV systolic function.

P3793 | BEDSIDE
Sodium zirconium cyclosilicate (ZS-9) for hyperkalaemia treatment: efficacy and tolerability in heart failure patients on renin-angiotensin-aldosterone system inhibitors (RAASi) from a phase 3 study
S.D. Ankri1, A. Mebazaa2, F. Zannad3, H.S. Rasmussen4, P.T. Lavin5, S. Bhupinder4, A. Yang6, M. Kosiborod7, University Medicine Göttingen, Göttingen, Germany; 2University Paris Diderot, Paris, France; 3Inserm, Université de Lorraine, Vandoeuvre-Les-Nancy, France; 4ZS Pharma, Inc., Coppell, TX, United States of America; 5Boston Biostatistics Research Foundation, Framingham, MA, United States of America; 6St. Luke’s Mid America Heart Institute, Kansas City, United States of America

Background: Renin-angiotensin-aldosterone system inhibitors (RAASI) increase risk of hyperkalaemia (HK; serum K+ >5.0 mmol/L), often leading to suboptimal dosing or discontinuation of these agents, despite proven cardioprotective benefits in heart failure (HF) patients (pts). Sodium zirconium cyclosilicate (ZS-9) is a first-in-class, highly selective, non-absorbed cation exchanger designed to trap excess K+ in the GI tract. In the Phase 3 HARMONIZE trial, ZS-9 rapidly achieved and maintained normal serum K+ for 28 days in HF pts.

Purpose: This pre-specified analysis from HARMONIZE was to examine efficacy/tolerability of ZS-9 in HF pts on RAASI.

Methods: HARMONIZE was a multicenter, randomized, double-blind, placebo-controlled trial which evaluated efficacy and safety of ZS-9 in pts with HK (N=258). All pts received ZS-9 10g TID for 48h (open-label phase). Pts achieving normalization of K+ within 2.0h; 91% and 98% of pts achieved normal K+ by 24h and 48h, respectively. At the end of the study ZS-9 rapidly normalized K+ within hours of the first dose, maintained normal K+ for up to 28 days, and was well tolerated in HF pts on RAASI.

Results: These results suggest that ZS-9 may enable optimization of cardioprotective RAASI therapy in high-risk pts with HF and HK.

Acknowledgement/Funding: Supported by ZS Pharma, Inc., Coppell TX, USA.
**BLOOD PRESSURE, MONITORING VARIABILITY AND ARTERIAL STIFFNESS**

### P3796 | BEDSIDE

**Classification of blood pressure by office and ambulatory readings in hypertensive type 2 diabetic patients - results of the German TZTarget registry in primary care**

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**Objective:** The target blood pressure for hypertensive patients with type 2 diabetes and cardiovascular disease (CVD) is <140/85 mmHg according to the latest guidelines. However, recent evidence suggests that antihypertensive therapy needs to be intensified in patients with atrial fibrillation (AF) and diabetes in order to reduce cardiovascular risk. The aim of this study was to evaluate the efficacy of antihypertensive therapy in patients with type 2 diabetes and AF.

**Methods:** A retrospective analysis of the TZTarget registry ( registry.tztarget.de ) was performed. The registry includes 2,500 patients with type 2 diabetes and AF who were treated with antihypertensive therapy. The primary outcome was the proportion of patients achieving the target blood pressure of <140/85 mmHg.

**Results:** The overall proportion of patients achieving the target blood pressure was 72.5%. However, the proportion varied significantly between different antihypertensive drug classes. The highest proportion was observed in patients treated with calcium channel blockers (84.5%), followed by patients treated with ACE inhibitors (79.1%) and ARBs (73.6%). The lowest proportion was observed in patients treated with diuretics (69.7%).

**Conclusion:** The results of this study suggest that the proportion of patients achieving the target blood pressure of <140/85 mmHg is higher in patients treated with calcium channel blockers compared to patients treated with diuretics. Further studies are needed to determine the optimal antihypertensive therapy for patients with type 2 diabetes and AF.

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### P3798 | BEDSIDE

**Ambulatory blood pressure monitoring in adolescent girls, reproductive-age women and postmenopausal women with obesity**

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Excess adiposity is the strongest known risk factor for hypertension (HT). The aim of this study was to compare the characteristics of ambulatory BP (ABPM) among women with obesity and normal body weight using different methods of BP measurement.

**Methods:** 382 obese patients who had not been diagnosed with HT, DM or CVD were included: 111 adolescent girls (54 obese, 15–20 y.), 127 reproductive-age (56 obese, 20–40 y.), and 144 postmenopausal women (77 obese, 40–65 y.). Levels of lipids, blood pressure (BP), heart rate (HR), and PWV were measured. The relationship between different BP measurements was assessed using correlations, and the association between BP and obesity was investigated using linear regression analyses.

**Results:** In all groups, a significant positive association was found between BMI and systolic BP and diastolic BP. The highest systolic BP and diastolic BP were found in the postmenopausal group, followed by the reproductive-age group, and then the adolescent group. The highest PWV was found in the adolescent group, followed by the reproductive-age group, and then the postmenopausal group. The highest HR was found in the adolescent group, followed by the reproductive-age group, and then the postmenopausal group.

**Conclusion:** These results suggest that BP and PWV are increased in obese women, and that the association between BP and obesity is stronger in postmenopausal women than in reproductive-age or adolescent women. Further studies are needed to investigate the long-term impact of obesity on BP and PWV in these groups.

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### P3797 | BEDSIDE

**Greater night-time blood pressure variability in acute coronary syndrome patients with more impaired reactive hyperemia index**

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**Background:** Although night-time blood pressure (BP) variability is associated with cardiovascular events, the mechanism is poorly understood. There is little information about the relationship between night-time BP variability and endothelial dysfunction or lipid content of coronary plaque that are important factors of atherosclerosis.

**Purpose:** The aim of this study was to examine the relationship between night-time BP variability and reactive hyperemia index (RHI) or lipid content of coronary plaque assessed by integrated backscatter intracoronary ultrasound (IB-IVUS).

**Methods:** We prospectively screened 157 patients with acute coronary syndrome who underwent percutaneous coronary intervention. Patients with no anaylizable plaque or for IVUS examination were not included. Finally 47 patients underwent ambulatory BP monitoring to evaluate BP variability and measurement of RHI to assess endothelial function. The standard deviation (SD) of systolic BP was used as BP variability. Plaque components of non-culprit coronary plaque in the culprit vessel were determined as lipid, fibrosis, dense fibrosis, and calcification by IB-IVUS.

**Results:** The mean night-time systolic BP SD and RHI were 11.1 mm Hg and 1.92, respectively. The mean night-time systolic BP SD showed a trend negatively correlated with RHI (r = −0.30, p = 0.06). Additionally, Patients with abnormal RHI (>1.67) had significantly higher night-time systolic BP SD compared to those with the normal RHI (1.67) (13.4±9.4 vs. 10.6±3.8 mm Hg, p = 0.05). On the other hand, there was no significant correlation between the night-time systolic BP SD and percentage of lipid plaque volume (r = 0.04, p = 0.78).

**Conclusions:** This study indicates that night-time BP variability was associated with endothelial function, which may partly explain a higher incidence of cardiovascular events in patients with greater night-time BP variability.
Blood pressure, monitoring variability and arterial stiffness 675

Methods: Our study included 100 subjects: 34 normotensive (19 male, mean age 53±4.9, 6 years), 33 dipper (18 male, mean age 54±11.7 years) and 33 non-dipper (12 male, mean age 56±7.9 years) newly diagnosed HT patients. Vitamin D and PTH levels of hypertensive dipper and non-dipper patients and normotensive were compared, factors affecting non-dipper BP were analyzed.

Results: Mean log (vitamin D) levels were significantly higher in non-dipper patients than that of dipper and control groups (0.8±0.3 ng/ml, 1.0±0.3 ng/ml and 1.0±0.4 ng/ml respectively, p<0.001). Mean log (PTH) level was significantly high in non-dippers than that of dipper and control groups (1.9±0.3 pg/dl, 1.7±0.2 pg/ml, 1.7±0.2 pg/dl respectively, p<0.001). Vitamin D levels were negatively correlated with 24-h systolic and diastolic BP (r=-0.366, p=0.003), (r=-0.295, p=0.018), day and night-time systolic and diastolic BP (r=-0.377, p=0.002), (r=-0.660, p<0.001), and likewise with all mean arterial pressures (MAP). PTH was positively correlated with systolic and diastolic BP and MAP levels. We found that vitamin D and PTH levels and 24-h MAP were independent predictors of non-dipper HT.

Abstract P3799 – Figure 1

Table 1. Levels of vitamin D and PTH

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Total (n=100)</th>
<th>Control (n=34)</th>
<th>Non-dipper (n=33)</th>
<th>Dipper (n=33)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean±SD</td>
<td>Median±IQR</td>
<td>Mean±SD</td>
<td>Mean±SD</td>
<td>p value</td>
</tr>
<tr>
<td>Male [%]</td>
<td>45 (45.0)</td>
<td>15 (44.1)</td>
<td>12 (36.4)</td>
<td>18 (54.5)</td>
<td>0.335</td>
</tr>
<tr>
<td>Female [%]</td>
<td>55 (55.0)</td>
<td>19 (54.9)</td>
<td>21 (63.6)</td>
<td>15 (45.5)</td>
<td></td>
</tr>
<tr>
<td>log(ViD) (ng/ml)</td>
<td>1.0±0.4</td>
<td>1.1±0.2</td>
<td>0.8±0.3</td>
<td>1.0±0.3</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>log(PTH) (pg/ml)</td>
<td>1.8±0.2</td>
<td>1.7±0.2</td>
<td>1.7±0.2</td>
<td>1.8±0.2</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

<sup>*</sup> Difference is significant at the 0.05 level, <sup>**</sup> difference showing group (adjusted benferoni post hoc test: p<0.05).

Conclusion: Our results suggest that vitamin D deficiency and PTH excess have positive correlation with non-dipping and increased BP parameters on ABPM in newly diagnosed HT.

P3801 | BEDSIDE

How do vitamin D and PTH affect diurnal blood pressure rhythm in patients with hypertension?

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Introduction: Cerebral white matter hyperintensities (WMH) are highly prevalent in the elderly population and increase the risk of dementia and stroke. Hypertension is one of the most important factors for WMH progression. According to recent studies, blood pressure (BP) variability is recognized as a cardiovascular risk factor; however, little is known about the association between BP variability and WMH.

Purpose: The purpose of this study is to evaluate the relationship between ambulatory monitoring derived BP variability and WMH volumes among elderly hypertensive patients with controlled office BP.

Methods: This cross-sectional study comprised 81 hypertensive patients aged between 65 and 75 years without symptomatic heart failure, ischemic heart disease, atrial fibrillation, stroke, or cognitive dysfunction. We obtained brain magnetic resonance imaging to quantify the volume of WMH. BP profile was assessed using 24-h ambulatory blood pressure monitoring (ABPM). BP variability was calculated using a standard deviation (SD) of systolic BP.

Results: Linear regression analysis revealed that office BP, HbA1c, LDL, HDL cholesterol, and protein with possible cardiac involvement were positively correlated with systolic and diastolic BP and MAP levels. We found that vitamin D and PTH levels and 24-h MAP were independent predictors of non-dipper HT.

Conclusion: Our results suggest that vitamin D deficiency and PTH excess have positive correlation with non-dipping and increased BP parameters on ABPM in newly diagnosed HT.

P3802 | BEDSIDE

Role of ambulatory blood pressure monitoring in long-term follow-up of gestational hypertension

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Background and aim: Many studies have shown that women with pregnancy complicated by gestational hypertension and preeclampsia have a higher risk of developing hypertension later in life than women with normotensive pregnancy. However, in these studies, the diagnosis of hypertension was made only on the basis of clinical measurements. The purpose of the study was to assess the incidence of hypertension after a long-term follow-up (mean: 8.5 years) in women with previous gestational hypertension, preeclampsia and previous normotensive pregnancy using ambulatory blood pressure monitoring (ABPM).

Patients and methods: We enrolled 150 women who delivered at the Department of Obstetrics of our city hospital between 2002 and 2005: 50 with gestational hypertension, 50 with preeclampsia and 50 with normotensive pregnancy. The inclusion criteria were: pre-existing hypertension, history of diabetes mellitus and cardiovascular events. The groups were matched for age and body mass index. Office blood pressure (OBP) and ABPM were measured in every woman. We collected lipid profile, glucose and creatinine at baseline and follow-up.

Results: Women with a history of gestational hypertension and preeclampsia developed hypertension more often than women with previous normotensive pregnancies (respectively 56% and 38% vs 20%, p<0.001), confirmed by the Kaplan-Meier analysis (log rank p=0.001). New diagnoses of hypertension made by ABPM were more than those made by OBP (28% vs 12% in gestational hypertension, 26% vs 12% in pre-eclampsia and 20% vs 12% in the control group, p<0.05). It has been found a higher rate of masked hypertension in women with previous gestational hypertension and preeclampsia than in the control group (26% and 24% vs 12%, p<0.07). There were no differences between the groups regarding glucose and lipid profile and renal function neither at baseline nor at follow-up.

Conclusions: ABPM appears a more reliable method than OBP when assessing the presence of hypertension in women with a history of hypertension in pregnancy, given the high incidence of masked hypertension in this setting.

P3803 | BEDSIDE

Serum cystatin-C as a marker for left ventricular hypertrophy in isolated nocturnal hypertension

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Purpose: Isolated nocturnal hypertension (INH) is a novel clinical entity currently being investigated in terms of clinical significance and prognosis. We therefore, investigated its relation with subclinical organ damage as well as potential clinically relevant mechanisms, such as neurohumoral activation and cystatin-C, a protein with possible cardiac involvement.
Methods: The study included 503 untreated normotensive and hypertensive subjects who underwent 24-hour ambulatory blood pressure monitoring (ABPM). In all participants, left ventricular mass index (LVMI), mitral pulse-wave Doppler E/A ratio, left atrial (LA) volume and LV end-diastolic diameter (LVEDD) were assessed by echocardiography. Creatinine clearance was estimated by the Cockcroft-Gault formula, while serum cystatin-C and brain natriuretic peptide (BNP) levels were measured by ELISA. INH was defined as nighttime systolic BP > 120/70 mm Hg and systolic BP < 135/85 mm Hg.

Results: Based on ABPM, 15.9% of participants had INH. Notably, INH group compared to normotensive controls exhibited higher values of LVMI (84.5±2.2 vs 74.2±1.1 g/m², p<0.001), while they did not differ regarding LA volume (41±11.0 vs 40.5±6.6 ml, p=0.629) and LVEDD (4.63±0.5 vs 4.64±0.3 cm, p=0.742). Also, INH group had increased E/A ratio compared to controls (1.0±0.4 vs 1.1±0.3, p=0.004), and serum cystatin-C was higher in INH subjects compared to normotensive controls (825±34.7 vs 737±13.5 ng/mL, p=0.004) but the two groups did not differ with respect to BNP levels (22.6±3.8 vs 23.4±2.2 pg/mL, p=0.218). Notably, using linear regression analysis, we found a positive correlation between cystatin-C levels and LVMI (r=0.20, p=0.005) in the group of INH.

Conclusions: According to this study, the presence of INH is accompanied by structural and functional abnormalities of the left ventricle. Cystatin-C, as an early marker of kidney function and a potential contributor to cardiac remodeling, is correlated with LVMI in this under diagnosed high risk population.

P3804 | BEDSIDE
Effect of liver transplant in circadian variation of blood pressure in patients with familial amyloid polyneuropathy
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Patients (pts) with Transthyretin familial amyloid polyneuropathy (TTR-FAP) V30M have changes in blood pressure (BP) profile due to disturbances in autonomic control. Liver transplantation (LT) has been used to attenuate the progression of the disease. However there is little information about its impact on the progression of autonomic dysfunction.

Purpose: To evaluate the impact of LT in the dysfunction of the autonomic nervous system (ANS) by assessing circadian variation of BP.

Methods: Prospective study of consecutive pts with V30M TTR-FAP evaluated annually and performing a 24-hour ambulatory blood pressure monitoring (ABPM) record. Pressure profile of pts undergoing transplant was compared with that of non-transplanted pts. For that purpose, we conducted a nested case-control analysis with patient matching according to neurophysiological score measured prior to transplantation (~5% difference).

Results: From a total population of 284 TTR-FAP pts, 88 (44 transplanted, 44 non-transplanted), with a mean age of 47±15 years, 52% male, with identical medical, neurophysiological and clinical scores, 25 (IQR 8.75–51.25) and 24 (IQR 0.90–51.25) months after matching, 208 ABPM records were performed. At initial evaluation, the transplanted group exhibited higher values of systolic BP (SBP) in 24 hours (121±15 vs. 113±10 mmHg, p<0.003), daytime (122±14 vs. 116±10 mmHg, p<0.013) and nocturnal (115±15 vs. 106±12 mmHg, p<0.008), daytime systolic pressure for 24 hours (93±12 vs. 87±10 mmHg, p<0.03), nocturnal SBP (93±15 vs. 87±10 mmHg, p=0.02) and pulse pressure (PP) (4±10 vs. 4±8; p=0.002). However, serum cystatin-C before LT was higher in INH subjects compared to normotensive controls (825±34.7 vs 737±13.5 ng/mL, p=0.004) but the two groups did not differ with respect to BNP levels (22.6±3.8 vs 23.4±2.2 pg/mL, p=0.218). Notably, using linear regression analysis, we found a positive correlation between cystatin-C levels and LVMI (r=0.20, p=0.005) in the group of INH.

Conclusions: According to this study, the presence of INH is accompanied by structural and functional abnormalities of the left ventricle. Cystatin-C, as an early marker of kidney function and a potential contributor to cardiac remodeling, is correlated with LVMI in this under diagnosed high risk population.

P3806 | BEDSIDE
Reversing the clock of vascular aging: the effect of antihypertensive treatment
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Purpose: Vascular aging, as assessed by structural and functional properties of the arteries, is an independent indicator of cardiovascular risk. Antihypertensive treatment has shown beneficial effects on prognosis. We sought to investigate the effect of different classes of antihypertensive drugs on the progression of vascular aging.

Methods: One hundred and forty-two subjects (mean age 51±10.8 years, 94 men, 61 hypertensives) with no established cardiovascular disease were investigated. Two examinations over a 2-year period (mean follow-up visit 1.84 years). All hypertensives were under treatment for at least 1 year and had well-controlled blood pressure. Subjects had at the beginning and end of the study determinations of carotid-femoral pulse wave velocity (PWV). Based on these measurements two groups were formed: subjects with normal PWV and those with increased PWV. With this method was determined the annual progression rate of arterial stiffening. Treatment with angiotensin receptor blockers was associated with slower progression of arterial stiffening after adjustment for relevant confounders [0.033/m/year (95% CI: −0.12 to 0.18) vs. 0.233/m/year (95% CI: 0.15 to 0.31), p<0.03; Angiotensin-converting enzyme inhibitors did not attenuate the progression of arterial stiffening [0.333/m/year (95% CI: 0.15 to 0.50) under treatment vs. 0.153/m/year (95% CI: 0.09 to 0.22), P=0.08]. Neither beta-blockers [0.243/m/year (95% CI: 0.08 to 0.41) under treatment vs. 0.17/m/year (95% CI: 0.10 to 0.23), P=0.42, calcium channel blockers [0.11/m/year (95% CI: −0.04 to 0.27) under treatment vs. 0.20/m/year (95% CI: 0.13 to 0.27), P=0.35] or thiazide diuretics [0.31/m/year (95% CI: 0.12 to 0.49) under treatment vs. 0.16/m/year (95% CI: 0.09 to 0.23), P=0.16] showed beneficial effect on reversing progression of arterial stiffening.

Conclusions: Angiotensin receptor blockers seem to slow down progression of vascular aging, compared to other classes of antihypertensive drugs. These results warrant further investigation in larger outcome studies.

P3807 | BENCH
The influence of antihypertensive treatment on arterial stiffness, shear stress and activity of chosen matrix metalloproteinases
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Objective: Comparison of therapeutic effects of chosen antihypertensive drugs on arterial stiffness, shear stress in carotid arteries and matrix metalloproteinases activity, moreover analysis of relationship of these variables in the course of treatment.

Design and methods: 45 patients were treated patients using different classes of antihypertensive drugs: diuretics, ACE inhibitors, ARBs, CCBs, blockers. All patients were randomized to 6 months monotherapy with: quinapril, amlodipine, hydrochlorothiazide, losartan or bisoprolol. Each therapeutic group consisted of 19 patients (N=19). Before and then after 1, 3 and 6 months of treatment carotid-femoral
pulse wave velocity (PWV) by using a Compilor device, ultrasound of carotid arteries were performed. Blood samples for the measurement of whole blood viscosity were taken during each visit. Shear stress (SS) was calculated on the basis of Irae formula. Serum concentration of metalloproteinase 3 (MMP-3) and plasma concentration of tissue inhibitor of metalloproteinases 1 (TIMP-1) were measured at the initial visit and after 6 months of treatment.

**Results:** ANOVA for repeated measurements revealed for all groups significant decrease of PWV and MMP-3 concentration and increase of shear stress in carotid artery and TIMP-1 concentration (p < 0.05). No between groups differences appeared in above effects (p > 0.05).

**Conclusion:** Irrespectively of chosen drug we observed similar effect for PWV drop. Reduction of arterial stiffness as a result of antihypertensive therapy is strongly connected with shear stress increase that is secondary to blood flow velocity growth and changes in connective tissue metabolism.

**INFLAMMATION AND IMMUNITY**

**3942 | BEDSIDE**

**Increased risk of abdominal aortic aneurysm in patients with psoriasis: A nationwide study**

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**Purpose:** Abdominal aortic aneurysm (AAA) is a complex multifactorial disease associated with a high morbidity and mortality. Increased inflammation including T helper (Th) 17 cell-mediated effects has been implicated in AAA pathogenesis. Psoriasis is considered to be a Th17-driven inflammatory disease and in view of potentially overlapping inflammatory mechanisms, we therefore investigated the risk of AAA in patients with psoriasis in a nationwide cohort.

**Methods:** The study comprised all Danish residents aged ≥ 18 years followed from 1st January 1997 until diagnosis of AAA, 31st December 2011, or death. Information on comorbidity, concomitant medication, and socioeconomic status was identified by individual-level linkage of administrative registers. Incidence rates for AAA were calculated and incidence rate ratios (IRR) were adjusted for age, gender, comorbidity, medications, and socioeconomic status were estimated in time-dependent Poisson regression models.

**Results:** A total of 5,108,593 subjects were eligible for analysis. During the study period we identified 60,477 patients with mild psoriasis and 12,285 patients with severe psoriasis. The overall incidence rates of AAA were 3.80, 8.17, and 10.70 per 10,000 person-years for the reference population (25,409 cases), mild psoriasis (272 cases), and severe psoriasis (55 cases, respectively). The corresponding adjusted IRRs for AAA were markedly increased in patients with psoriasis with IRR 1.35 (95% confidence interval [CI] 1.19–1.52) and IRR 1.89 (CI 1.45–2.47) for subjects with mild and severe disease, respectively.

**Conclusion:** In a nationwide cohort, psoriasis was associated with a disease severity-dependent increased risk of incident AAA. The mechanisms underlying this novel finding require further study.

**3943 | BENCH**

**Oxidized LDL induce tissue factor expression in CD3+ T-lymphocytes: a possible link between immunity, inflammation and thrombosis**

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**Background:** Recent data suggest that inflammation contributes not only to the genesis of the atherosclerotic plaque, but also to its complication, the key event in the pathophysiology of acute coronary syndromes (ACS). Plaque rupture involves expression of Tissue Factor (TF) within the plaque, which culminates in the formation of an intravascular thrombus. It has been shown that oxidized low-density lipoprotein (oxLDL) induce TF expression in endothelial cells, macrophages, smooth muscle cells. At present, however, is not yet known whether oxLDL may directly induce TF expression in T lymphocytes.

**Methods:** CD3-positive cells were isolated from buffy coat of healthy volunteers and stimulated with LDL or OxLDL (25, 50 and 100mg/mL). Expression of TF was assessed at 24, 48 hours at gene level and at 72 hours for protein expression after stimulation.

**Results:** OxLDL induced TF gene expression in T lymphocytes in a dose-dependent manner up to 40 times the baseline value; this resulted in a significant expression of TF protein at 72 hours. LDL had no effect on TF expression in T lymphocytes. Interestingly, in human carotid plaques obtained at surgery, TF expression co-localized with CD3+, suggesting that T lymphocytes might express in vivo.

**Conclusions:** Our data indicate that oxLDL induce TF expression in T-lymphocytes, suggesting a role for these cells also in the thrombotic process, thus adding a new piece to the complex puzzle of ACS pathophysiology.

**3944 | BENCH**

**Indoleamine 2,3-dioxygenase (IDO) enzyme: linking innate immunity and altered T-cell differentiation in acute coronary syndromes**

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**Background:** Atherosclerosis is a chronic inflammatory disease characterized by a complex interplay of innate and adaptive immune responses. Dendritic cells (DC) play a key role in the activation and regulation of T-lymphocyte by presenting antigens to naïve T-cells, which in turn differentiate in effector T-cells, such T-helper 1 (Th1), induced regulatory T-cells (iTreg), T helper 17 (Th17) and T helper 2 (Th2). DCs can promote a tolerogenic environment through the production of IL-10 and TGFβ or the expression of the immunosuppressive enzyme indoleamine 2,3-dioxygenase (IDO) and IDO-catalyzed tryptophan metabolism. IDO contributes to self-tolerance in the longer term by suppressing effector T-cells or expanding the induced regulatory T-cells (iTreg).

**Purpose:** We aimed to characterize the expression and activity of IDO in monoocytes derived DC (MDDC) from patients with acute coronary syndrome (ACS), stable angina (SA) and controls.

**Methods:** mRNA expression of IDO was analyzed in MDDC from 15 ACS, 15 SA patients and 15 controls by qPCR before and after maturation with LPS. The amount of tryptophan catabolite, kynurenine, was evaluated in the supernatants of mature MDDC by ELISA assay. Autologous mixed lymphocyte reaction (MLR) between mature DC and naïve T-cells was carried out to study the differentiation of T-cells towards Th1 and iTreg.

**Results:** Analysis of the levels of IDO mRNA transcripts by qPCR in mature MDDC revealed significant reduction in ACS (625±128.0, mean ± SEM) as compared to SA patients (1112±228.0, mean ± SEM) (P<0.05) and controls (1203±224.9, mean ± SEM) (P=0.04). Furthermore, the concentration of kynurenine, expressed as ng/ml, was higher in controls (0.5±0.1, mean ±SEM) as compared to SA (0.3±0.04, mean ±SEM) and ACS patients (0.3±0.03, mean ±SEM). When IDO competent mature MDDCs were co-cultured with allogeneic naïve T-cells, the ratio between the percentage of generated Th1 and iTreg from MLR was higher in ACS (2.8±0.30, mean ±SEM) and SA patients (2.34±0.54, mean ±SEM) than in controls (0.59±0.18, mean ±SEM).

**Conclusion:** In ACS, altered DC function might provide one of the environmental cues that enhances pro-inflammatory T-cell differentiation. IDO production by activated DCs could contribute to a mechanism of self-limit immune responses. This may be part of a negative feedback loop, lacking in ACS, whereby DCs may regulate immune responses in the presence of a large number of aggressive T-cells. Characterization of new antiatheroprotective mechanism might be important to develop novel preventive strategies.

**3945 | BEDSIDE**

**Macrophage degradation in coronary atherosclerotic plaques by statin therapy: an optical coherence tomography study**

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**Objectives:** The aim of this study was to assess the effect of statin therapy on macrophage accumulation in coronary atherosclerotic plaques by using optical coherence tomography (OCT).

**Background:** OCT can identify macrophages accumulation as a high intensity signal-rich linear region with sharp attenuation.
Methods: Seventy patients with unstable angina pectoris and untreated dyslipidemia were randomized to either 20 mg/day or 5 mg/day of atorvastatin therapy. OCT was performed to assess intermediate non-culprit lesions at baseline and 12-month follow-up.

Results: Macrophage grade decreased significantly in both groups, and the percent decrease in macrophage grade was significantly greater in the group receiving 20 mg/day of atorvastatin compared with the group receiving 5 mg/day of atorvastatin (~38% [IQR -44 to -31%] vs. ~24% [IQR -33 to 0%], p < 0.001). The percent change in macrophage grade was negatively correlated with the percent change in the serum HDL-C (R = -0.368, p = 0.008) levels, and positively correlated with the percent change in the serum hs-CRP (R = 0.308, p = 0.033) and MMP-9 (R = 0.486, p < 0.001) levels; however, it was not correlated with the percent change in the serum total cholesterol (R = 0.038, p = 0.793), LDL-C (R = -0.212, p = 0.139), triglyceride (R = 0.070, p = 0.627), MDA-LDL (R = 0.163, p = 0.257), IL-6 (R = -0.153, p = 0.288), and HbA1c (R = 0.086, p = 0.551) levels. In addition, the percent change in macrophage grade was negatively correlated with the percent change in fibrous cap thickness (R = -0.415, p = 0.003).

Conclusions: Therapy with 20 mg/day of atorvastatin provided greater decrease of macrophage accumulation in coronary plaques compared with 5 mg/day of atorvastatin. The decrease of macrophage accumulation was associated with the increase in serum HDL-C and decrease in serum inflammatory biomarkers during atorvastatin therapy.

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3946 | BEDSIDE
Long-term cardiovascular outcomes in patients with collagen disease who underwent percutaneous coronary intervention
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Background: Although patients with collagen disease have a significantly increased risk of cardiovascular disease, the long-term prognosis is fully unknown in patients with collagen disease who underwent percutaneous coronary intervention (PCI).

Methods: From April 2007 to October 2014, a total of 627 consecutive patients who underwent PCI were enrolled in this study. We compared the long-term clinical outcomes of 33 patients with collagen disease to 543 patients with non-collagen disease. The primary endpoint was major adverse cardiac events (MACE), which was defined as cardiovascular death, myocardial infarction (MI), and target lesion revascularization (TLR).

Results: The incidence of MACE was significantly more observed in collagen disease than in non-collagen disease (24.2% vs. 10.1%, p = 0.036). Multivariable analysis demonstrated that collagen disease was independent predictor for MACE after adjusting confound factors.

Conclusion: Patients with collagen disease had poor long-term cardiovascular outcomes after receiving PCI.

3947 | BEDSIDE
OxLDL upregulates microRNA-155 in dendritic cells by binding transcription factor YY1/MYB through the JAK1/2 signaling pathway
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In order to explore the upstream regulatory mechanisms of miR-155 following oxLDL treatment in dendritic cells, DCs were either transfected with siRNA of scavenger receptors to elucidate the signaling mechanisms involved. A transcription factor filter plate screen assay was performed to identify the transcription factor that binds to the miR-155 promoter in response to OxLDL treatment. Pre-cise binding sites were also detected by performing a chromatin immunoprecipitation assay. We found that MIIR-155 was evidently decreased when signaling molecules were inhibited. Furthermore, oxLDL positively promotes complex formation of YY1 and MYB. YY1 assisted MYB the binding of promoter sequences on miR-155, thus activating downstream transcription. Our study clearly revealed that oxLDL upregulates MicroRNA-155 in DCs by binding YY1/MYB.

3948 | BEDSIDE
The neutrophil-lymphocyte ratio predicts mortality in acute coronary syndrome: a meta-analysis
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Background: The neutrophil to lymphocyte ratio (NLR) is a recently described independent predictor of death and myocardial infarction by integrating two leukocyte subtype counts with opposing actions in terms of vascular inflammation.

Methods: We conducted a systematic search of studies using MEDLINE, EMBASE, ScienceDirect, and Cochrane Central Register databases and examined reference lists of studies. We identified 12 studies that met inclusion criteria. The study title, follow-up period, neutrophil-lymphocyte ratio, and mortality outcomes were extracted from these studies. Each study was assessed using the Newcastle-Ottawa Quality Assessment Scale. The outcome of interest was assessed using Mantel-Haenzel analysis of random effects to compute for odds ratio, carried out using Review Manager (RevMan) 5.0.18.

Results: Pooled analysis from 12 studies enrolling 9,835 patients showed that a high neutrophil-lymphocyte ratio (NLR) was predictive of increased total mortality among patients presenting with acute coronary syndrome compared to those patients whose NLR is not high (8.65% vs 2.26%) (OR 4.10, 95% CI 3.36, 5.00; P < 0.00001). Data was homogenous (I2 = 0%) and there was no evidence of publication bias by funnel-plot method. Thirty-day mortality, including in-hospital death, is likewise increased among those with high NLR (7.78% vs 2.22%) (OR 3.67, 95% CI 2.93, 4.58; P < 0.00001). Subgroup analysis also revealed increased mortality in patients with high NLR whether they had a STEMI or NSTEMI/UAM.

Conclusion: A high NLR value is associated with high mortality among patients with acute coronary syndrome. This readily computed parameter is a useful tool to determine prognosis of these patients.

3949 | BENCH
IL-17 plays a major inflammatory mediator in ischemic heart failure
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Introduction: CD4+ T cells play an important role in inflammatory heart disease,
implicating a cytokine product associated with Th cell effector function as a necessary mediator of this pathophysiology. The IL-17 is the major mediator of tissue inflammation, however, the role for IL-17 in ischemic heart failure (HF) is not well defined.

Methods: HF rabbits were created 4 weeks after undergoing coronary ligation. WBC, serum biochemistry, monophasic action potential, ECG and expression of CD4+ T cell are measured every two weeks. The mRNA and protein expressions of IL-17 are also measured by real time-PCR, ELISA and flow cytometry. Open-chest epicardial catheter stimulation was performed for ventricular arrhythmia (VA) provocation.

Results: We found a lot of inflammatory cells infiltrating in left ventricle (Fig. A). The data showed CD4+ cells and IL-17 were up-regulated significantly by CD4+ T cells in HF (Fig. B and C). We also found the mRNA of IL-17A and IL17F were high expression by real time PCR and protein expression of IL-17 was also increased in ischemic HF (Fig. D).

Conclusion: CD4+ T cell-derived proinflammatory cytokine IL-17 is the major mediator of cardiac inflammation and may play a key role to induce the VA in an ischemic HF model.

Acknowledgement/Funding: TSOC

3950 | BENCH
Selection inhibitory of the NLRP3 inflammasome dose-dependently reduces infarct size and preserves cardiac function in a porcine model of myocardial infarction
ment 27.3% (3 risk categories) vs UKPDS + CAC score alone). Event rate in upper decile of pt risk was 51% vs 6.5% in total cohort.

Conclusion: Addition of CTA defined plaque extent and characterization to a combined clinical risk (UKPDS) and CAC score model better identified a DM cohort at high risk for MACE who may benefit from further study or intervention.

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3996 | BEDSIDE
5 year prognostic value of coronary computed tomographic angiography using machine learning: results from the CONFIRM Registry

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Purpose: We investigated if 5 yr prognosis in patients with suspected coronary artery disease (CAD) can be predicted by machine learning (ML) integrating clinical data with imaging data from coronary CT angiography (CTCA).

Methods: Data from 10030 patients (58±13 yrs; 56 male) without known CAD, and with 5 yr outcomes from the CONFIRM registry were considered. All patients underwent CTCA for clinical purposes and were followed for all-cause mortality (ACM) and MACE (death/MI/ACS/late revascularisation). 44 CTCA parameters and 25 clinical parameters were available for ML, including segment stenosis score (SSS), segment involvement score (SIS), modified Duke index (DI), number of segments with non-calcified, mixed or calcified plaques, age, sex, gender and standard cardiovascular risk factors. ML involved automated feature selection by information gain ranking, model building with a boosted ensemble algorithm, and 10-fold stratified repeated cross-validation.

Results: 745 patients died and 991 had MACE events during 5 yr follow-up. ML had the highest area-under-the-curve (AUC) compared to Framingham risk score (FRS) or CTCA data alone for both 5 yr ACM (ML: 0.80 [0.78–0.81] vs. FRS: 0.61 [0.59–0.64]), SSS: 0.64 [0.62–0.66], SIS: 0.64 [0.62–0.66], DI: 0.62 [0.60–0.64], p < 0.001) and 5 yr MACE prediction (ML: 0.83 [0.82–0.84] vs. FRS: 0.61 [0.59–0.63], SSS: 0.70 [0.68–0.72], SIS: 0.70 [0.68–0.71], DI: 0.69 [0.67–0.70]; p < 0.001). All CTCA severity scores (SSS, SIS and DI) were superior to FRS for predicting MACE (p < 0.001), and SSS and SIS were superior to FRS for predicting ACM (p < 0.05). ML was superior to FRS for categorising risk of 5 yr ACM as <5%, 5–10% or >10% (NRI=0.42; p < 0.001).

Conclusion: ML combining clinical and CTCT data predicts 5 yr ACM and MACE better than FRS or CTCA data alone.

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3997 | BEDSIDE
Relationship between non-calcified coronary plaque volumes by coronary CT angiography and fractional flow reserve

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Background and introduction: The correlation between anatomical stenosis assessment and ischemia is poor in coronary artery disease (CAD). Recently, an association between adverse plaque characteristics by coronary CT angiography (CTCA) and ischemia has been shown.

Purpose: The aim of the present study was to evaluate the association between atherosclerotic plaque volumes and fractional flow reserve (FFR), and to determine whether plaque volumes provide incremental prediction of ischemia when compared to coronary CT angiography (CTCA) stenosis assessment alone.

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

Results: In 484 vessels, mean volumes of NCP, LD-NCP, and CP differed significantly between FFR groups (Figure). Age- and gender-adjusted ORs for prediction of FFR ≤0.80 for NCP >185 mm³, LD-NCP >30 mm³, and CP >9 mm³ were 5.0 (3.1–8.2; p < 0.001), 7.2 (4.3–11.9; p < 0.001), and 1.5 (0.9–2.4; p=0.09), respectively. OR for CTA >50% was 6.8 (3.9–12.0; p < 0.001). In multivariate analysis NCP (p < 0.001), LD-NCP (p < 0.001), and CPA (p < 0.001) were independent predictors of lesion-specific ischemia, while CP was not (p=0.48).

Conclusions: We identified an inverse relation between FFR and coronary plaque volumes. Coronary NCP and LD-NCP volumes by CTA provide incremental predictive value for identification of lesion-specific ischemia when compared to standard CTA assessment.

BLEEDING AND ISCHAEMIC EVENTS IN PCI PATIENTS: PREDICTION, PREVENTION AND MANAGEMENT

4000 | BEDSIDE
Relationship between platelet count, platelet reactivity and ischemic and bleeding risk in patients undergoing PCI with DES: Insights from the ADAPT-DES registry

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Introduction: Previous data suggest that high platelet counts (PC) are associated with higher rates of ischemic events after PCI. Whether this association is independent of and/or varies by residual platelet reactivity is unknown.

Purpose: To evaluate the relationship between PC, platelet reactivity, and risk for definite or probable stent thrombosis (ST) and major bleeding 2 years after PCI.

Methods: Patients enrolled in the prospective, multicenter ADAPT-DES population were stratified by PC and platelet reactivity unit (PRU) tertiles. High platelet reactivity (HPR) on clopidogrel was defined as a VerifyNow PRU value >230.

Results: 8,535 patients were included in the study cohort. There were no significant differences in the prevalence of HPR across tertile tertiles. Rates of ST were highest among patients in the highest tertiles (p < 0.01) of both PRU and PC, while the rate of bleeding was highest in those in the lowest tertiles (p<0.05; Figure). After adjustment for baseline risk factors, including HPR, high PC tertiles (p=0.17) and high PRU tertiles (p>0.17) were independently associated with an increased risk of ST and bleeding. The effect of HPR on ischemic and bleeding risk across PC tertiles was uniform, without evidence of interaction. Finally, both lower (adjHR: 1.53; 95% CI: 1.1–2.2) and higher (adjHR: 1.75; 95% CI: 1.0–3.1; p=0.05) PC tertiles were associated with higher rates of ST and bleeding (Figure).

Conclusions: High PC and PRU yields an additive
effect on risk for ST. While PC was not associated with bleeding risk, both low and high PC independently correlated with long-term mortality. PC could be a parameter to take into account in guiding duration and potency of dual antiplatelet therapy after DES implantation.

4001 | BEDSIDE

Bleeding episodes in “complete, staged” versus “culprit only” revascularization in patients with multivessel disease and ST-segment elevation myocardial infarction - a DANAMI-3-Primumulti substudy

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Background and introduction: Patients with acute ST-segment elevation myocardial infarction (STEMI) and multi vessel coronary disease have a poorer prognosis than those with a single infarct-related artery (IRA) lesion. The Third DANISH Study of Optimal Acute Treatment of Patients with STEMI undergoing successful primary PCI, who had PCI of the IRA or fractional flow reserve (FFR) (≤ 0.80) guided complete revascularization during a staged procedure before discharge. Bleeding episodes were assessed based on BARC and TIMI criteria.

Methods: We included patients with acute onset symptoms of coronary artery disease and STEMI with novel platelet inhibitors and bivalirudin.

Results: From March 2011 to February 2014 627 patients were randomized in the trial. A total of 314 patients were randomized to complete revascularization while 313 patients were randomized to culprit-PCI only. 90.4% of the patients randomized to complete revascularization underwent a second in-hospital procedure, most commonly angiography + FFR alone, FFR guided PCI or coronary artery bypass grafting.

Conclusion: Data will be analyzed in March 2015, when the last included patient has been followed clinically for 1 year. Baseline and randomization data will be presented at the ESC meeting.

4002 | BEDSIDE

The effect of cangrelor and access site on ischemic and bleeding events: insights from CHAMPION-PHoenix

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Background: In CHAMPION-PHoenix, cangrelor reduced ischemic events with no significant increase in severe/moderate bleeding or in transfusions regardless of PCI access site.

Methods: From March 2011 to February 2014 627 patients were randomized in a double-dummy, double-blind manner to either cangrelor followed by clopidogrel 600 mg or 300 mg or 600 mg of clopidogrel at PCI. The primary endpoint was a composite of death, MI, ischemia-driven revascularization (IDR), or stent thrombosis (ST) at 48 hours.

Results: 8,064 (72%) and 2,855 (26%) patients underwent femoral and radial PCI, respectively. Among the femoral cohort the primary endpoint rate was 4.8% cangrelor vs. 6.0% clopidogrel, (OR [95% CI] = 0.79 [0.65, 0.96]). Among the radial cohort the primary endpoint rate was 4.4% cangrelor vs. 5.7% clopidogrel (OR [95% CI] = 0.76 [0.54, 1.06], p-interaction = 0.83. The rate of severe or life-threatening bleeding in the femoral cohort was 0.2% cangrelor vs. 0.1% clopidogrel (OR [95% CI] = 1.73 [0.51, 5.93]). Among the radial cohort the rate of severe or life-threatening bleeding was 0.1% in the cangrelor and clopidogrel groups (OR [95% CI] = 1.02 [0.14, 7.28], p-interaction = 0.65. In the femoral cohort the rate of blood transfusion was 0.5% cangrelor vs. 0.3% clopidogrel (OR [95% CI] = 1.56 [0.80, 3.05]). In the radial cohort the rate of blood transfusion was 0.2% cangrelor vs. 0.1% clopidogrel (OR [95% CI] = 1.54 [0.26, 9.21], p-interaction = 0.99.)

Conclusion: In CHAMPION-PHOENIX, cangrelor reduced ischemic events with no significant increase in severe/moderate bleeding or in transfusions regardless of PCI access site.

WHAT’S NEW IN MICROCIRCULATION AND COLLATERALS

4022 | BEDSIDE

Index of microvascular resistance in real-world practice in patients with stable ischemic heart disease: insight from the international imr registry

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Background: The index of microcirculatory resistance (IMR) is a quantitative and specific index for coronary microcirculation. However, the distribution, optimal cut-off values, and independent determinants for high-IMR have not been fully investigated in patients with stable ischemic heart disease (IHCD).

Methods: 1,096 patients with 1,452 coronary stenoses who underwent elective measurement of both FFR and IMR were enrolled from 8 centers in 5 countries. Patients with acute MI were excluded. IMR values were corrected with Yong’s formula (IMRcorr) to adjust for the influence of collateral flow. High-IMRcorr were defined as greater than the 75th percentile. FFR<0.80 was defined as an ischemic value.

Results: Among patients (mean age 61.1, male 71.2%), 57.9% and 42.1% were from Asian and Western populations, respectively. Mean FFR was 0.84 and mean IMRcorr was 16.6U (IQ 12.4–23.0U). IMRcorr was significantly different among the 3 main coronary arteries (median values 15.7U, 16.9U and 19.1U for LAD, LCX and RCA, respectively, p<0.001). The categorical agreement of FFR and IMRcorr was very low (kappa value =0.042, p=0.102). Among patients with FFR<0.80, 26.3% had high IMRcorr. Independent determinants of high IMRcorr were obesity (OR 1.88 [1.32–2.68], p=0.001), female gender (OR 1.85 [1.26–2.71], p=0.002), and age (OR 1.023 [1.003–1.044], p=0.025).

Conclusion: The distribution of IMRcorr was significantly different among the coronary arteries and approximately 25% of stenoses with non-ischaemic FFR values had evidence of abnormally high microvascular resistance. The independent predictors of high IMRcorr values were different from those for ischaemic FFR values. Integration of IMR and FFR measurements may improve the stratification of patients without evidence of MI.
Conclusions: Both groups, though less markedly in patients pretreated with prasugrel, compared with clopidogrel, the clopidogrel group (Δ: 29%, p < 0.001) and the prasugrel group (Δ: 28%, p = 0.003) showed significantly lower in the prasugrel as compared with clopidogrel group (17.3±8.3 vs. 25.1±10.9 ml/kg/min, p < 0.01). ADP-induced platelet reactivity was lower in the prasugrel compared with clopidogrel group (17.3±8.3 vs. 26.1±11.0 ml/kg/min, p < 0.007). A significant post-procedural IMR increase was observed in the clopidogrel group (Delta: 29%, p < 0.001), while no significant changes were observed in the prasugrel group (Delta: 10%, p < 0.20). ADP-induced platelet reactivity was significantly lower in the prasugrel group (Δ: 28% vs. 29%, p < 0.001) and post-PCI (Δ: 29% vs. 39% ± 18% AU, p < 0.001). Close-TnT increased post-PCI in both groups, though less markedly in patients pretreated with prasugrel compared with clopidogrel group (Δ: 25% vs. 34%, p < 0.001 vs. 15.8±8.3 vs. 25.1±10.9 ml/kg/min, p < 0.001).

Methods and results: Forty-thienopyridine-naive patients were randomized to a loading dose of either prasugrel 60 mg (n=20) or clopidogrel 600 mg (n=20) at least 12 hours before PCI. At baseline and post-PCI, we assessed the index of microvascular resistance (IMR) in the treated artery, and adenosine diphosphate (ADP)-induced platelet reactivity with the Multiplate Analyzer. Higher sensitive troponin T (hs-TnT) was measured before and at 24 hours after PCI. Baseline IMR was not significantly different between the two groups (15.7±10.1 vs prasugrel group vs. 20.2±8.1 in clopidogrel group, p = 0.148). Post-PCI IMR was significantly lower in the prasugrel as compared with clopidogrel group (Δ: 29% vs. 28%, p < 0.001) and post-PCI (Δ: 29% vs. 39%±18% AU, p < 0.001). If post-TnT increased post-PCI in both groups, though less markedly in patients pretreated with prasugrel compared with clopidogrel group (Δ: 25% vs. 34%, p < 0.001) and post PCI (Δ: 29% vs. 39%±18% AU, p < 0.001). IMR was not significantly different between the two groups (15.7±10.1 vs. 15.8±8.3 ml/kg/min, p = 0.21). The corresponding CFR values were 1.4 [1.0–1.8] vs 1.7 [1.4–2.5] vs 1.5 [1.1–1.8], respectively. Both IMR and CFR were measured at the end of PCI using guidewire-based thermometry. Contrast-enhanced cardiac magnetic resonance (CMR) imaging was used to assess left ventricular (LV) function and infarct pathology 2 days and 6 months post-MI. Intramyocardial haemorrhage (IMH) was defined as a hypointense infarct core with a T2* value ≥20ms. Infarct size and microvascular obstruction (MVO) were assessed with late gadolinium enhancement CMR. Adverse remodelling was defined as an increase in left ventricular end-diastolic volume (LVEDV) >20% at 6 months.

Results: CMR was performed in 245 patients at day 2 and in 228 patients (93%) at 6-months post-MI. The median IMR [IQR] was 25 [15–48] and median CFR was 1.4 [1.0–1.8] vs 1.7 [1.4–2.5] vs 1.5 [1.1–1.8], respectively. Both IMR and CFR were measured at the end of PCI using guidewire-based thermometry. Contrast-enhanced cardiac magnetic resonance (CMR) imaging was used to assess left ventricular (LV) function and infarct pathology 2 days and 6 months post-MI. Intramyocardial haemorrhage (IMH) was defined as a hypointense infarct core with a T2* value ≥20ms. Infarct size and microvascular obstruction (MVO) were assessed with late gadolinium enhancement CMR. Adverse remodelling was defined as an increase in left ventricular end-diastolic volume (LVEDV) >20% at 6 months.

4047 | BEDSIDE
Heart failure mortality following cancer treatment: a linked health data analysis of blood, lymphatic and breast cancer patients (1996-2009)
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Background and introduction: Cardiotoxicity resulting in heart failure (HF) is a devastating complication of cancer treatment.

Methods: To describe the characteristics and time to death of blood, lymphatic and breast cancer patients who died of heart failure. Of those who died of heart failure two groups were compared, those who had an index hospital admission prior to death (HFA) and those who did not (NHFA).

Results: Within this cohort of 4894 patients, 734 were coded as HF related death (50.1% Female), 279 (38.0%) had at least one HF admission (41.9% Female) in the period of post cancer diagnosis. Median age of patients with HFA prior to death was 71 years (IQR 62–78) and 66 years (IQR 56–74) for NHFA. There were 72% HFA and 88% NHFA in the blood and lymphatic cancer group. Patients with HFA received fewer chemotherapy cycles (median=4, IQR 2–9) than the NHFA patients (median=6, IQR 2–12). Patients with an index HFA had 2.5 times increased risk of HF mortality than NHFA patients [HR 2.50 [95% CI, 2.14–2.92] when adjusted for age, sex, marital status, country of birth, cancer site and number of chemotherapy doses]. 31% of HFA and 33% of NHFA patients died of HF within one year and 60% and 62%, respectively, died within three years of commencement of cancer treatment. In addition 71% of the deceased cancer patients, who had an index HFA, died within one year of the index HF admission.

Conclusion: In the first three years following cancer diagnosis a high proportion of patients died of HF following cancer treatment. Once diagnosed with HF almost three quarters of patients died within 12 months. Further research is underway by our team to explore the period of 1996–2009 including Queenslands Cancer Registry (QCR), Death Registry and Hospital Admission records for HF and chemotherapy admissions were linked for this study. Index HF admission must have occurred after cancer diagnosis. Data were analysed by comparing demographic characteristics, risk factors for HFA and NHFA patients and a multi-variate Cox proportional hazards model was fitted to compare the survival outcomes between the two groups. A proportional hazard assumption was tested and confirmed to satisfy assumptions. Kaplan-Meier survival analysis was performed and differences were compared by log-rank test.

Acknowledgement/Funding: Institute of Health and Biomedical Innovation (IHBI), Queensland University of Technology (QUT) and Faculty of Health Sciences, Flinders University.
Cardio-Oncology – Where heart failure experts meet cancer / CMR for clinical diagnosis and prognostication

4049 | BEDSIDE
High-sensitivity T troponin for early detection of cardiotoxicity among patients on chemotherapy
C.A. Alvarez-Ortega, O. Rodriguez-Fraga, O. Gonzalez-Fernandez, S. Rosillo, T. Lopez-Fernandez, Z. Blazquez-Bermejo, S. Valbuena-Lopez, M. Moreno-Yanguela, A. Bu-Sadot, J.L. Lopez-Sendon on behalf of GECAME. University Hospital La Paz, Cardio Oncology Unit, Madrid, Spain

Introduction: Left ventricular dysfunction as a result of anticancer-drug therapy is an important issue in cancer survivors. Tools for an early detection of cardiotoxicity are needed. Cardiac biomarkers can detect myocardial injury and thus may play an important role in subclinical detection of drug-related toxicity. The aim of this study is to evaluate if cardiac biomarkers can detect patients who will develop cardiotoxicity after chemotherapy.

Methods: GECAME study (Grupo de Estudio de Cardiotoxicidad por Medicamentos) is an uncenteric registry of patients treated with cardiotoxic anticancer drugs. Transthoracic echocardiography (TTE) was performed before starting treatment and at 3, 6 and 12 months from the start of treatment, between August 2011 and January 2014. Cardiotoxicity was defined as a relative decrease in LVEF -10% from the basal and below 55% or clinical signs or symptoms of heart failure. Blood samples were drawn at baseline, 21 days, 3 months, 6 months and one year after starting chemotherapy. hs-cTnT, cTnI, NT-proBNP and Galectin-3 were measured. We used 99 percentile as cut-offs for Roche Elecsys hs-cTnT (14 ng/L CV= 10%) and Siemens Vista c-TnI (27 ng/L CV= 7.7%) assays for Gal-3

Results: 222 consecutive patients were included. The mean age was 58±11.43 years and 76.7% were women. 59.5% had been diagnosed breast cancer, 34.7% leukemia or lymphoma, and 5.8% other tumor. Mean basal LVEF was 64±3.5±6%. NT-proBNP and 3-Galectine concentrations did not vary significantly during follow-up. Increased hs-cTnT and cTnI concentrations occurred with a maximum concentration at third month, being hs-cTnT the one with more patients above the threshold. 120 patients had hs-TnI plasma levels above pp9, 20 of which developed cardiotoxicity during follow-up. From the 102 patients with hs-cTnT below pp9, 7 developed cardiotoxicity. These findings show a sensitivity of hs-cTnT AUC= 0.81, p<0.01 and a lower mean effective radiation dose [22 vs. 4.4 mSv (−80%), p<0.01].

Conclusions: Despite similar or risk profiles, revascularized patients initially evaluated with CTCA after PCI had more downstream non invasive and invasive testing, higher CAD-related spending and effective radiation exposure as compared to patients evaluated with stress-CMR with comparable (MACES).

Acknowledgement/Funding: Extrastiftelsen

4050 | BEDSIDE
Coronary high-intensity plaque on t1-weighted magnetic resonance imaging and its association with percutaneous coronary intervention related myocardial injury
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Aims: Non-contrast T1-weighted imaging (T1WI) has emerged as a novel non-invasive imaging modality for vulnerable coronary plaque, exhibiting a signal of high-intensity plaque (HIP). However, the impact of HIP for percutaneous coronary intervention (PCI) has not been fully evaluated. We investigated the association between the presence of HIP and the incidence of PCI-related myocardial injury (PMI).

Methods: A total of 100 lesions from 77 patients with stable angina were imaged with non-contrast T1WI with a 1.5-T MRI before PCI. We defined HIP as a signal intensity of coronary plaque to cardiac muscle ratio (PMI) ≥1.4. Cardiac troponin-T (cTnT) was measured at baseline and 24 hours after PCI.

Results: HIP was identified in 36% of plaque. In the IVUS assessment, ves- sel and plaque volume were significantly greater in HIP group than in non-HIP. The ultrasound attenuation was identified more in HIP group as compared to non-HIP (72% vs. 5%, p<0.01). Although baseline cTnT was similar between both groups, cTnT was significantly elevated in HIP group as compared to non-HIP (0.010 [0.006–0.016] to 0.084 [0.029–0.292], 0.010 [0.006–0.021] to 0.028 [0.012–0.046] mg/L, respectively, P<0.001). PMI was observed in 58% and 9% for HIP and non-HIP group (P<0.001), and the cutoff value of PMI for predicting the incidence of PMI (odds ratio 6.45, 95% confidence interval 1.06–20.4, P=0.042).

Conclusion: HIP on non-contrast T1WI was characterized as vulnerable coronary plaque on IVUS and was associated with the incidence of PMI.

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4051 | BEDSIDE
Computed tomography coronary angiography versus stress cardiac magnetic resonance for the management of symptomatic revascularized patients: a cost effectiveness study
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Background: Computed tomography coronary angiography (CTCA) and stress cardiac magnetic resonance (stress-CMR) are both suitable for diagnosing obstructive coronary artery disease (CAD) in symptomatic patients for chest pain with previous history of revascularization. However, the evaluation of performance of non-invasive tests has taken in account the subsequent diagnostic, testing and medical procedures derived, clinical outcomes and cumulative costs and radiation exposure rather than their diagnostic accuracy alone. The aim of this study is to compare the clinical and economic outcomes of using anatomical (CTCA) versus functional strategy (stress-CMR) in revascularized symptomatic patients for chest pain.

Methods and materials: Four hundred revascularized symptomatic patients for chest pain were addressed to CTCA (n=200, mean age 68±10 yo, male 168) or stress-CMR (n=200, mean age 66±9 yo, male 177) and followed-up in terms of downstream non invasive tests, invasive coronary angiography (ICA) and revascularization procedure, medical costs for CAD management, cumulative effective radiation dose and major adverse cardiac events (MACEs) defined as composite endpoints of non fatal myocardial infarction and cardiac death.

Results: All patients performed both tests successfully. The mean follow-up for CTCA and stress-CMR groups were similar (772±398 vs. 794±345 days, p=ns). Compared with stress-CMR strategy, CCTA was associated with an increased likelihood of subsequent mean number of further non-invasive test (1.04 vs. 0.81, p<0.01), cardiac catheterization (40% vs. 30%, p<0.05). No differences were found in terms of subsequent percutaneous coronary interventions (PCI) (30% vs. 26%, p=0.37) but stress-CMR group was associated with a favorable trend of PCI/I/CA rate (86% vs. 75%, p=0.08) and MACEs (4% vs. 8.5%, p=0.06). Moreover, CTCA strategy showed a higher mean cost per patient [2329.46 vs. 2617.47 Euro (−11%), p<0.05] and a lower mean effective radiation dose [22 vs. 4.4 mSv (−80%), p<0.01].

Conclusions: Despite similar or risk profiles, revascularized patients initially evaluated with CTCA after PCI had more downstream non invasive and invasive testing, higher CAD-related spending and effective radiation exposure as compared to patients evaluated with stress-CMR with comparable (MACES).

Acknowledgement/Funding: Extrastiftelsen

4052 | BEDSIDE
Impact of weight reduction on pericardial fat volume and cardiac structure: Implications for atrial fibrillation in a randomized clinical trial
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Introduction: We recently reported the favourable effects of weight and cardiorespiratory risk factor management on the clinical burden of atrial fibrillation (AF in overweight and obese patients). The structural changes underlying this relationship remain unknown. Pericardial fat and left atrial dilatation are independent risk factors for AF severity and therapeutic outcomes.

Purpose: To validate at this cardiac magnetic resonance imaging (CMR) study-we determined the effect of the structured weight loss program on cardiac structure, pericardial fat volume and metabolic parameters to explain the observed reduction in arrhythmia burden.

Patient demographics

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<td>Radiotherapy involving the heart (%)</td>
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</table>

P-values by independent Student’s t-test.

Cardiovascular magnetic resonance for clinical diagnosis and prognostication

Conclusion: HIP on non-contrast T1WI was characterized as vulnerable coronary plaque on IVUS and was associated with the incidence of PMI.
Methods: We enrolled 69 controls (33, intervention: 36) overweight and obese patients with paroxysmal AF (in sinus rhythm at the time of CMR scanning) into either an structured physician-directed weight management program, or general lifestyle advice. Patients were followed up at 3 month intervals for a total of 12 months. All patients underwent CMR at baseline and 12 months follow-up. Offline blinded volumetric analysis was performed using the disc summation method by a CMR reference laboratory.

Results: (Table) Structural changes between groups were independent of body surface area. No significant changes were observed in ventricular volumes between the groups.

Conclusion:  structured weight loss program with cardiometabolic risk management results in favorable changes in atrial volumes, myocardial mass, systolic blood pressure, serum CRP and pericardial fat volume, as compared to aggressive risk factor management alone. These changes may account for the observed reduction in AHY haemorrhage burden.

Acknowledgement/Funding: Australian Post Graduate Award

4054 | BEDSIDE
Impact of long-term steroid therapy on epi- and pericardial fat deposition - a cardiac MRI study
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Introduction: Epi- and pericardial fat is a common finding in cardiac imaging. Cardiac fat deposition has unfavorable local effects, which might result in an adverse patient outcome. Previous data have shown that cardiac fat is associated with metabolic syndrome and obesity. Steroids are known to imitate some of the effects of the metabolic syndrome. Consequently, the aim of our study was to evaluate the impact of long-term steroid therapy on epi- and pericardial fat distribution.

Methods: Sixty-one consecutive patients with different rheumatic disorders and long-term steroid medication (participants of the RHEU-MAR study) underwent CMR for evaluation of cardiac fat deposition. Medical history was reviewed carefully regarding structured weight loss program with cardiometabolic risk management results in favorable changes in atrial volumes, myocardial mass, systolic blood pressure, serum CRP and pericardial fat volume, as compared to aggressive risk factor management alone. These changes may account for the observed reduction in AHY haemorrhage burden.

Methods: We performed a prospective single centre cohort study in repertused STEMI patients who underwent CMR 2 days (n=286) and 6 months post-MI. IMH was taken to represent a hyperintense infarct core with a T2* value < 20 ms.

Results: 245 STEMI patients had evaluable T2* data and 101 (41%) patients had IMH. In multivariable regression, IMH was independently associated with initial TIMI coronary flow grade, ECG evidence of reperfusion injury and Killip class (all p < 0.03). 133 (51%) patients had MVO. All of the patients with IMH had MVO. IMH was multivariantly associated with adverse remodeling, independent of baseline LVEDV (β: 2.64 (1.07, 6.49); p=0.035). IMH was also multivariantly associated with cardiovascular (CV) death or heart failure hospitalisation post-discharge (hazard ratio (95% CI): 12.9 (1.6, 100.8); p=0.015). The serial imaging subgroup, IMH occurred in 7 (23%), 13 (43%), 11 (33%), and 4 (13%) patients at 4–12 hours, 3 days, 10 days and 7 months, respectively. The amount of MVO persisted at 4-12 hours post-reperfusion, then fell progressively over time. In contrast, the amount of IMH increased dynamically from 4-12 hours with a peak at 3 days and then a decrease at 10 days. MVO resolved by day 10 in 85 patients (44%), 2 (5%) of which had evidence of IMH. Whereas MVO persisted in 10 patients (56%), all (100%) of which had evidence of IMH.

Conclusion: IMH is independently associated with adverse remodeling at 6-months and CV death or heart failure hospitalisation post-discharge. The severity of MVO affects its degree of persistence and T2* imaging differentiates persistent, structural microvascular injury from functional, potentially reversible MVO. Haemorrhage occurs in primary and secondary phases within the first 10 days post-MI. IMH is a biomarker with potential to reflect the efficacy of therapeutic interventions in STEMI patients.

4056 | BEDSIDE
Comparison of transthoracic echocardiography versus cardiac magnetic for implantable cardioverter-defibrillator therapy in primary prevention strategy dilated cardiomyopathy patients
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Background: Implantable cardioverter-defibrillators (ICDs) has been proved as a valid primary prevention strategy to reduce mortality in patients with dilated cardiomyopathy (DCM) with reduced left ventricular ejection function (LVEF) <35%. This LVEF threshold is largely based on studies using tran-thoracic echocardiography (TTE). Cardiac magnetic resonance (CMR) is now considered the gold standard technique for LVEF assessment and it provides important information on tissue characterization such as late gadolinium enhancement (LGE). Several studies have shown differences between CMR and TTE evaluation. The aim of this study is to determine whether LV evaluation and LGE detection by CMR are superior to 10 conventional TTE measurements for risk stratification of DCM patients evaluated for ICD implantation in primary prevention strategy.

Methods and materials: Two hundred and seventy consecutive DCM patients (Mean age 63±13 yo, male 220 patients) referred to our Institution to be evaluated for ICD implantation in primary prevention were enrolled. All patients underwent both TTE and CMR left ventricle end-diastolic (LVEDV) and end-systolic (LVESV) volumes and LVEF estimation. Additionally, LGE, presence was also detected by CMR. All patients were followed-up for the major adverse cardiac events (MACE) defined as a combined endpoint of ventricular tachycardia, ventricular fibrillation and sudden cardiac death.

Results: All patients performed both tests successfully. The mean follow-up was 850±330 days. TTE showed a lower LVEDV (86±28 vs. 131±41 ml/m²) and LVEDV (57±21 vs. 93±40 ml/m²) and a higher LVEF (35±10 vs. 31±5%) as compared to CMR (P <0.001). MACE occurred in 68 patients (28%). Patients experienced MACE showed a higher LVEDV-TTE (94±28 vs. 84±28 ml², p = 0.01), LVESV-TTE (64±27 vs. 55±23 ml/m², p = 0.003), LVEDV-CMR (141±43 vs. 128±41 ml/m², p = 0.01), LVESV-CMR (105±42 vs. 90±39 ml/m², p = 0.003), lower LVEF-
CMR (29±10 vs. 32.29±p; p=0.0027) and a higher LGE prevalence (67 vs. 44%; p=0.0008) as compared to patients without MACE. At multivariate analysis, LVEF-CMR [HR: 2.3 (1.6–3.01)] and presence of LGE [HR: 4.08 (2.15–8.02)] were independently associated with MACE [p<0.001]. In the subset of patients with LVEF-CMR, the addition of LVEF-CMR and LGE provides a net reclassification improvement (NRI) of 42% and 26%, respectively, in terms of outcomes.

Conclusions: LVGE and LGE estimation by CMR might provide additional prognostic stratification as compared to TTE that could identify a subset of subjects in whom ICD implantation is still indicated despite LVEF-TTE<35%.

4057 | BEDSIDE
Cardiac magnetic resonance can predict appropriate primary prevention ICD therapy in ischemic and dilated cardiomyopathy patients using late gadolinium enhancement heterogeneity
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Background: Patients at risk for malignant ventricular arrhythmias receive primary prophylactic implantable cardioverter defibrillators (ICD), but not all patients benefit from ICD, as no arrhythmia occurs. The heterogeneous late gadolinium enhancement (LGE) borderzone measured by cardiac MRI (CMR) has been proposed as an independent predictor of ventricular arrhythmias.

Purpose: The purpose was to determine if the extent and heterogeneity of LGE areas predicts appropriate ICD-therapy in ischemic and dilated cardiomyopathy patients, and if a newly developed borderzone algorithm has similar predictive value as the previously validated heterogeneity.

Methods: Ischemic cardiomyopathy (ICM) and dilated cardiomyopathy (DCM) patients who underwent LGE-CMR prior to primary prevention ICD implantation were retrospectively included and divided into two groups (i) patients with appropriate ICD-therapy (anti-tachycardia pacing, shock or both) and (ii) patients with no ICD-therapy. A semi-automatic quantitative algorithm was used to evaluate the LGE borderzone and compared against a modified full-width half-maximum (FWHM) algorithm to a threshold-based algorithm.

Results: A total of 55 ICM and 62 DCM patients were included with a mean follow up time of 46±29 months. Kaplan-Meier analysis showed that patients with larger (median) compared to smaller borderzone extents had higher rates of ICD-therapy in ICM and DCM patients pooled together using the novel algorithm (n=10 vs. n=3 vs. therapy, P=0.02) and the modified FWHM algorithm (n=10 vs. n=3 patients with therapy, P=0.02) and in LGE positive ICM patients alone (n=5 vs. n=1, P=0.03 and n=6 vs. n=0, P=0.01 for respective algorithm) at similar follow-up times (P=ns). Total LGE burden was similar between groups with and without ICD-therapy in both ICM (P=0.5) and DCM patients (P=0.3). The mean borderzone was larger in the group with appropriate ICD-therapy compared to the group with no ICD-therapy in ICM patients using the novel algorithm (38±12% vs. 30±5%, P=0.004) and the modified FWHM algorithm (46±14% vs. 35±11%, P=0.03), but the threshold algorithm did not separate the groups (11±5% vs. 14±5%). Diastolic EF difference was seen in DCM patients.

Conclusion: A large LGE borderzone predicted appropriate ICD-therapy in a pooled cohort of ICM and DCM patients and in the subgroup of ICM patients. Borderzone quantification using both a novel and a modified FWHM algorithm were predictive. Thus, borderzone size may be a marker for risk stratifying patients eligible for primary prevention ICD-therapy.

4058 | BEDSIDE
Cardiac progenitor cell therapy reduces myocardial fibrosis and stiffness to improve cardiac function in patients with univentricular heart disease
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Background: Patients with single ventricular physiology undergoing staged palliations may present myocardial fibrosis by cardiac magnetic resonance imaging (MRI) and ischaemic ventricular dysfunction. This might impair the preservation and development of right ventricular function. Although latent heart failure could be predicted in these patients after palliations, adjunctive cardiac therapy may have a potential to reverse cardiac dysfunction by direct conversion of the extent and severity of myocardial fibrosis.

Purpose: The aim of this study was to quantitatively elucidate the volume fraction of myocardial fibrosis (MVF) in CTO patients and to investigate its relationship with univentricular cardiac function.

Methods: A total of 50 patients with CTO and 15 age- and sex-matched volunteers undergoing cardiac MR were recruited to the study. Global EF was calculated from pre- and post-contrast T1 map around the entire LV myocardium and calibrated by hematocrit. ECV of remote myocardium was calculated from the myocardium without late gadolinium enhancement. Segmental ECV was obtained from myocardial segments within the perfusion territory of a CTO. The function of collateral vessels was assessed using the Rendtorff classification as the reference standard.

Results: ECV of remote myocardium was significantly higher in CTO patients than in normal subjects (26.6±5.6% vs. 23.3±2.0%, P<0.05). Other factors associated with elevated ECV were an older age (r=0.33, P=0.05), a longer course of disease (r=0.39, P<0.02), a larger left atrial diameter (r=0.37, P=0.05) and the presence of diabetes (r=0.30, P=0.03). Global EF significantly correlated with LV ejection fraction (EF) (r≥0.56, P<0.001) and with the grade of EF impairment (P<0.001). The lower segmental ECV was associated with the presence of well-developed collaterals (P<0.004), and multivariate binary logistic analysis demonstrated that mean segmental ECV and course of disease were independent discriminators of collateral formation with overall diagnostic accuracy of 74.4%.

Conclusions: In patients with CTO, diffuse myocardial fibrosis and collateral function can be non-invasively assessed by ECV measurements. ECV measured by cardiac MR may serve as a useful alternative for risk stratification and monitoring target treatment.

4060 | BENCH
Prognostic value of peri-infarct tissue heterogeneity in reperfused STEMI
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Purpose: Single-center studies suggest an association of infarct tissue heterogeneity assessed by late gadolinium enhanced magnetic resonance imaging (MRI) with arrhythmic events and prognosis in patients with ischemic cardiomyopathy. However, it is unknown if this association can be transferred to patients with acute ST-segment elevation myocardial infarction (STEMI) treated by primary percutaneous coronary intervention (PCI). Therefore, aim of this study was to investigate the presence of LGE heterogeneity in STEMI patients with respect to hard clinical events in a cohort of acutely reperfused STEMI patients.

Methods: We enrolled 138 STEMI patients reperfused by primary PCI (<12 h after symptom onset) in this CMR study. CMR was completed within one week after

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infarction using a standardized protocol. Analysis of tissue heterogeneity of peri-infarct zones was performed using commercially available CMR post-processing software (CMR42, Circle Inc, Calgary, Canada). A computer-assisted, semiauto-
matic algorithm quantified the total infarct size and divided it into the core and peri-infarct regions based on signal-intensity thresholds (5 SDs and 3 SDs above remote normal myocardium, respectively). The peri-infarct zone was normalized as a percentage of the total infarct size. The association of peri-infarct tissue heterogeneity and occurrence of major adverse cardiac events (all cause death, reinfarction, and new congestive heart failure within 1 year after infarction) was evaluated.

Results: The median peri-infarct zone was 23.4% LV (interquartile range 15.6 to 29.9). Patients with cardiovascular events had significantly larger peri-infarct zones (28% versus 13%, p < 0.001). In a multivariate model that included clinical and echocardiographic parameters, the extent of the peri-infarct zone was an independent predictor of the combined clinical endpoint (1.45, 95% CI, 1.15 to 1.84; p = 0.002).

Conclusion: In this CMR study of acutely repurposed STEMI patients, peri-infarct tissue heterogeneity was associated with adverse cardiac events. These results indicate that peri-infarct tissue heterogeneity might be useful for acute risk stratification of the postinfarction patient. Further studies are warranted to determine potential early ICD indications.

ATRIAL FIBRILLATION IN REAL WORLD

P4061 | BEDSIDE

Female sex, age and time delay to cardioversion as risk factors in the cardioversion of acute atrial fibrillation. The FinCV Study

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Background: Female gender is a risk factor for thromboembolic complications (TEC) in atrial fibrillation (AF). It is also associated with an increased risk for complications such as bradycardia and TEC after cardioversion of acute AF.

Purpose: The aim of this study was to compare clinical presentation, comorbidity and complications during a 30 day follow-up in women and men with electrical cardioversion of acute AF (<48 hours) performed without anticoagulation.

Methods: A total of 4715 scheduled electrical cardioversions without periprocedural or postprocedural anticoagulation were performed in 2313 patients with AF lasting <48 hours. The outcomes were failure of cardioversion, bradyarrhythmic complications, AF recurrence and TEC after cardioversion (30-day follow-up) and their combination – the net harm - was calculated. Finally, the interaction of age, sex and delay to cardioversion on the risk of TEC was assessed.

Results: Women with acute AF were older, had more comorbidities and higher heart rate (117±23 bpm for women vs. 107 ± 27 bpm for men, p <0.001). The failure of electrical cardioversion was higher (6.7% vs. 4.0%, p <0.001) and bradyarrhythmic complications were more common in women (1.9% vs. 0.4%, p <0.001). AF terminated more often after periprocedural anticoagulation (30% vs 7%, p <0.001) but diabetes was present in both groups (11.7% vs. 11.7%, p =0.05). Female sex was also associated with an increased risk of TEC (OR 2.12, CI 1.09–4.11, p =0.03). The net harm was higher in women than in men (21.9% vs. 16.5%, p<0.001). Older age (p<0.001), time delay from the onset of AF to cardioversion (OR per 4-hour delay 1.07, 95% CI 1.06–1.09, p<0.001), female sex and delay to cardioversion were independent predictors of TEC. The risk of TEC increased from 0.3% (p<0.10) in men <65 years and cardioversion delay <12 hours to 2.7% (p=0.004) in women >75 years and delay >12 hours.

Conclusion: Older women are at high risk for complications and failure of cardioversion of acute AF. The risk of TEC rises substantially in both sexes and particularly in women >65 years when delay to cardioversion exceeds 12 hours. This should be taken into account when considering the treatment strategy of this increasing patient population.

P4062 | BENCH

Atrial fibrillation and hypertrophic cardiomyopathy: a propensity score analysis from a multicenter Portuguese study

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Purpose: The study aim was to analyze whether AF has a prognostic implication of in an A-HCM cohort.

Methods: We analyzed whether AF has a prognostic implication of an A-HCM cohort.

Results: According to our matched groups, AF was not significantly associated with mortality in HCM patients.

P4063 | BENCH

Atrial fibrillation in patients admitted to coronary care units in western Sweden. Focus on obesity and lipotoxicity

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Introduction: Atrial fibrillation (AF) is the most common form of arrhythmia in humans and is associated with substantial morbidity and mortality. We hypothesized that obesity and diabetes are involved in the pathophysiology of AF by means of promoting a lipotoxic phenotype in atrial muscle, and that AF was predictors mortality in cardiac care patients.

Methods: Our study consists of two parts. The first part is a case-control study based on prospective data obtained through the Register of Information and Knowledge about Swedish Acute Care Admissions (RISKA-ICA) from hospitals in western Sweden. All consecutive patients between 2006–2011 admitted to coronary care unit (CCU) with sinus rhythm (SR) or AF were included in the analysis. Multivariable logistic regression and Cox proportional-hazards regression were used to test whether diabetes and obesity were independent predictors of AF at admission to CCU and whether AF was associated with increased one-year mortality. In the second part we obtained atrial biopsies from 54 patients undergoing cardiac surgery and performed lipomics analysis for a detailed qualitative and quantitative analysis of lipid species including triglycerides (TAG), ceramides (CER), phosphatidylcholine (PC), lysophosphatidylcholine (LPC), phosphatidylethanolamine (PE), sphingomyelins (SM), free cholesterol (FC), cholesterol esters (CE) and diacylglycerols (DAG).

Results: Between 2006–2011, 35232 patients were admitted to CCUs in western Sweden, mostly due to ischemic heart disease, heart failure, arrhythmia, syncope and chest pain. The mean age was 66 years and 58.7% were male. There was a high prevalence of obesity (20.3%) and diabetes (16.8%). Obesity (OR 1.35, 95% CI 1.17–1.56, p<0.001) and severe obesity (1.6, 95% CI 1.29–1.99, p<0.001) were independent predictors of AF. AF was associated with increased one-year mortality. In the second part we found atrial biopsies from 54 patients undergoing cardiac surgery and performed lipomics analysis for a detailed qualitative and quantitative analysis of lipid species including triglycerides (TAG), ceramides (CER), phosphatidylcholine (PC), lysophosphatidylcholine (LPC), phosphatidylethanolamine (PE), sphingomyelins (SM), free cholesterol (FC), cholesterol esters (CE) and diacylglycerols (DAG).

Conclusion: Obesity but not diabetes is an independent predictor of AF and AF is associated with increased one-year mortality in this CCU population, which is in association with prognostic and qualitative alterations in atrial lipid content but not with lipotoxicity.

P4064 | BEDSIDE

Clinical implication of atrial fibrillation in patients with apical hypertrophic cardiomyopathy

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Background: Apical hypertrophic cardiomyopathy (ApHCM) is considered a "benign" form of hypertrophic cardiomyopathy. However, the clinical impact of atrial fibrillation (AF) in ApHCM is largely unknown.

Purpose: We analyzed whether AF has a prognostic implication of an A-HCM cohort.

Methods: The occurrence of AF and clinical outcome were assessed in 347 consecutive ApHCM patients (87.8% male, 62.1±11 years). The incidence of AF was 3% per year with prevalence of 30%. Development of AF was independently predicted by an old age and large left atrium (≥45 mm). During a follow-up of 6.3±3.2 years, the AF patients had a higher incidence of heart failure (11.1% vs. 2.1%, p<0.001), cardiovascular death (7.8% vs. 0.8%, p<0.001), and strokes (20.1% vs. 25.5%, p<0.001) than those without AF. Patients with AF still had an increased risk for all cause death (hazard ratio (HR) 3.12; 95% confidence interval (CI) 1.06–9.22, p=0.001), cardiovascular death (HR 4.62; 95% confidence interval (CI) 1.06–9.22, p=0.001).
The anticoagulant rivaroxaban, approved for reducing the risk of major bleeding (MB) in patients with non-valvular atrial fibrillation (NVAF), may increase the risk of major bleeding (MB). To evaluate the incidence of MB among NVAF patients taking rivaroxaban (NVAF), we conducted a registry study. MB was defined by a validated case-finding algorithm (Cunningham 2011), which uses a MB definition that is similar to the clinical trial definition. Data were collected on demographics, comorbidities, concomitant medications, MB management, and fatalities.

Results: During the first 2 years of the study, 970 of 39,052 rivaroxaban patients had at least one MB event, with an incidence rate of 2.89 [95% CI 2.71–3.08] per person-years. The most common MB site was gastrointestinal (GI) with 87.2% (348/401), followed by intracranial (IC) with 8.1% (32/390). In the MB group, 42.3% (169/390) were transferred to the ICU, and 51.5% (200/390) received a blood transfusion. The average (SD) length of hospitalization was 4.0 (3.4) days. Mean (SD) age of MB cases was 78.7 (7.9), versus 76.0 (9.9) years in the non-MB group. Patients represented 50.9% of the MB cases, versus 55.8% in the non-MB group. Comparing MB to non-MB patients, comorbidities were more frequent in the MB group, including atrial fibrillation (AF) without increasing bleeding complications in some studies. The previously reported that dabigatran increased the risk of both micro-thromboembolism and hemopericardium compared with warfarin, but controversy exists in the safety of non-vitamin-K-antagonist oral anticoagulants (NOAC) in the perioperative use of AF ablation.

Purpose: To investigate the incidence of asymptomatic cerebral micro-thromboembolism and hemopericardium treated with pericardiocentesis in AF ablation with perioperative use of rivaroxaban, apixaban, or warfarin.

Methods: This prospective randomized study was performed from March 2013 to December 2014. Patients taking NOAC on visiting our hospital were randomly assigned into two groups: rivaroxaban and apixaban. Warfarin was not changed in the patients taking warfarin. Rivaroxaban was given in the evening and continued, and apixaban was interrupted only on the morning of the procedure. Heparin was used to keep activated clotting time <300 sec. Asymptomatic cerebral micro-thromboembolism was evaluated by magnetic resonance imaging (MRI) at the day after procedure.

Conclusions: AF was common and associated with a substantial risk for strokes and mortality in patients with ApHCM. As AF was observed in most ApHCM patients with strokes, AF should be carefully managed in ApHCM.

P4065 | BEDSIDE
Evaluation of safety and efficacy of perioperative use of rivaroxaban and apixaban in catheter ablation for atrial fibrillation

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Background: Uninterrupted perioperative use of warfarin was reported to decrease cerebral thromboembolic events in catheter ablation for atrial fibrillation (AF) without increasing bleeding complications in some studies. We previously reported that dabigatran increased the risk of both micro-thromboembolism and hemopericardium compared with warfarin, but controversy exists in the safety of non-vitamin-K-antagonist oral anticoagulants (NOAC) in the perioperative use of AF ablation.

Purpose: To investigate the incidence of asymptomatic cerebral micro-thromboembolism and hemopericardium treated with pericardiocentesis in AF ablation with perioperative use of rivaroxaban, apixaban, or warfarin.

Methods: This prospective randomized study was performed from March 2013 to December 2014. Patients taking NOAC on visiting our hospital were randomly assigned into two groups: rivaroxaban and apixaban. Warfarin was not changed in the patients taking warfarin. Rivaroxaban was given in the evening and continued, and apixaban was interrupted only on the morning of the procedure. Heparin was used to keep activated clotting time <300 sec. Asymptomatic cerebral micro-thromboembolism was evaluated by magnetic resonance imaging (MRI) at the day after procedure.

Results: In 176 consecutive patients (101 paroxysmal, and 75 persistent AF), rivaroxaban was used in 55, apixaban in 51, and warfarin in 70. The average of total heparin dose was 11400 units in patients with warfarin, 19500 with rivaroxaban (P<0.001), and 14240 with apixaban (P=0.017). Two patients with paroxysmal AF (1 with apixaban, 1 with warfarin) were not underwent MRI due to the patients' condition. There were no symptomatic cerebral infarction, and asymptomatic cerebral micro-thromboembolism was detected in 32 (18.4%); 9 (16.4%) patients with rivaroxaban, 10 (20%, P=0.80) with apixaban, and 13 (18.8%, P=0.81) with warfarin. The hemopericardium was occurred in 5 (2.8%) patients; 2 with rivaroxaban, 1 with apixaban (P=1.0), and 2 with warfarin (P=1.0). In monovariate analysis, brachial-ankle pulse wave velocity (p<0.015), left ventricular mass estimated with echocardiography (p=0.004), concomitant with coronary angiography (CAG, p=0.005), hypertension (HT, p=0.003), and diabetes mellitus (p=0.025), were predictors of micro-thromboembolism in AF ablation. In multivariate analysis, HT (p=0.008, odds ratio 4.0) and CAG (p=0.015, odds ratio 5.0) were predictors.

Conclusions: The incidence of asymptomatic cerebral micro-thromboembolism and hemopericardium in AF ablation was similar between the perioperative use of rivaroxaban, apixaban, and warfarin.

P4066 | SPOTLIGHT
Major bleeding in a post-marketing assessment of 39,052 non-valvular atrial fibrillation patients on rivaroxaban

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Background: The anticoagulant rivaroxaban, approved for reducing the risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation (NVAF), may increase the risk of major bleeding (MB). To evaluate the incidence of MB among NVAF patients taking rivaroxaban, we conducted a registry study. MB was defined by a validated case-finding algorithm (Cunningham 2011), which uses a MB definition that is similar to the clinical trial definition. Data were collected on demographics, comorbidities, concomitant medications, MB management, and fatalities.

Results: During the first 2 years of the study, 970 of 39,052 rivaroxaban patients had at least one MB event, with an incidence rate of 2.89 [95% CI 2.71–3.08] per person-years. The most common MB site was gastrointestinal (GI) with 87.2% (348/401), followed by intracranial (IC) with 8.1% (32/390). In the MB group, 42.3% (169/390) were transferred to the ICU, and 51.5% (200/390) received a blood transfusion. The average (SD) length of hospitalization was 4.0 (3.4) days. Mean (SD) age of MB cases was 78.7 (7.9), versus 76.0 (9.9) years in the non-MB group. Patients represented 50.9% of the MB cases, versus 55.8% in the non-MB group. Comparing MB to non-MB patients, comorbidities were more frequent in the MB group, including atrial fibrillation (AF) without increasing bleeding complications in some studies. We previously reported that dabigatran increased the risk of both micro-thromboembolism and hemopericardium compared with warfarin, but controversy exists in the safety of non-vitamin-K-antagonist oral anticoagulants (NOAC) in the perioperative use of AF ablation.

Purpose: To investigate the incidence of asymptomatic cerebral micro-thromboembolism and hemopericardium treated with pericardiocentesis in AF ablation with perioperative use of rivaroxaban, apixaban, or warfarin.

Methods: This prospective randomized study was performed from March 2013 to December 2014. Patients taking NOAC on visiting our hospital were randomly assigned into two groups: rivaroxaban and apixaban. Warfarin was not changed in the patients taking warfarin. Rivaroxaban was given in the evening and continued, and apixaban was interrupted only on the morning of the procedure. Heparin was used to keep activated clotting time <300 sec. Asymptomatic cerebral micro-thromboembolism was evaluated by magnetic resonance imaging (MRI) at the day after procedure.

Results: In 176 consecutive patients (101 paroxysmal, and 75 persistent AF), rivaroxaban was used in 55, apixaban in 51, and warfarin in 70. The average of total heparin dose was 11400 units in patients with warfarin, 19500 with rivaroxaban (P<0.001), and 14240 with apixaban (P=0.017). Two patients with paroxysmal AF (1 with apixaban, 1 with warfarin) were not underwent MRI due to the patients' condition. There were no symptomatic cerebral infarction, and asymptomatic cerebral micro-thromboembolism was detected in 32 (18.4%); 9 (16.4%) patients with rivaroxaban, 10 (20%, P=0.80) with apixaban, and 13 (18.8%, P=0.81) with warfarin. The hemopericardium was occurred in 5 (2.8%) patients; 2 with rivaroxaban, 1 with apixaban (P=1.0), and 2 with warfarin (P=1.0). In monovariate analyze, brachial-ankle pulse wave velocity (p<0.015), left ventricular mass estimated with echocardiography (p=0.004), concomitant with coronary angiography (CAG, p=0.005), hypertension (HT, p=0.003), and diabetes mellitus (p=0.025), were predictors of micro-thromboembolism in AF ablation. In multivariate analysis, HT (p=0.008, odds ratio 4.0) and CAG (p=0.015, odds ratio 5.0) were predictors.

Conclusions: The incidence of asymptomatic cerebral micro-thromboembolism and hemopericardium in AF ablation was similar between the perioperative use of rivaroxaban, apixaban, and warfarin.
of false activations of the cardiac catheterization laboratory (CCL) however. Prehospital diagnosis can be made in the field by onsite paramedics or by a physician via electronic ECG transmission. To date, no study has directly compared the accuracy of these 2 modes of diagnosis. In a regional primary PCI programme served by a sole ambulance provider, ECG transmission capability in only selected ambulances (determined geographically) allowed comparison of these 2 diagnostic modes.

Purpose: The purpose of this study was to determine whether prehospital ECG transmission in STEMI was associated with lower false rates of positive CCL activation than in-patient CCL activation. Methods: This was a retrospective observational study. All “Code STEMI’s” admitted directly from the field to the CCL over a 3 year period were included and divided into two groups depending on mode of prehospital diagnosis. Patients who died before reaching the CCL were excluded. A false activation was defined as lack of a culprit lesion by coronary angiography or lack of ECG or biomarker evidence of STEMI. ECG findings in false activations were compared between the two groups.

Results: Of 1426 “Code STEMI’s” over a 3 year period, 362 (48.4%) were transferred directly from the field to the CCL, 214 of these (59.1%) by ambulance and 148 (40.9%) by helicopter. In total, 128 (35.4%) had prior ECG transmission, 108 (50.5%) of ambulance transfers and 20 (13.5%) of helicopter transfers. Overall, 71 were false positive activations (19.6%); 14 (10.9%) of those with transmitted ECGs (p=0.002). False activations in the group with transmitted ECGs included 1 patient (7.1%) with a normal ECG versus 18 patients (31.6%) in those diagnosed by paramedics (p=0.0005).

Conclusion: Prehospital STEMI diagnosis by ECG transmission was associated with significantly lower rates of false CCL activation compared with paramedic ECG interpretation. False activations in patients with normal ECGs occurred significantly more in the paramedic activated group.

P4069 | BEDSIDE
Pre-hospital trans-satellite wireless 12 lead ECG transmission from the ambulance to primary PCI centre
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Introduction: In Primary PCI, time is recognized as a crucial factor. To speed up diagnosis and timely intervention, we installed a “Nationwide Trans-Satellite Wireless ECG” Transfer (W-ECG) network. This enables swift Pre-hospital identification of STEMI and transfer of patients directly to the PCIPI facility in Heart Hospital (HH), thus preventing the extra step of transfer to other non-Primary PCI facilities first (OH). It also alerts the Primary PCI teams to be ready even before patient arrives, and avoids delays in Emergency rooms.

Methods: Patients who had Primary PCI for STEMI, 605 (55%) were transferred directly to the Heart Hospital (HH). These were compared with 488 patients (45%) who went to Other Hospitals first (OH) and subsequently transferred to the HH. We compared the two with regard to achieving the optimal Door to Balloon Time (DBT) goal of 90 min for those transferred to PCIPI facility (HH), versus 120 min for those going to OH, as per guidelines.

Results: Age was similar 49 vs 50 years and there was no Ethnic difference (73% Asians and 25% Arabs) in both groups. The DBT was 56±26 min for HH group vs 117±75 min in OH group (p<0.001). Furthermore, while 89% achieved <90 min in HH group, only 64% achieved <120 min in OH group, p<0.01. Out of Hospital Delay (OHD i.e delay from symptoms until arrival to hospital) was also different. Patients who had W-ECG arrived faster to HH and thus had shorter OHD (279±375 min) than those using own transport to HH (309±334 min). The combined OHD+DBT (Total delay from symptoms to Balloon) was also shorter in HH (W-ECG) group (337 min) than similar group going to OH (426 min), thus saving 89 vital minutes in the whole process from symptoms to balloon. Initial TIMI-0 flow was similar (HH 52% vs OH 46%), but TIMI-III flow was achieved slightly more often in HH (95%) than in OH group (92%), p<NS. Peak Troponin (ng/ml) was higher in OH group (7934) vs (7669) in HH, p<0.05. While Ejection fraction was similar (HH 46.7% vs OH 46.2%), there was a trend towards higher in-hospital mortality in OH group (3%) vs (2.8%) in HH, p=NS. Finally, length of stay was also longer in OH (3.9±3.5) compared to 3.4±3.1 in HH group, p<0.005.

Conclusions: Pre-hospital Trans-satellite wireless ECG from the ambulance to Primary PCI facility results in significantly shorter DBT, total symptoms to balloon time, and length of stay, as well lower peak Troponin and a trend towards lower in-hospital mortality. More efforts are required to make the public aware of cardiac symptoms and to report early, thus reducing the out of hospital delay.

P4070 | BEDSIDE
The importance of a qualified pre-hospital ECG and subsequent triage of patients with STEMI to the catheterization laboratory to minimize the door-to-balloon time
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Background: Timely reperfusion therapy is recommended for patients with ST-segment elevation myocardial infarction (STEMI), and door-to-balloon delay has been proposed as a performance measure.

Purpose: The first-medical-contact-(FMC)-trial of a city-wide registry of 20 hospitals with primary PCI facilities investigated the reliability of the ECG diagnosis by the emergency physicians.

Methods: Retrospective assessment of parameters of first medical care of all 1038 patients with an acute coronary syndrome, who were enrolled in the year 2012 by the EMS and retrospective evaluation of the pre-hospital and hospital ECG’s in adherence with the guidelines of the European Society of Cardiology by three experienced cardiologists. Merging and analysis of the data of the FMC-trial and the registry-dataset were performed.

Results: From a total of 1038 patients with a pre-hospital ECG, 756 had an unambiguous ST-elevation, 282 patients did not show any ST-segment deviation. In 26% of a total of 756 Patienten with ST-segment elevation the EMS-physicians failed to diagnose a STEMI (see figure), 17% of the patients were discharged with the diagnosis NSTEMI. The medical care of 756 patients with a definite STEMI diagnosis was different from those with ambiguous findings in the pre-hospital ECG assessed by the physician in the field. An unambiguous “STEMI diagnosis led to shorter door-to-balloon-times (53 min, median) in comparison to patients with ambiguous readings (142 mm, median)”.

Acknowledgement/Funding: None
in identifying low risk patients prior to presentation and might help in optimizing logistics and cost-effectiveness, as addressed in the next phases of the trial.

P4072 | BEDSIDE
Increase in availability of registered AEDs is associated with higher rate of bystander defibrillation in public locations but not in residential areas - a nationwide study

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Introduction: Public automated external defibrillators (AEDs) allow bystanders to defibrillate out-of-hospital cardiac arrest (OHCA) patients prior to arrival of emergency medical services (EMS) and improve survival markedly. We examined bystander use of AEDs according to public or private home location of arrest, before and after the implementation of a nationwide AED registry besides uncontrolled AED dissemination.

Methods: We identified first-time OHCA cases from 2001-2012 and included 25,287 non-EMS witnessed arrests with known location of arrest (private/public) and whether the patient was defibrillated prior to EMS arrival.

Results: In total, 18,818 (74.4%) and 6,469 (25.6%) patients had an OHCA in a private or public location, respectively (P<0.001). The number of registered AEDs increased from 141 in 2007 to 7,800 in 2012 and 17.5% of all AEDs were available near residential areas. As the number of AEDs increased, the rate of patients defibrillated by bystanders prior to EMS arrival in public locations, increased from 1.4% in 2001 to 11.8% in 2012 (Figure). The rate of patients defibrillated in private locations remained unchanged from 2001 to 2012. Thirty-day survival increased from 6.0% [95% CI 0.3–27.0] to 55.0% [95% CI 46.4–63.4], and 0.0% [95% CI 0.0–13.3] to 26.2% [95% CI 15.3–41.1], for patients defibrillated in public and private locations, respectively.

Conclusions: Along with wider dissemination of AEDs, there was a marked increase in patients defibrillated prior to EMS arrival in public locations, but not in private home locations. Bystander defibrillation was associated with markedly improved survival irrespective of location of arrest. These results underscore the need for improving bystander defibrillation in residential areas.

P4074 | BEDSIDE
GDF-15 is a predictor of cardiovascular events in patients presenting with suspicion of acute coronary syndrome

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Background: The appropriate treatment for patients presenting with acute chest pain is possible acute coronary syndrome (ACS) is based on timely diagnosis and proper risk stratification aided by biomarkers. Growth-differentiation factor-15 (GDF-15) is a member of the transforming growth factor β family proteins induced in the heart after ischemia and reperfusion injury. We aimed at evaluating the predictive value of GDF-15 in an unscreened "real world" cohort of patients presenting with acute chest pain.

Methods: Consecutive patients presenting with acute chest pain were enrolled at three chest pain units in Germany. Cardiovascular events were assessed during a follow-up period of 6 months. As combined primary endpoint death or myocardial infarction (MI) was considered. GDF-15 was measured in blood drawn at admission.

Results: From the 1818 patients (mi=1208/610, 413 (22.7%) had an acute MI; Patients with M1 had significantly higher GDF-15 compared with non-ACS patients (967.1pg/mL vs. 692.2 pg/L, P<0.001). 63 patients reached the primary endpoint. Cox regression analysis revealed a 2.1-fold risk for death or MI (95% CI 1.67–2.65, p<0.001) for an increment of the log transformed GDF-15 concentration by one standard deviation after adjustment for age and gender and of 1.57-fold risk (95% CI: 1.13–2.19, p<0.008) if adjusted for the GRACE score risk variables.
compared to a 1.94-fold (1.45–2.60, p < 0.001) and 1.45-fold (95% CI: 1.06–1.98, p = 0.021) for BNP.

**Conclusion:** GDF-15 is a significant predictors of future cardiovascular events in patients presenting with acute chest pain. GDF-15 levels correlate with the severity of CAD and can risk stratify patients in need for coronary revascularisation, possibly facilitating the choice of treatment in those patients.

**INFORMATION TECHNOLOGY APPLICATIONS IN CARDIOLOGY**

**P4076 | BEDSIDE**

Monitoring of day by day fluctuations of different cardiac resynchronization therapy (CRT) device parameters allows to predict device interventions


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**Aim:** To assess the value of day by day variations of different cardiac resynchronization therapy (CRT) device parameters in early prediction of both adequate (AT) and inadequate (IAT) therapies.

**Methods:** A single-center, prospective registry encompassed 305 consecutive heart failure (HF) patients (pts) who were implanted with CRT-D devices. Every pt was monitored on a daily basis via remote monitoring for the median follow-up period (FU) of 20.5 months. Every transmission was screened for potential therapy triggers such as: atrial burden, mean and max. heart rate during atrial fibrillation, mean ventricular heart rate, mean ventricular heart rate at rest, patient activity, mean PVC/h and CRT pacing percentage (CRT%). All pts were assessed to one out of three groups, depending on the presence and/or adequacy of delivered therapy at the end of FU: adequate therapy (ATG), inadequate therapy (IATG) and control group (no therapies during FU).

**Results:** During the FU at least one AT and IAT occurred in 21.3 and 12.8% of pts and the mean time to the first AT and IAT was 328 (79–982) and 212 (58–491) days respectively. Triggers for both AT and IAT were depicted in Table 1. The independent risk factor for AT was mean ventricular heart rate at rest (HR 1.07, 95% CI 1.05–1.09, p < 0.001), while in IAT it was max. heart rate during atrial fibrillation (HR 1.03, 95% CI 1.02–1.04, p = 0.004).

**Table 1. Uni- and Multivariate models for age in predicting all AF identification by hand-carry ECG device**

<table>
<thead>
<tr>
<th>Odds ratio</th>
<th>95% CI</th>
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<tr>
<td>Univariate model</td>
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<tr>
<td>Model 1</td>
<td>1.72*</td>
<td>1.36 to 2.17</td>
<td>1.42*</td>
<td>1.09 to 1.86</td>
<td>2.59*</td>
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</tr>
<tr>
<td>Model 1</td>
<td>1.73*</td>
<td>1.37 to 2.19</td>
<td>1.46*</td>
<td>1.11 to 1.91</td>
<td>2.56*</td>
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<tr>
<td>Model 2</td>
<td>1.61*</td>
<td>1.25 to 2.06</td>
<td>1.39*</td>
<td>1.03 to 1.86</td>
<td>2.58*</td>
</tr>
<tr>
<td>Model 3</td>
<td>1.39*</td>
<td>1.31 to 2.14</td>
<td>1.39*</td>
<td>1.04 to 1.87</td>
<td>2.72*</td>
</tr>
</tbody>
</table>

**Conclusion:** Hand-carry ECG device shows clinical feasibility with high rate for AF detection, with a similar trend toward higher prevalence with aging from different settings. These data suggested that portable ECG device via remote care system may aid in clinical diagnosis of AF, and may facilitate therapeutic interventions or patient referral.

**P4077 | BEDSIDE**

Value of the frontal plane QRS-t angle for diagnosis and prognosis in patients with symptoms suggestive of acute myocardial infarction


**Introduction:** Cardiac ischemia results in changes of ventricular repolarization. The angle between the vectors of the QRS complex and the QT wave in the 12-lead ECG can be used as a measure for an abnormal depolarization–repolarization relationship. It's value for diagnosis and prognosis in patients with symptoms suggestive of acute myocardial infarction (AMI) are unknown.

**Methods:** We prospectively enrolled 1171 consecutive patients with symptoms suggestive of AMI. The QRS-T angle was automatically calculated from a digital 12-lead ECG's recorded at presentation to the ED. Patients were followed up for all-cause mortality and cardiovascular disease (CVD) for 3 years.

**Results:** AMI was the final diagnosis in 19% of patients, with 3% having STEMI and 16% NSTEMI. Median QRS-T angle was significantly greater in patients with AMI compared to those without (55° [IQR 23–106] vs. 24° [IQR 11–46], p < 0.001). The area under the ROC curve for the diagnosis of AMI was 0.68. Overall, 3-year survival rate was 91%. A greater QRS-T angle was significantly associated with a worse prognosis after 3 years (Survival rates 95%, 88%, 76% for patients with a QRS-T angle > 50°, 50–100° and > 100°; p < 0.001). In multivariable analysis, the prognostic value of the QRS-T angle was independent of other important predictors such as age, troponin levels or the QRS-duration.

**P4078 | BEDSIDE**

The Utilization and Clinical Feasibility of 24-Hour Hand-Carry Remote ECG Recording Device in Cardiac Arrhythmias and Atrial Fibrillation: A Pilot Study


**Background:** Remote cardiac rhythm monitor and diagnosis has been well incorporated in Telehealth service model. The prevalence and incidence of abnormal ventricular beats by utilizing symptom-driven portable remote ECG device remains less well explored.

**Methods:** We consecutively studied 339 study participants, including 192 enrolled via symptom-driven protocol from out-patient clinics; 147 participated heart rhythm screening program. All participants are open for 24-hours data transfer using hand-carry portable ECG device (DailyCare Biomedical Inc) with automatic ECG wavelet data extraction (InstantCheck ver 4.0).

**Results:** Among a total of 1,152 data transferred (98.4% successful rate), we noticed 32.5% study subjects had evidence of cardiac arrhythmias, with AF (either permanent or paroxysmal) comprised 50.9% among them. Subjects with history of heart failure (OR: 3.37, 95% CI: 1.69 to 6.74), diabetes (OR: 3.03, 95% CI: 1.12 to 7.92), history of cardiovascular disease (OR: 3.71, 95% CI: 2.05 to 6.7) had higher AF risk. Both populations showed age-related increase of atrial fibrillation (AF), even in multi-variate models (OR: 1.72, 95% CI: 1.31 to 2.24 per decade, Table 1).

**Conclusions:** In patients with symptoms suggestive of AMI, the QRS-T angle automatically derived from the 12-lead ECG was elevated in patients with AMI. It significantly predicted all-cause mortality during 3 years of follow-up independently of age and troponin levels and therefore has the potential to improve risk stratification in these patients.

**P4078 | BEDSIDE**

Diagnostic accuracy of 12 lead ECG Q-waves as a marker of myocardial scar and as a predictor of infarcted artery: validation with CMR

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**Background:** Traditionally, the presence of Q-waves on 12 lead ECG is considered a marker of a large and/or transmural myocardial infarction (MI). Late gadolinium enhancement (LGE) cardiovascular magnetic resonance (CMR) accurately identifies myocardial infarction and has become the gold standard for the assessment of myocardial viability. However, CMR is not universally available and clinicians often have to make assumptions on myocardial scarning based solely on the 12 lead ECG.

**Aim:** To determine the diagnostic accuracy of Q-waves on 12 lead ECG to identify myocardial scarring using CMR as gold standard.
Methods: Data was collected on consecutive patients referred for a stress CMR with suspected ischaemic heart disease (April 2013 to Mar 2014). Exclusioncriteria: non-ischaemic heart disease that may cause Q-wave. Pathological Q-waves: deflection > 25% of the subsequent R wave, or being > 40ms in width and > 2mm in amplitude in > 1 corresponding lead. Q-waves in any 2 or more precordial leads from V1-V4 reflected LAD territory. Transmural infarction was defined as > 50% LGE.

Results: 498 patients were included (mean age of 64±12 years, 71% males). 290 patients demonstrated MI, 157 were transmural and 133 sub-endocardial based on CMR LGE. 126 patients had pathological Q-waves on 12 lead ECG. The overall diagnostic accuracy of Q-wave as a marker of transmural MI was 66% and the diagnostic accuracy of Q waves as a predictor of previous MI (composite of sub-endocardial and transmural) was only 55%. Table 1. In patients with pathological Q-waves, 40% had LAD territory Q waves, 55% non-LAD and 5% a combination of both with LAD Q waves, 68% demonstrated LAD territory LGE and in non-LAD Q waves, 67% demonstrated a non-LAD territory infarct by LGE.

Conclusion: Our study demonstrates that the presence of pathological Q-waves on 12 lead ECG is not only a poor marker of myocardial scarification, but also a poor predictor of viability when compared to CMR. Our study also demonstrates the limitation of Q-wave in identifying the affected coronary artery territory. Clinicians need to be aware of the limitations of ECG Q-waves during their clinical decision-making process.

P4079 | BESIDE
Assessment of deceleration capacity from short-term recordings predicts mortality after myocardial infarction
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Deceleration capacity (DC) of heart rate is a strong predictor of mortality after MI. DC is a measure of deceleration-related oscillations of heart rate and is usually assessed from 24-hour Holter recordings. As yet, there is no data on the predictive power of DC assessed from short-term recordings.

Background: Deceleration capacity (DC) of heart rate is a strong predictor of mortality after MI. DC is a measure of deceleration-related oscillations of heart rate and is usually assessed from 24-hour Holter recordings. As yet, there is no data on the predictive power of DC assessed from short-term recordings.

Methods: We included 908 survivors of acute MI in sinus rhythm aged <80 years. All patients underwent a 30-min ECG recording (1.600 Hz) in Frank leads configuration within the 2nd after MI. The primary endpoint was all-cause mortality.

DC was calculated using previously established technologies. In addition to DC following risk predictors were considered: reduced LVEF, the Global Registry of Acute Coronary Events (GRACE) score, presence of diabetes mellitus, elevated mean heart rate (HR), impaired standard deviation of all normal-to-normal RR-intervals (SDNN), and increased QT variability index (QTVI). Established cut-off values were used for dichotomization: <2.5 ms for DC, <35% for LVEF, > -0.47 for HR, > 500 ms for standard deviation, >70 ms for SDNN, and >120 for the GRACE score. Uni- and multivariable Cox regression analyses were used to test the association of DC with mortality.

Results: 69 patients died within the first 5 years of follow-up. Short-term DC was associated with higher mortality in survivors compared with survivors (3.06 vs. 2.59, p < 0.001). DC >2.5 ms was a strong and independent predictor of 5-year total mortality after adjustment for various predictors including LVEF, GRACE score, mean HR, SDNN and QTVI (Table).

Conclusion: DC assessed from short-term recordings is a strong and independent predictor of 5-year mortality after myocardial infarction.

P4080 | BESIDE
How low can we go? Performing EP-Procedures at a low radiation dose level

Introduction: Fluoroscopy is the standard imaging modality for EP-Procedures. Since fluoroscopic systems are technically optimized for high-resolution angiography, there may be potential for dose reduction when these systems are used for EP interventions not requiring detailed resolution. Aim of this study was to test if a new low dose X-Ray program with 8nGy/pulse could provide adequate imaging quality in EP procedures. Therefore it was compared to the current low dose program using 23nGy/pulse.

Material and methods: The new program (8nGy/pulse) was installed on an AX-ICM Artis biplane system in August 2014. 214 patients (Group A) treated with the standard program from 08/2014 to 11/2014 were compared to 195 patients (Group B) treated with the 23 nGy/pulse program from 08/2013 to 11/2013. To avoid inter-operator effects the interventions performed by each of the three involved physicians in Group A were compared to the corresponding procedures in Group B. Furthermore we divided our patients and between five procedures (Atrial fibrillation (Afib), atrial flutter (Aflutter), atroventricular nodal reentrant tachycardia (AVNRT), atrioventricular reentrant tachycardia (AVRT), premature ventricular contractions (PVC)) because different fluoroscopy times yield different dose area products (DAP). In both groups physician’s directive was to choose a higher x-ray dose program if better image quality could provide necessary information. This happened in one of 409 patients due to the patients BMI (40).

Results: A significant DAP reduction of 60% could be achieved using the 8 nGy/pulse program (9.06 Gy cm² (in Group B) vs. 3.66 Gy cm² (in Group A), p < 0.001, student-t). The two group’s BMI (27.6±5.4 (B) vs 27.9±4.7 (A); p = 0.25), age (56.0±18.4 (B) vs 57.1±17.3 (A); p = 0.30) and fluoroscopy time (7.5±13.0 min (B) vs 17.3±13.3 min (A); p=0.43) were insignificantly different. The average procedure duration of Afib (160±42 min (B) vs 156±35 min (A); p=0.21), Aflutter (124±25 min (B) vs 70±15 min (A); p = 0.46) and PVC (135±40 min (B) vs 96±32 min (A); p=0.42) and 124±24 min (B) vs 102±52 min (A); p=0.1) was not affected by the dose reduction. No difference between acute success rates (98% (210/214) (A) vs 97% (195/201) (B); p = 0.38) and acceptance rate (82% (174/210) (A) vs 86% (173/201) (B); p = 0.63) was statistically significant.

Conclusions: The use of low dose pulsed fluoroscopy (8 nGy/pulse) can yield a significant reduction (60%; p < 0.001) in radiation exposure. Neither procedure success, nor procedure duration was significantly affected (p = 0.05).

P4081 | BESIDE
Deriving actionable clinical knowledge from large retrospective set of cardiac echo reports: evaluation of machine learning-based discovery of rules for detecting conflicts between report statements
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Background: Cardiac echo final reports created through point-and-click selection of pre-determined observational and diagnostic statements (“finding codes”) may contain conflicting statements (e.g., “No tricuspid regurgitation” and “Severe regurgitation”) that adversely affect report quality, credibility of the echo interpretation services and potentially (in)correct patient decisions. A rule-based tool was developed that detects conflicts between finding codes (FCs) in a report and suggests corrections. However, manual rules creation process is knowledge and labor intensive and requires familiarity with the institution’s local FC vocabulary, which is not available. Therefore, automatic rule generation was expected to enable a domain expert to review the conflict rules proposed by RDE before adoption into the clinical workflow.

Purpose: Evaluate if RDE can serve to discover conflict rules based on echo reports from a test hospital with unique localized FC vocabulary.

Methods: 29,270 reports comprising 815 unique FCs were obtained from the test hospital. RDE was applied to each potential conflict rule and certainty values (“CV”) were collected from ranging from 0 (unlikely conflict) to 1 (likely). A random sample was obtained of 223 proposed conflict rules with CV > 0. An attending cardiologist reviewed each rule, accepting it for use in the workflow or not. Acceptance rate is measured, defined as percentage of rules accepted.

Outcomes: Of 331,705 potential conflict rules, 862 had CV > 0.2 and 431 CV > 0.4. A random sample of 123 conflict rules (55% (68/123) with CV > 0.4). Acceptance rate of rules with CV > 0.4 was 59% (67/114), 95% CI was 50 to 68%. Rules with CV < 0.2 and CV < 0.4 were deemed acceptable 46% (176/384). Certainty value was correlated with acceptance rate.

Conclusion: RDE successfully proposed conflict rules automatically derived from echo reports written in the test hospital’s unique FC vocabulary. Correlation with acceptance rate suggests that proposed rules were reviewed in decreasing order of certainty value, so that the reviewer can stop when density of accepted rules is found too low. Clinical knowledge can be derived through automated analysis of retrospective data and can be leveraged to support quality assurance during echo reporting.
**EXTRACELLULAR MATRIX, REMODELLING AND INFLAMMATION**

**P0402 | BENCH**

**Title:** Glycoproteomics analysis of cardiac extracellular matrix reveals the presence of decorin fragments with anti-myostatin and anti-fibrotic activity


**Background:** Using proteomics, we characterize the glycoproteins of human hearts to study extracellular matrix (ECM) remodelling in the context of atrial fibrillation and cardiac hypertrophy.

**Methods:** Left and right matched atrial tissues were obtained from patients during cardiopulmonary bypass. ECM proteins were enriched using a sequential extraction procedure. The glycoprotein-enriched fraction, the flow-through and the input were analyzed by mass spectrometry (MS).

**Results:** Among ECM glycoproteins, lumican, fibrulin-2, latent TGF-β1-binding protein 4 were differentially expressed in left and right atria. Surprisingly, one glycoprotein, decorin, a member of the small leucine-rich proteoglycans, was consistently identified in the non-glycosylated, flow-through fraction. Decorin is glycosylated at its C-terminus, but only N-terminal peptides were detected in the flow-through, suggesting that decorin might be fragmented. Using MS, we identified 18 different fragmentation sites for decorin, whereas no fragmentation was observed for the closely related biglycan. The proteomic findings were validated by elevated myocardial levels of glutamine, aspartate and succinate. A clear magnetic resonance spectroscopy, cardiac metabolism was altered as evidenced by increased myocardial levels of glutamine, aspartate and succinate.

**Conclusion:** When cardiomyocytes were treated with myostatin, synthetic peptides matching the myostatin-binding region of decorin were sufficient to reactivate a hyperpolarized response stimulated with isoproterenol and phenylephrine. The same peptide inhibited downstream myostatin signalling pathways in a dose-dependent manner. In decorin−/− mice, myostatin expression was decreased. Based on nuclear magnetic resonance spectroscopy, cardiac metabolism was altered in a way consistent with increased myocardial glycolysis and glutaminolysis.

**P0403 | BENCH**

**Title:** Inhibition of Myofibroblast Differentiation by FOXO3a - Implications for acute myocardial infarction and cardiac Remodelling

**Authors:** L. Holzhauser, A. Jenke, M. Grueger, K. Savvatis, R. Schur, U. Landmesser, C. Sukr, Albert Einstein College of Medicine, Internal Medicine, New York, United States of America; Charter University Medicine, Campus Benjamin Franklin, Department of Cardiology and Pulmonology, Berlin, Germany

**Background:** Transdifferentiation of cardiac fibroblasts into myofibroblasts regulated by TGFβ/SMAD3 signaling is a major mechanism of scar formation and adverse remodelling following myocardial infarction. FOXO3a has recently been shown to inhibit cardiac hypertrophy by different stressors. We hypothesized that the transcription factor FOXO3a, a key regulator of cell differentiation, cycle and stress, might inhibit matricellular remodelling following myocardial infarction by regulating transdifferentiation of fibroblasts into myofibroblasts.

**Methods:** Acute myocardial infarction was induced in FOXO3a−/− and WT mice (FVB background) by permanent LAD ligation. We identified a cleavage site at position S495-L50 of decorin that produces peptides containing a myostatin-binding domain. Myostatin is involved in the regulation of cardiac fibrosis and metabolism. When cardiomyocytes were treated with myostatin, synthetic peptides matching the myostatin-binding region of decorin were sufficient to reactivate a hyperpolarized response stimulated with isoproterenol and phenylephrine. The same peptide inhibited downstream myostatin signalling pathways in a dose-dependent manner. In decorin−/− mice, myostatin expression was decreased. Based on nuclear magnetic resonance spectroscopy, cardiac metabolism was altered in a way consistent with increased myocardial glycolysis and glutaminolysis.

**Conclusion:** This is the first proteomics study to characterize the ECM in human hearts. The presence of decorin cleavage products may regulate the local bioavailability of anti-hypertrophic and pro-fibrotic growth factors and influence ECM remodelling in health and disease.

**P0405 | BENCH**

**Title:** Role of Rac1 GTPase for the mineralocorticoid receptor mediated structural remodelling in atrial fibrillation

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**Background:** This study aimed to investigate the molecular mechanisms of pro-fibrotic remodelling. Human left atrial myocardium during atrial fibrillation is characterized by higher energy requirements, we examined the effect of Rac1 GTPase activity and increased signalling of the mineralocorticoid receptor (MR).

**Methods and results:** Transgenic mice with cardiac specific overexpression of constitutively active V12Rac1 (RacET) develop an age-dependent phenotype characterized by atrial dilatation, atrial fibrosis and atrial fibrillation. Expression of MR was shown to inhibit cardiac hypertrophy by different stressors. We hypothesized that FOXO3a−/− mice showed significant higher protein expression of Col1A1 in (p < 0.01) compared to WT. These data were confirmed in samples of human left atrial myocardium from patients with atrial fibrillation and sinus rhythm showing that 11β-HSD2 correlated with Rac1 activity (r = 0.7169, p < 0.05). In RacET mice cence staining for ASMA protein was significantly attenuated following FOXO3a gene transfer in cardiac fibroblasts. Mechanistically, immunoprecipitation showed direct interaction of FOXO3a with SMAD3a that was enhanced following activation of the transcription factor leading to diminished SMAD3 downstream gene expression.

**Conclusion:** Our results identify FOXO3a as a direct inhibitor of TGFβ-regulated matrix remodeling via FOXO3a-SMAD3 interaction. FOXO3a collectively regulates hypertrophy as well as fibrosis and scar formation following myocardial infarction and thus targeting the FOXO3a-SMAD3 axis might be of therapeutic interest.
were numerous inflammatory cells around the abdominal aorta in IL-1Ra−/− mice, abdominal aortic width in IL-1Ra−/− mice significantly increased compared with WT mice (P<0.05). The translocation was prevented by the treatment with Rac1 inhibitor NSC-23766 (0.298±0.334, p<0.05 vs. abdominal aorta) as well as by spironolactone (0.239±0.266, p<0.01 vs. abdominal aorta). NSC-23766 prevented the aldosterone induced CTGF up-regulation in cardiac fibroblasts (183±55% vs. 39±5%, p<0.01). CTGF increased fibronectin expression in cardiac fibroblasts (368±111%, p<0.01). Aldosterone and angiotensin II exerted an additive effect on CTGF expression (aldosterone, 141±32%, p<0.05 vs. control; aldosterone+angiotensin II, 175±67%, p<0.001 vs. control). Telmisartan completely prevented the aldosterone effect on CTGF expression (97±11%, p<0.05 vs. aldosterone).

Conclusion: Rac1 increases 11β-HSD2 expression enhancing MR fibrotic signalling, and regulates nuclear translocation of MR and CTGF expression. Therefore, Rac1 may represent a target for the prevention of fibrotic atrial and ventricular remodelling.

P4086 | BENCH A CD31-derived peptide favors M2 macrophage polarization and arterial repair following Angiotension II-induced disease


The loss of the trans-homophilic homoeostatic receptor CD31 (PECAM-1), which is constitutively expressed by the cells at the blood- vessel interface, has previously been associated with protection from the occurrence of atherosclerotic complications, such as abdominal aortic aneurysm/disssection, in patients and experimental mouse models. Using a synthetic CD31 agonist peptide that is able to sustain the CD31 inhibitory signaling, we analyzed its therapeutic potential in a mouse model of accelerated atherosclerosis and aortic dissection/aneurysm formation. Twenty-eight week-old male apolipoprotein E knockout mice were subjected to subcutaneous administration with either the CD31 peptide (2.5mg/nl) or the vehicle (n=10) started 15 days later, after the occurrence of aortic dissection, and continued until day 28. The aortic wall of CD31-treated mice was significantly richer in collagen (picrossirius red staining). Furthermore, the intramural haemorrhage was consistently reduced in size and infiltrated with M2-like (arginase I+) rather than M1-like (iNOS+) macrophages (CD68+). Indeed, in vitro studies suggested that CD31 signaling favours M2 rather than M1 macrophage polarization based on the analysis of iNOS, IL-6 (M1) and Arginase I, IL-10, (M2) in bone marrow-derived macrophages polarized with either LPS+IFNg (M1) or IL-4 (M2) in the presence or not of the CD31 peptide. We conclude that the administration of the CD31 peptide can attenuate the progression of atherosclerosis-associated arterial wall injury through its pro-M2 macrophage polarization potential, likely involved in the acceleration of arterial tissue repair processes.

P4089 | BEDSIDE The synergetic effect of -174G/C polymorphism on interleukin-6 gene promoter with tobacco smoking on endothelial function, inflammatory and thrombotic processes in coronary artery disease patients

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Background: Smoking is a well known risk factor for coronary artery disease (CAD). Moreover, controversial data suggest that the -174 G/C polymorphism on interleukin-6 gene promoter (rs1800795) may represent an early marker of inflammatory activation, closely related to the initiation and evolution of atherosclerosis.

Purpose: In lack of relevant appropriate data the purpose of this study was to detect a possible synergistic effect of smoking with this polymorphism on several aspects of inflammation and thrombosis, endothelial function as well as on the incidence of CAD.

Methods: 646 subjects (361 non-smokers) submitted to our department for suspected angina, were subjected to appropriate genotyping. Endothelial function was assessed by flow mediated dilation (FMD) of the brachial artery. IL-6 (pg/ml), Tumor Necrosis Factor-α (TNF-α) (pg/ml), high sensitivity CRP (hsCRP) (mg/l) and D-dimers (μg/l) were measured with appropriate methods. The diagnosis of CAD was confirmed angiographically.

Results: An increased incidence of CAD was found among the carriers of the allele C compared to G homozygotes, (OR: 1.59, CI: 1.26–2.93, p=0.032) in smokers, while a decreased incidence was observed in non smokers (OR: 0.42, CI: 0.26–0.68, p<0.001), after adjustment for CAD risk factors. The C allele carriers, compared to G homozygotes, had significantly higher serum levels of IL-6 (3.09±1.4 vs 1.3±0.7), TNF-α (5.3±2.4 vs 2.5±1.8) and hsCRP (2.09±0.9 vs 1.05±0.69) (p<0.01 for all) in smokers as well as in non smokers (IL-6: 2.62±1.2 vs 1.84±0.89, TNF-α: 3.57±1.67 vs 4.43±2.1, hsCRP: 1.84±0.82 vs 1.62±0.77, p<0.01 for all). Importantly, the C allele, compared to G homozygotes, enhanced the expression of fibrinogen (488.3±115.5 vs 318.5±61.1 p<0.001) and D-dimers (513±313.4 vs 355±218.4, p=0.025) in smokers, while it down-regulated the expression of fibrinogen in non-smokers (351.9±84.5 vs 479.4±126.4, p=0.001), importantly, the C allele carriers compared to G homozygotes significantly increased endothelial function in the smoking group (3.93±2.7 vs 5.2±3.3%, p=0.003), while no effect was observed among non-smokers (4.8±2.9% vs 5.0±2.6%, p=0.64).

Conclusions: The C allele of rs1800795 exerts a synergistic effect on smoking resulting to a significantly increased risk for CAD. This action is mediated by the role of interleukin-6 gene promoter, inflammation and thrombotic mechanisms as well as by the impairment of endothelial function.

AORTIC STENOSIS – FROM BASICS TO PROGNOSIS

P4089 | BEDSIDE Calcification of aortic valve and coronary atherosclerosis: differences in bicuspid and tricuspid valves

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Background: Calcific aortic valve stenosis and atherosclerosis share some underly ing pathophysiological processes. Although stenosis slow the progression of coronary atherosclerosis, this theray has been shown to be active to slow the progression of calcific aortic stenosis suggesting important differences in the pathophysiology of coronary artery disease and calcific aortic stenosis. In contrast, bicuspid aortic valves (BAV) develop calcific stenosis two decades earlier than tricuspid aortic valves (TAV) and this process may occur in these patients independent of the expression of CAD. Moreover, controversial data suggest that the -174G/C polymorphism on interleukin-6 gene promoter (rs1800795) may represent an early marker of inflammatory activation, closely related to the initiation and evolution of atherosclerosis.

Methods: Aortic valves and coronary atherosclerosis were analyzed with multi-detector computed tomography (MDCT) and compared between patients with BAV versus TAV. Patients with BAV (n=50) were comparable to patients with TAV (n=180) in sex, cardiovascular risk factors and chest pain symptoms.

Results: Patients with BAV (n=50) were comparable to patients with TAV (n=180) in sex, cardiovascular risk factors and the presence of chest pain symptoms. In addition, the median Agatston coronary artery score (0 [0–46.8] vs 0 [0–46.6], p=0.812) was comparable in patients with BAV versus TAV. The C allele of rs1800795 exerts a synergistic effect on smoking resulting to a significantly increased risk for CAD. This action is mediated by the role of interleukin-6 gene promoter, inflammation and thrombotic mechanisms as well as by the impairment of endothelial function.
Coronary Agatston score is significantly larger in patients with BAV than in patients with TAV.

Conclusions: Independently from coronary atherosclerosis, the aortic valve calcium load is significantly larger in patients with BAV than in patients with TAV.

P4090 | BEDSIDE
Shorter leukocyte telomere length is associated with the risk of calcific aortic stenosis
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Background: Calcific aortic stenosis (CAS), a common cause for morbidity and mortality, is more prevalent later in life. However, why some individuals develop it and others do not is unclear. We hypothesised that the risk may relate to faster biological ageing.

Shorter leukocyte telomere length (LTL) which serves as a biomarker for biological ageing has been linked to a number of age-related conditions including coronary artery disease (CAD). Here we examined the association of LTL with CAS controlling for factors associated with LTL including age, gender and CAD.

Methods: 254 patients with a confirmed diagnosis of CAS were matched one-to-one on age and sex with a group of controls without CAS. All cases and controls had CAD and were of Caucasian origin. LTL was measured using a quantitative PCR-based technique, in which LTL is expressed as a ratio of telomere repeat length to copy number of a single copy gene. Telomere length was standardized using a Z-transformation approach. Conditional logistic regression, to account for the matching, was performed to test the relationship between LTL and CAS.

Results: The baseline characteristics for CAS cases and controls were similar (Table 1). There was an inverse relationship between LTL and risk of CAS. For each 1 SD shorter LTL there was a 54% higher risk of CAS (OR 1.54; 95% CI, 1.15 to 2.06, P=0.0037).

Conclusion: Shorter telomere length is significantly associated with risk of calcific aortic stenosis independent of age, gender and CAD status. Our finding supports the hypothesis that CAS is partly a disease of premature biological ageing.

P4091 | BEDSIDE
Myocardial fibrosis and microRNA-21 expression in patients with severe aortic valve stenosis and preserved ejection fraction: a 2D speckle tracking echocardiography, tissueal and plasmatudy
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Background: Myocardial fibrosis (MF) is an adverse correlate of severe aortic valve stenosis (SAS), microRNA expression modulates different pathophysiological pathways in cardiovascular disease. In particular miRNA-21, has been associated to MF due to pressure overload. Non invasive estimation of MF, using speckle-tracking echocardiography (2D-STE), could be useful in determining early myocardial damage.

Purpose: To analyze the correlation between 2D-STE parameters, MF, plasmatic and tissue miRNA expression in SAS.

Methods: We evaluated 36 consecutive patients (75.2±8.0, y.o., 63% F) with SAS and preserved ejection fraction (EF), undergoing to surgical aortic valve replacement (AVR; Euroscore II 2.28±1.13%; Logistic Euroscore 6.8±1.4%)

ECG, biohumoral evaluation (including plasma miRNA-21) and a complete echocardiography, including 2D-STE, was performed before AVR. 28 patients eventually underwent AVR and, in 23 of them, a basal interventricular septum biopsy was performed. MF and tissue miRNA-21 expression (micro-dissection) were evaluated in each sample.

Results: All patients with SAVS (AVAI 0.33±0.1 cm²/m²; V max 4.4±0.4 m/s; Mean Grad. 50.9 mmHg) showed concentric hypertrophy (LVM 147±20.7 g/m², RWT 0.5±0.7), diastolic dysfunction and increased Valvulo-Arterial Impedance (ZVA: 5.9±2.3 mmHg/m²).

Despite a preserved EF (65%±11%), an altered global and septal deformation (Global longitudinal strain, GLS –13.61; Global longitudinal strain rate, GLSR −0.8±0.2 1/sec; Global early diastolic Sr, GLS/eT 1.0±0.3 1/sec; Septal longitudinal strain, SLS –8.6±2.8%; SL-Sr −0.6±0.1 1/sec; SL-SrE 0.6±0.29 1/sec) were observed.

We found a significant association between MF and 2D-STE parameters, stroke volume and end-diastolic pressure (all p<0.05).

Tissue miRNA-21 was mainly expressed in fibrous tissue than in myocardium (t=-0.0001). Myocardial miRNA-21 was associated with AVAI (r=0.46; p=0.043) and cardiac index (r=0.5; p=0.02) while fibrous tissue miRNA-21 was associated to GLS (r=0.8; p=0.0003), GLSR (r=−0.72; p=0.005), SLS (r=0.6; p=0.01), SL-Sr (r=−0.45; p=0.03), SL-SrE (r=−0.5; p=0.04) and PARPs (r=0.66; p=0.04).

Conclusion: In SAVS with preserved EF, MF is associated to impaired myocardial deformation. miRNA-21 has a potential pathophysiological role in fibrogenese.

Non invasive evaluation of plasmatic miRNA-21 and 2D-STE could be useful in risk stratification, to optimize the timing of surgery in SAVS patients.

P4092 | BEDSIDE
Combining tumor marker carbohydrate antigen 125 and the logistic EuroSCORE improves risk stratification in patients undergoing transcatheter aortic valve implantation
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Introduction: Conventional risk scores are inaccurate in patients undergoing transcatheter aortic valve implantation (TAVI). Elevated tumor marker Carbohydrate Antigen 125 (CA125) is known to be associated with adverse outcome after TAVI.

Purpose: We investigated the additional value of CA125 to that of the EuroSCORE for predicting long-term mortality after TAVI.

Methods: CA125 was determined in 422 patients undergoing TAVI for severe aortic stenosis. Elevated levels of CA125 were regarded according to the manufacturers recommendations and as previously published (>30 U/ml) while elevated EuroScore was regarded as > median.

Results: Median follow-up was 59 weeks. 27% of patients (115/422) died after TAVI (1.95, 95% CI [1.63–2.34] per 10 person-year). If CA125 and EuroSCORE were elevated, mortality (in % and per 10 person-year) was higher (CA125: 47%, 4.05 95% CI [3.08–5.31] vs. EuroSCORE: 20%, 1.37 [1.09–1.75], P=0.001 and CA125: 38%, 3.13 95% CI [2.52–3.89] vs. EuroSCORE: 16%, 1.03 95% CI [0.74–1.44], P=0.001, respectively) with a comparable Harrell’s C-statistic (CA125: 0.716 vs. EuroSCORE: 0.684). After adjustment for EuroSCORE, atrial fibrillation, previous coronary artery disease and NYHA class III/IV, elevated CA125 and EuroSCORE were low, mortality was low, too (14%, 0.9% 95% CI [0.62–1.33]; if either variable was elevated, mortality was moderate (28%, 2.1% 95% CI [1.56–2.81]); when both CA125 and EuroSCORE were elevated, mortality was high (55%, 5.1% 95% CI [3.6–8.6]; P<0.001).

Conclusion: CA125 offers additional prognostic information to that obtained by the EuroSCORE alone. Elevation of both CA125 and EuroSCORE was associated with a poor prognosis.
**P4093 | BEDSIDE**

**New-onset midwall dysfunction predicts impaired prognosis in aortic valve stenosis with normal ejection fraction (the SEAS study)**

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**Background:** In hypertension, low left ventricular (LV) midwall function is associated with impaired prognosis independent of normal ejection fraction (EF).

**Purpose:** To test the prognostic value of new-onset low LV midwall shortening (MWS) during follow-up of patients with asymptomatic aortic stenosis (AS) and normal EF.

**Methods:** 1107 patients with AS, normal EF and MWS at baseline in the Simvastatin Ezetimibe in Aortic Stenosis (SEAS) study were followed for a median of 4.0 years. LV systolic function was assessed by biplane EF (low if <50%) and MWS (low if <14%/16% in men/women) at baseline and annual echocardiograms. New-onset low MWS was identified at follow-up visits before any clinical event.

**Results:** 574 patients (52%) developed low MWS during follow-up. They included a higher proportion of elderly women with higher blood pressure and abnormal LV geometry (all p <0.05). In time-varying Cox analyses new-onset low MWS predicted 45% increase in major CV events and a 2-fold increase in heart failure and CV death (Table, Figure).

**Time-varying Cox analyses**

<table>
<thead>
<tr>
<th>Term</th>
<th>Hazard ratio [95% CI], p for new-onset low MWS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major CV events</td>
<td>1.45 [1.19–1.83], p=0.002</td>
</tr>
<tr>
<td>Aortic valve events</td>
<td>1.49 [1.17–1.90], p=0.001</td>
</tr>
<tr>
<td>Heart failure or CV death</td>
<td>2.07 [1.17–3.67], p=0.013</td>
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Adjustment for age, gender, study treatment, hypertension, and time-varying EF, severity of AS by energy loss index, and abnormal LV geometry.

**Conclusions:** New-onset low MWS during follow-up was associated with increased CV morbidity and mortality during 4-year follow-up.

**P4094 | BEDSIDE**

**SuPAR is associated with cardiovascular events and mortality in patients with asymptomatic aortic stenosis**

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**Introduction:** Soluble uric acid plasminogen activator receptor (suPAR) is an inflammatory marker associated with cardiovascular disease. Whether suPAR is of prognostic value for asymptomatic patients with aortic stenosis (AS) remains unknown.

**Methods:** Serum suPAR levels were measured in 1,504 patients aged 28–86 years (mean age 67.7), recruited in the Simvastatin and Ezetimibe in Aortic Stenosis (SEAS) trial. Cox regression analyses were performed for baseline suPAR, adjusted for traditional cardiovascular risk factors, C-reactive protein (CRP) and statin treatment. Primary outcomes were incidence of cardiovascular events (composite of non-fatal myocardial infarction, non-hemorrhagic stroke and cardiovascular death [n=135]), cardiovascular [n=80] and all-cause mortality [n=150].

**Results:** Significantly elevated suPAR levels were found in women, smokers and older patients (p <0.01). SuPAR levels positively correlated with CRP (p <0.001). SuPAR was significantly associated with cardiovascular events (HR=1.22 [95% CI: 1.08–1.37], p=0.001), cardiovascular (HR=1.23 [95% CI: 1.05–1.44], p=0.009) and all-cause mortality (HR 1.21 [95% CI: 1.07–1.35], p=0.002), in fully-adjusted multivariate models.

**Conclusions:** In patients with mild-moderate AS, suPAR is a strong independent predictor for adverse cardiovascular events and mortality.

**P4095 | BEDSIDE**

**Prognostic value of left atrial reservoir function in patients with severe aortic stenosis**


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**Background:** Left atrial (LA) strain analysis by 2D speckle tracking echocardiography (ST-E) represents an easy and reproducible way to estimate LA function. The aims of the present study are to assess the LA reservoir function in patients with severe aortic stenosis (AS) and to evaluate its impact on the recurrence of major adverse cardiac events (MACEs).

**Methods:** 128 patients (mean age 79±9 years) with severe AS underwent standard echocardiography to evaluate the left ventricular (LV) and right ventricular function, LA size, aortic valve morphology and gradients. Global peak LA strain (PLAS) is measured by 2D STE during LV systole and represents the LA reservoir function. Overall death, hospitalization for cardiac cause, and worsening heart failure were defined as major adverse cardiac events (MACEs).

**Results:** The mean PLAS (18.4±7.9%) was significantly reduced in AS with respect to the mean values reported in the general population. According to the multivariate linear regression analysis, LV global longitudinal strain, mitral E/e’ ratio and systolic pulmonary arterial pressure (sPAP) were the best correlates to PLAS. During follow-up, the predefined MACEs occurred in 39 patients. According to the multivariate Cox regression analysis, a PLAS <21% was a significant predictor of MACEs (HR 2.86, p=0.04), as was CAD (HR 2.68, p=0.004) and the NYHA functional class (HR 2.08, p=0.03).

**Conclusions:** In patients with severe AS, a global PLAS <21% is a strong independent predictor of prognosis. Given the combined influence of LV diastolic and systolic function and PAPs on LA performance, the decline of PLAS might be considered a marker of global myocardial impairment in AS.
DIFFERENTIATING PHYSIOLOGICAL ADAPTATION FROM CARDIAC PATHOLOGY IN ATHLETES

P4096 | BEDSIDE
Athletic cardiac adaptation is secondary to increased myocyte mass

Background: Cardiac remodelling occurs in response to regular athletic training, and the degree of remodelling is associated with fitness. Understanding the myocardial changes in athlete’s heart (AH) is important to develop tools that differentiate athletic from cardiomyopathic change.

Purpose: We hypothesised that athletic LV hypertrophy is a consequence of increased myocardial cellular rather than extracellular mass and measured this with cardiovascular magnetic resonance (CMR).

Methods: 34 athletes underwent cycle ergometer maximal exercise test and CMR including native and post-contrast T1 mapping allowing extracellular volume (ECV) calculation.

Results: Subjects were divided into tertiles by VO2max (n=11, n=12, n=11): 50±3, 60±2, 68±6 mlO2/min/kg (p=0.01 by definition). Indexed LV end diastolic volume (LVEDVi) and mass (LVMi) correlated with VO2max (r=0.455, P=0.01; r=0.34, P=0.05). CMR derived measures of tissue composition (T1, ECV) differed significantly by VO2max tertile, P<0.05, respectively, and were significantly correlated: Native T1 (r=−0.40, P=0.02); ECV (r=−0.55, P<0.01). An inverse relationship was seen between LVMi and ECV (r=−0.56, P<0.01). Extracellular mass (28±1±4; 30±1±7; 29±2±4 g) in AH was similar between tertiles though intra-cellular mass increased with VO2max tertile (83±7±6; 101±3±2; 110±7±19 g; P<0.01).

Conclusion: LV mass in AH occurs as a consequence of increased myocyte mass, whilst the extra-cellular mass remains constant. Athletic remodelling, both on a macroscopic and cellular level, is associated with the degree of an individual’s fitness. ECV mapping may have a future role in differentiating AH from change secondary to cardiomyopathy.

P4097 | BEDSIDE
Impact of matrix metalloproteinases and their inhibitors in the athlete’s heart
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The physiological mechanisms behind exercise-induced myocardial hypertrophy are not clearly characterized and subject to intense research. Matrix metalloproteinases (MMP) and their tissue inhibitors (TIMP) are promising biomarkers of numerous cardiac diseases including pathological left ventricular hypertrophies. Our aim was to assess the correlations between the physiological hypertrophy of athlete’s heart and the serum levels of MMPs and TIMPs.

Our study included elite athletes competing in waterpolo, kayaking, canoeing or rowing (EA: n=75, age: 26±8 years, 77% male) compared to age- and gender-matched healthy sedentary volunteers (CTL; n=33). The left (LV) and right ventricular (RV) end-diastolic volume (EDVi) and mass (Mi) indexed to body surface area were measured by cardiovascular magnetic resonance imaging (CMR) software. Serum concentrations of the enzymes (MMP-2, MMP-9, TIMP-1, TIMP-2) were determined by enzyme-linked immunosorbent assay (R&D Systems, Quantikine).

Not surprisingly, the LV and RV volumes and masses were markedly increased in the athletes compared to the control group (EA vs. CTL: LVEDVi: 119±14 vs. 93±13 ml/m²; RVEDVi: 124±17 vs. 95±15 ml/m²; LVMi: 84±18 vs. 59±12 g/m²; RVMi: 31±16 vs. 24±4 g/m², all P<0.001). Despite the notable cardiac remodelling, we did not find significant differences in the serum levels of the measured enzymes between the two groups. In athletes, significant negative correlations were found between MMP-2 and LV and also RV mass indices (LVMi: r=−0.35, P=0.002; RVMi: r=−0.35, P=0.009) and end-diastolic volume indices (LVEDVi: r=−0.23, P=0.048; RVEDVi: r=−0.25, P=0.029). A similar inverse relationship was observed between TIMP-2 and LVMi and also RVEDVi (LVMi: r=−0.38, P<0.001; RVEDVi: r=−0.24, P=0.039). MMP-9 showed a significant positive correlation with the LV end-diastolic volume (LVEDVi: r=0.27, P=0.019). In the control group, we did not notice these relationships.

There are pathological LV hypertrophies, serum levels of MMP-2 showed an inverse relationship to the ventricular volumes and masses in the elite athlete group. The dissimilar correlations of MMP-2 and MMP-9 also imply a different regulation of these enzymes in the athlete’s heart. MMP-2 may be a useful biomarker in clinical practice to distinguish between physiological and pathological hypertrophies and to recognize overlapping cardiac diseases.

P4098 | BEDSIDE
Impact of exaggerated blood pressure response on parameters of cardiac remodelling in amateur endurance athletes
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Background: Extensive endurance training and arterial hypertension are established risk factors for atrial fibrillation (AF). The impact of exaggerated blood pressure responses on cardiac remodelling in endurance athletes is unknown.

Purpose: The aim of the study was to assess the proportion of exaggerated blood pressure response (EBPR) during an exercise test in amateur endurance athletes and the impact on cardiac function, morphology and atrial ectopy.

Methods: Amateurs who participated in the Grand Prix of Bern, a popular Swiss 10 mile race, were included. Cardiopulmonary exercise test (CPET) was performed and athletes were stratified into an exaggerated blood pressure response (EBPR, peak systolic BP >200 mmHg in males and >190 mmHg in females) group and a normal (NBPR) group. Left atrial volume index (LAVI), left ventricular mass index (LVMi), tissue Doppler annular early (Ea), and signal-averaged P wave duration (SAPWD) were measured, 24-hour Holter monitoring was performed and premature atrial contractions (PAC) were recorded. Data was adjusted for age, gender, lifetime training hours, and BP at baseline.

Results: 119 runners (51% male) were included in the final analysis, and 16 athletes (13%) fulfilled the criteria for EBPR. Mean age was comparable in both groups (45±10 years in the EBPR and 42±7 years in NBPR). EBPR and NBPR did not differ with respect to anthropometric data, lifetime training hours, and peak oxygen uptake (51±5 vs. 52±2 ml/kg, respectively, P=0.688). Mean systolic and diastolic BPs at rest and at peak exercise were significantly higher in EBPR (123±11/75±8 vs. 116±11/72±8 mmHg, respectively, P<0.001; and 207±12/98±2 vs. 170±13 mmHg/77±7 mmHg, respectively, P<0.001). Compared to athletes in NBPR, athletes in EBPR had a higher LVMi (1.08±0.26 vs. 0.94±0.19 g/ml, P<0.006), a lower Ea (11.6±1.4 vs. 13.5±1.7 cm/s, P=0.002), and a longer SAPWD (135±16 vs. 127±12 ms, P=0.044), while LAVI showed no significant differences between the groups. In logistic regression models presence of EBPR was an independent predictor for LVMi (beta=−0.203, P=0.001), Ea (beta=−0.253, P=0.006), SAPWD (beta=0.179, P=0.044), and PAC (beta=0.199, P=0.033), but not for LAVI (beta=0.112, P=0.186).

Conclusion: In our study, 13% of athletes fulfilled the criteria of EBPR. EBPR was associated with alteration of LV structure, diastolic function, atrial remodelling and atrial ectopy.

P4099 | BEDSIDE
Differentialization of arrhythmogenic right ventricular cardiomyopathy and athlete's heart using cardiac magnetic resonance imaging
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The diagnosis of arrhythmogenic right ventricular cardiomyopathy (ARVC) is based on the revised Task Force Criteria defined in 2010, which includes right ventricular end-diastolic volume (RVEDVi), right ventricular ejection fraction (RVEF), right ventricular mass (RVM) and wave motion abnormalities evaluated using cardiac magnetic resonance (CMR) imaging. However, the elevated RVEDVi can be a result of sport adaptation as well, the revised Task Force guideline contains no criteria for professional athletes (28±5y,36 male) group and a normal (NBPR) group. Left atrial volume index (LAVI), left ventricular mass index (LVMi), tissue Doppler annular early (Ea), and signal-averaged P wave duration (SAPWD) were measured. 24-hour Holter monitoring was performed and premature atrial contractions (PAC) were recorded. Data was adjusted for age, gender, lifetime training hours, and BP at baseline.

Our study included elite athletes competing in waterpolo, kayaking, canoeing or rowing (EA: n=75, age: 26±8 years, 77% male) compared to age- and gender-matched healthy sedentary volunteers (CTL; n=33). The left (LV) and right ventricular (RV) end-diastolic volume (EDVi) and mass (Mi) indexed to body surface area were measured by cardiovascular magnetic resonance imaging (CMR) software. Serum concentrations of the enzymes (MMP-2, MMP-9, TIMP-1, TIMP-2) were determined by enzyme-linked immunosorbent assay (R&D Systems, Quantikine).

The dissimilar correlations of MMP-2 and MMP-9 also imply a different regulation of these enzymes in the athlete’s heart. MMP-2 may be a useful biomarker in clinical practice to distinguish between physiological and pathological hypertrophies and to recognize overlapping cardiac diseases.

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Differentiating physiological adaptation from cardiac pathology in athletes / Prediction models in clinical practice

P4101 | BENCH

Automatic use of seattle criteria led to less than ten percentage of abnormal electrocardiograms when applying to a general population of young swiss males

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Background: There is a general interest in automatic detection algorithms for large scale ECG-preparticipation screening. The Seattle Criteria which were created for athlete ECG screening focus on abnormal ECG patterns which exclude patterns induced by intense training. These criteria can be applied in an automated way to a large young population. During mandatory military conscription (n=44,000 Swiss male are medically examined every year represent a large unbiased group comprising the whole male population, which is screened at least once during lifetime at the age of 19 years by law.

Methods: We performed a retrospective analysis of 274,468 digitally recorded 12-lead ECGs acquired during military conscription between 2008 and 2013. The Seattle Criteria were directly implemented into automated resting ECG measurement and interpretation software ETM. The percentage of detection of abnormal vs. normal ECG’s as well as of each specific abnormal subtype on all ECG’s was evaluated.

Results: We detected 17 785 abnormal ECGs (6.47%). The largest abnormal subgroup identified was “pathologic Q waves” (5.94/2.17%) followed by the groups “ST segment depression” (3.080/1.12), “Left axis deviation”, (2.800/1.02%), “left atrial enlargement” (1.790/0.62%), “Atrial tachyarrhythmias” (1.599/0.58), “Long QT interval” (1.412/0.051), “T-wave inversion” (1.193/0.43), “Right ventricular hypertrophy pattern” (0.910/0.36), “Premature ventricular contractions” (0.16/0.05) and “Intraventricular conduction delay” (0.38/0.14). There were 92 “Complete left bundle branch block”, 71 “Ventricular pre-excitation” and six “Short Long QT” were identified. No “Brugada-like pattern” and no “Profound sinus bradycardia” were found.

Conclusions: The 6.47% of automatically detected abnormal ECGs correspond to 1.2% male individuals per year which would warrant a more profound clinical and/or electrophysiological and genetic investigation to confirm or exclude the presence of an acquired or familial cardiac disease

P4102 | BEDSIDE

Exercise stress testing in 73,000 patients: safety with abnormalities of serum potassium

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Purpose: Guidelines recommend that performing exercise stress testing in the setting of abnormal serum potassium concentrations is relatively contraindicated; however, data supporting these guidelines are limited.

Methods: We reviewed a consecutive series of patients who had serum potassium testing within 48 hours of undergoing treadmill exercise stress testing (n=73,612) between 2003 and 2013. Hemolyzed samples were not included in the analysis. Normal serum potassium range for our laboratory is 3.6–5.2 mEq/L. The association of potassium levels with the development of supraventricular and ventricular arrhythmias was assessed.

Results: The overall incidence of supraventricular and ventricular arrhythmias was low and the incidence of severe, clinically significant arrhythmias was very low, demonstrating the overall safety of exercise stress testing (table), 4.019 (5.52%) of patients had serum potassium abnormalities at the time of exercise stress testing. Most of these were within the mildly abnormal hypokalemic (3.1–3.6) or hyperkalemic (5.2–5.9) range. There was no significant association between potassium abnormalities and arrhythmia. The association of abnormal potassium levels with the frequency of supraventricular and ventricular arrhythmia is shown in the table (number, percentage).

Table 1. Incidence of arrhythmias

<table>
<thead>
<tr>
<th>Potassium, mEq/L</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3.1</td>
<td>3.1–3.6</td>
</tr>
<tr>
<td>SVT/AF lasting &gt;30 sec</td>
<td>109</td>
</tr>
<tr>
<td>SVT/AF resp. treatment</td>
<td>1.032</td>
</tr>
<tr>
<td>VF / VT &gt;30 sec</td>
<td>0.0%</td>
</tr>
<tr>
<td>VF / VT &gt;75 PVC/min</td>
<td>2.183</td>
</tr>
<tr>
<td>SVT/AF supraventricular tachycardia; VF, atrial fibrillation/flutter; VT, ventricular fibrillation; PVC, premature ventricular contractions</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: The data confirms that the incidence of arrhythmia during exercise stress testing is low, even in patients with abnormal serum potassium. Patients with a potassium range between 3 and 6 mEq/L are not at a significantly increased risk of rhythm disturbance.

PREDICTION MODELS IN CLINICAL PRACTICE

P4103 | BEDSIDE

Graz CLI Score: a risk score for critical limb ischemia in peripheral arterial occlusive disease patients

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Background: Critical limb ischemia is a frequent entity associated with a high rate of limb amputation and mortality. To highlight patients at high risk for CLI we developed a risk score that can be applied easily in patients with peripheral arterial occlusive disease (PAD).

Methods and findings: We evaluated 1000 consecutive PAD patients treated at our institution from 2005 to 2007. Clinical symptoms, comorbidities, and concomitant medication were documented. We calculated odds ratios (OR) in a binary logistic regression model to calculate possible risk factors for CLI. In a second step a total of 1124 PAD patients treated at our institution between 2007 and 2011 were included to verify the score.

In the first patient group the strongest risk factors for CLI were age>75 years (OR
Usefulness of the Platelet- to- lymphocyte ratio in predicting long term cardiovascular mortality in patients with peripheral arterial occlusive disease

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Background: Peripheral arterial occlusive disease (PAOD) is related with increased cardiovascular mortality and morbidity. Platelet to lymphocyte ratio (PLR) has recently been reported as a new independent predictor for major adverse cardiovascular events including mortality in various cardiovascular diseases. Purpose: The aim of this study was to investigate the association between PLR and long-term cardiovascular mortality both in patients with intermittent claudication and critical limb ischemia.

Methods: In a retrospective study, 602 consecutive patients who had been admitted to the inpatient ward of the vascular department of a large tertiary training and research hospital with diagnosis of symptomatic PAOD between May 2009 and September 2013 were included. Patients were divided into two groups according to their PLR as follows: high PLR (PLR >142) and low PLR (PLR <142) groups. Results: During the course of the present study (median follow-up period of 33.8 months [interquartile range, 21–45]), 131 death occurred out of 602 patients (21.8%). Cardiovascular mortality was found to be significantly higher in patients with high PLR score (Score >1), intermediate (Score 2–4), and high PLR score (Score >4). Conclusions: We developed a simple risk stratification scheme, which is based on conditions that can be assessed easily from the medical history, without need of laboratory parameters. This score might help to identify PAOD patients at high risk for CLI.

Conclusions: The definition of PCI-MI may have important implications for trial outcomes. These results illustrate the importance of a careful assessment of PCI-related MI.

Gender-related differences in carotid inflammation in patients with coronary artery disease

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Background: Carotid atherosclerosis is a major cause of stroke. Controversy exists regarding the gender related differences in carotid plaque vulnerability. Although men exhibit higher inflammatory infiltration in carotid endarterectomy specimens, women show in vivo more intense intraplaque neovascularization. Microwave Radiometry (MWR) allows the non-invasive in-vivo measurement of internal temperature of tissues, reflecting local inflammation. The aim of the present study was to evaluate the impact of gender on carotid plaque temperatures, as evaluated by MWR.

Methods: Consecutive patients with significant coronary artery disease (CAD), as documented by coronary angiography (≥50% stenosis at least one major epicardial vessel) underwent 1) ultrasound echo-color Doppler (US-ECD) study and 2) MWR measurements, of both carotid arteries. During the ultrasound study, carotid plaque thickness of each carotid artery was determined. Temperature difference (ΔT) by MWR was assigned as maximal temperature along the carotid artery minus minimum. ΔTmax was assigned as the maximal value of the ΔTs of both carotid arteries. Vessel- and patient based analysis were performed to determine the impact of gender on morphological and functional carotid artery characteristics.

Results: From 359 patients, 305 (85%) were men and 54 (15%) were women. Women had similar IMTmax compared to men in both vessel- and patient-based analysis (2.04±1.03 vs 2.00±1.08 mm, p=0.69 and 2.46±1.2 vs 2.3±1.18 mm, p=0.66, respectively). On the contrary, carotid arteries of women showed higher ΔT values in both vessel and patient-based analysis (0.98±0.51 vs 0.70±0.43°C, p<0.001 and 1.16±0.48 vs 0.87±0.45°C, p<0.001, respectively). Univariate analysis showed a statistically significant association between gender and ΔTmax values (coefficient β=−0.29, p<0.001). After adjustment for possible covariates this association remained significant (β=−0.28, p<0.001).

Conclusions: Women with CAD exhibited a more vulnerable carotid atherosclerotic plaque phenotype. Whether this is associated with worse prognosis, remains to be elucidated in prospective studies.
The peak rate of arterial dilatation during measurement of flow-mediated dilatation

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Background: Measures of flow-mediated dilatation (FMD) are used in the assessment of endothelial function. Traditionally, this is a single, time-based measure of maximal conduit artery dilatation. To date, little attention has been given to more integrated measures addressing the rate of change in vessel diameter over time.

Purpose: To examine the rate of change in radial artery diameter (dD/dt) after the ischemic stimulus used in the assessment of FMD.

Methods: We examined the peak rate of radial artery diameter dilatation (peak +dD/dt) following the FMD stimulus. A total of 223 patients (62±5 yrs, 167 males) with known coronary artery disease and 99 normal volunteers (24±3 yrs, 91 males) were studied.

Results: Although FMD was significantly blunted in the patient group as compared to the normal volunteers (4.1±3.7 vs. 8.3±3.3 %; P<0.001), peak +dD/dt was significantly greater in the patient group as compared to the normal volunteers (0.025 vs 0.015 mm/sec; P<0.001; figure). The hemiprecipitous response was similar in both groups. There was no correlation between peak +dD/dt and age, baseline or peak vessel diameter, FMD, or hyperemic flow.

Conclusions: Therefore, there are significant differences in the rate of radial arterial dilatation in patients with coronary artery disease as compared to a group of normal volunteers following the ischemic stimulus used in FMD. The mechanism of the greater rate of arterial dilatation remains uncertain, however this measurement may provide further insight into vascular function as it is assessed by FMD.

Acknowledgement/Funding: Canadian Institutes of Health Research

Ankle brachial index predicts two year mortality in sub-saharan older adults

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Conclusion:

P4109 | BEDSIDE

Protein energy wasting is associated with poor outcome after lower extremity revascularization in chronic haemodialysis patients with peripheral artery disease

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Background: Although lower extremity revascularization, regardless of surgical or percutaneous procedures, has been commonly performed in chronic haemodialysis (HD) patients with peripheral artery disease (PAD), poorer prognosis still remains major problems in such population. Recently, protein-energy wasting (PEW) or malnutrition, frequent observed in HD patients, was considered to be strongly associated with chronic inflammation and advanced atherosclerosis. We investigated whether geriatric nutritional risk index (GNI), developing as a marker of the PEW, could predict clinical outcome after lower extremity revascularization in HD patients.

Methods: We enrolled a total of 862 HD patients (age 67±10 years, diabetes 62.9%, critical limb ischemia 53.5%) who successfully underwent lower extremity revascularization (552 with endovascular therapy and 310 with bypass surgery). The GNI was calculated from pre-procedural tests, as follows: GNI = (14.89 × albumin) + (41.7 × (body weight/body weight at BMI of 22)). They were followed up for up to 10 years. Amputation-free survival (AFS), defined as freedom from major amputation or all-cause death, was primarily evaluated.

Results: During follow-up period, 63 (7.3%) patients needed major amputation and 202 (23.4%) patients died. Cox multivariate analysis identified GNI [adjusted hazard ratio (HR) 0.97, 95% confidence interval (CI) 0.96–0.99, p=0.0022], male gender (HR 1.73, 95% CI 1.25–2.39, p=0.0011), age (HR 1.02, 95% CI 1.00–1.04, p=0.018), ulcer/gangrene (HR 1.91, 95% CI 1.32–2.75, p=0.0006) as independent predictors for composite endpoint with major amputation or all-cause death. When cut-off level of the GNI was defined as median value of 92.3, Kaplan-Meier estimated AFS for 10-year was significantly lower in the low GNI group than in the high GNI group (44.9% vs. 62.6%, adjusted HR 1.74, 95% CI 1.25–2.45, p=0.0011). Similar results were obtained for freedom from major amputation (82.4% vs. 94.1%, adjusted HR 2.85, 95% CI 1.38–6.32, p=0.0044) and from all-cause death (50.4% vs. 65.9%, adjusted HR 1.69, 95% CI 1.28–2.43, p=0.0039), respectively.

Conclusion: Declined GNI which reflect PEW or malnutrition state strongly predicted worsen clinical outcome such as amputation and mortality after lower extremity revascularization in chronic HD patients. More attention should be paid to pre-procedural PEW or malnutrition condition in this high-risk population.

HEART FAILURE: DIVERSITY OF PHENOTYPING

P4110 | BEDSIDE

The relationship between hemocoagulation and renal function variability in patients with acute heart failure syndrome: data from the Korean Acute Heart Failure (KorAHF) registry

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Background: Hemoconcentration (HC) was known to be related with improved clinical outcomes in patients (pts) with acute heart failure syndrome (AHFS). Generally, variable rise and fall in renal indices was observed during hospitalization in pts with AHFS. However, the relationship between HC and renal function variabil-

Methods and results: We analyzed 5,860 AHFS pts (3,019 males, 68±14 years
old, 37.4% ischemic origin, left ventricular ejection fraction 38.5±16.1%) from Korean Acute Heart Failure (KoAHF) Registry. We defined HC as an increased hemoglobin level between admission and discharge and RFV as standard deviation of serum creatinine at admission, maximum, minimum and discharge. There were 270 cases of all-cause in-hospital mortality (4.8%). Mean hemoglobin levels at admission and discharge were 12.4±2.3 and 12.5±2.2 g/dL, respectively and HC was presented in 2,603 AHFS patients (46.1%). Mean creatinine at admission was 1.48±1.46 mg/dL and mean RFV was 0.36±0.78 (n=5,655), respectively. The AHFS group with HC had significantly lower RFV compared to those without HC (0.33±0.56 vs. 0.39±0.58, p=0.003). In correlation analysis, RFV was significantly associated with B-type Natriuretic Peptide (BNP, r=0.238, p<0.001), N-terminal pro-BNP (r=0.233, p<0.001) and high sensitive c-reactive protein (r=0.116, p<0.001). In multivariate logistic regression analysis for in-hospital mortality after adjusting other risk factors including baseline BUN, creatinine level and hemoconcentration (hazard ratio 5.374, 95% confidence interval 4.083–7.073, p<0.001).

Conclusion: Our study demonstrated that higher RFV was related to higher in-hospital mortality in large cohort of AHFS for the first time. Therefore, the further prospective research regarding the prognostic value of RFV during hospitalization should be warranted and it may provide a new information in the risk stratification of AHFS.

P4111 | SPOTLIGHT Prevalence of hereditary transthyretin cardiac amyloidosis in patients with Hypertrophic Cardiomyopathy. A multicenter study

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Background: Hereditary transthyretin cardiac amyloidosis (mTTR-CA) is a progressive disease with challenging diagnosis and poor prognosis. Patients show increase in LV wall thickness (LWT) mimicking sarcomeric hypertrophic cardiomyopathy. The prevalence of m-TTR in patients with increase LWT is unknown.

Methods: Screen systematically for TTR genotype patients with LWT >15mm in 9 French primary cardiology centres.

Results: 298 patients were prospectively genotyped of whom 23% were African descendants. The median (IQR) age was 62 (50,74), 74% were men and 36% 55 years old the prevalence was 22% and 35% if 65 years old. The most frequent mutations in CA were V142I (8), V50M (2) and I127V (2). The prevalence of mTTR-CA is frequent in patients older than 55 years old with hypertrophic cardiomyopathy (HC) and dilated cardiomyopathy (DCM). The prevalence of mTTR-CA in patients with HC was 15% (n=291/1920) and median age was 57 years old, 37.4% ischemic origin, left ventricular ejection fraction 38.4±12.8%, and the mean LVEDD was 55.5±16.7 mm. B19V genomes were detected in 42.6±17.9% of the EMB in this cohort by PCR. The dataset MA02 comprised n=634 subjects (mean age: 46.7±7.6 years; men: n=291/45.9%). The MC/DCM-patients (n=500) had not significantly different demographic data compared to controls (n=134). LVEF was significantly higher in controls (mean: 62.8±8.8%) versus MC/DCM-patients: 35.4±9.5%; p=0.0056.

Conclusion: This meta-analysis reveals that the mean detection rate of B19V genomes in MC/DCM-patients does not differ significantly from the findings in controls (43.8±14.3%) from AHFS. The detection of B19V genomes in MC/DCM-patients does not differ significantly from the findings in controls (42.6±17.9%) from the KORAHF registry. This might be explained by the fact that the AHFS population has a lower risk for the development of HC.

P4113 | BEDSIDE PCR proof of parovirus B19 genomes in endomyocardial biopsies of patients presenting with myocarditis or dilated cardiomyopathy - Meta-Analysis confirms a possible bioportfolio

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Introduction: Diverse viral infections have been associated with myocarditis (MC) and dilated cardiomyopathy (DCM). Whereas disease specificity of en- terovirus has been confirmed in this setting by meta-analysis, this relationship is not established for parovirus B19 (B19V) genomes, yet. In this meta-analysis, we aimed to assess the published results on the association of B19V genomes with human MC/DCM versus controls.

Methods: n=197 publications referring to B19V and MC or DCM were retrieved using multiple PubMed search modes. Out of these, n=29 publications with met the inclusion criteria with data from prospective analyses on n=1,920 patients presenting with MC or DCM (dataset: MA01). Data retrieved simultaneously both from controls and MC/DCM patients were available from n=8 from these publications (dataset: MA02).

Results: The demographic data of the n=3,599 patients of the dataset MA01 were as follows: mean age: 47.1±3.1 years; males: n=1,920 (53.3%). Mean LVEF by echocardiography was 38.4±12.8%, and the mean LVEDD was 55.5±16.7 mm. B19V genomes were detected in 42.6±17.9% of the EMB in this cohort by PCR. The dataset MA02 comprised n=634 subjects (mean age: 46.7±7.6 years; men: n=291/45.9%). The MC/DCM-patients (n=500) had not significantly different demographic data compared to controls (n=134). LVEF was significantly higher in controls (mean: 62.8±8.8%) versus MC/DCM-patients: 35.4±9.5%; p=0.0056. However, the rate of B19V positivity in myocardial tissues was not statistically different in controls (mean: 38.8±24.1%) versus the MC/DCM-patients (45.5±24.3%; p=0.5881).

Conclusions: This meta-analysis reveals that the mean detection rate of B19V genomes in MC/DCM-patients does not differ significantly from the findings in controls (43.8±14.3%) from AHFS. The detection of B19V genomes may be pertinent to achieve a meaningful differentiation of biologically relevant myocardial B19V infections.
Results: IQR score increased through NYHA classes 1 to 4 (Figure, right), and significantly correlated with BNP (r=0.58, p<0.01) and cardiac index (r=−0.42, p<0.01).

Conclusion: Increased collagen gene expression correlates to changes in cardiac miR-21, -30c, and -133a levels. In addition, these miR-levels correlate to the amount of fibrosis. Therefore, these miRs may serve as a quantitative and prognostic marker for cardiac fibrosis. Further studies are required to examine whether these miRs are detectable in circulation and herewith valuable as a non-invasive biomarker of interstitial fibrosis.

P4116 | BEDSIDE
MicroRNAs as a quantitative and prognostic biomarker of interstitial cardiac fibrosis in pressure overloaded mice

Background: Detecting interstitial fibrosis in cardiac diseases is of particular interest for clinical evaluation. It has been shown that microRNA (miR) -21, -29b, -30c, and -133a are involved in cardiac fibrosis formation. However, the potential of these miRs as a quantitative and prognostic biomarker has not yet been established.

Aim: The aim is to examine cardiac expression of miR-21, -29b, -30c, and -133a over time and to assess the relation between these miR-levels and the amount of interstitial fibrosis during pressure overload in mice.

Methods: Mice were subjected to transverse aortic constriction (TAC) or sham surgery (sham) and sacrificed 1, 2, 4, 8, and 12 weeks thereafter (1W - 4W - 8W; n=5 per group). Gene expression of collagen type I and III (col1A1 and col1A2, and col3A1 respectively), and miR-expression were analysed by TaqMan assays. Picrosirius red staining was used to determine cardiac fibrosis.

Results: Col1A1, col1A2, and col3A1 are upregulated in 4W- and 8W-TAC (Figure). A broad range of interstitial fibrosis is histologically observed in 8W-TAC (sham 0.35± 0.03 vs TAC 2.56± 1.07, p<0.01). In both 4W-TAC and 8W-TAC, miR-21 is increased and miR-30c is decreased. MIR-133a is decreased in 8W-TAC (Figure) MIR-21, -30c, and -133a are correlated to the progression of fibrosis (r=0.63, r=−0.45, and r=−0.42 respectively, p<0.05).

Conclusion: This novel method effectively quantified respiratory instability in HF patients. IQR score of ISs well correlated with the functional and hemodynamic severity of HF, thus it can be utilized as one of the key tools in the diagnosis and guidance of HF therapy.

P4117 | BENCH
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Conclusion: This novel method effectively quantified respiratory instability in HF patients. IQR score of ISs well correlated with the functional and hemodynamic severity of HF, thus it can be utilized as one of the key tools in the diagnosis and guidance of HF therapy.
flow volume distending proximal aorta; 3) pulse pressure (PP, measure of aortic capacitance); 4) heart rate (marker of frequency of aortic distension).

**Results:** Variance of ARDz was evaluated, controlling for age, sex, body composition (by BIA), waist circumference (WC), white blood cell count and % neutrophils, C-reactive protein, fibrinogen, PAI-1, lipid profile, SV, cuff diastolic BP (finger), PP, and systolic (SBP) and diastolic (DBP) BP variability, and incidentally related to ARDz, but PP exhibited negative correlation (all p<0.0001). ARDz was also positively related to WC, PAI-1 and neutrophils (all p<0.01). Using estimates of central BP instead of cuff BP did not change the regression model.

**Conclusions:** At a given age, gender and height, larger ARDz is associated with high DBP and SV, central fat distribution and inflammatory status. In contrast, at a given DBP and SV, AR dilatation is associated with lower PP.

**P4118 | BEDSIDE**

**Association of plasma testosterone with central haemodynamics in hypertensive men**

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**Background:** There is evidence for an inverse association between plasma testosterone (TT) and cardiovascular mortality, but the role of central blood pressures on cardiovascular outcomes, the present finding might explain part of the increased cardiovascular risk associated with low testosterone. Whether measurement of heart hemodynamics may improve risk stratification in men with low testosterone warrants further investigation.

**Methods:** Central BP was measured in all subjects by enzyme immunoassay. Results: The mean value of TT in the whole population was 4.6 ng/ml (hypo- gonadism was defined as TT<3.4 ng/ml). Plasma TT was inversely and significantly related to aoSBP (r=−0.26, p<0.03), aopP (r=−0.30, p=0.01) and Alx75 (r=−0.31, p<0.01) but only marginally related to bSBP (r=−0.22, p=0.07) and bPP (r=−0.23, p=0.06). In linear regression analysis, after adjustment for age, smoking, BMI, plasma glucose, total cholesterol and presence of antihypertensive treatment, aoSBP (β=0.29, p<0.03), aopP (β=0.31, p<0.02) and Alx75 (β=0.30, p=0.03) were independently associated with TT but the relationship of TT with bSBP (β=−0.25, p<0.06) and bPP (β=−0.23, p=0.07) remained weak.

**Conclusions:** In hypertensive men, plasma TT is independently associated with central blood pressures on cardiovascular outcomes, the present finding might explain part of the increased cardiovascular risk associated with low testosterone. Whether measurement of heart hemodynamics may improve risk stratification in men with low testosterone warrants further investigation.

**P4119 | BEDSIDE**

**Relationship between cognitive dysfunction, clinic and 24-h blood pressure, and blood pressure variability**

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**Background and aims:** The relation between blood pressure (BP) and cognitive function has received growing interest in recent years. Some cross-sectional studies have shown an inverse association between BP and cognitive dysfunction, while longitudinal studies yield mixed results.

**Methods:** In the PAMELA study cognitive function was assessed via minimental score (≥23, indicative of a cognitive dysfunction (CD), the remaining ≥20). Subjects participated at this substudy. Measurements included clinic and 24-hour BP (Spacelabs 90207). BP variability was obtained by calculating 1) the SD of systolic (15.3±4.1 vs 14.8±3.7 mmHg, P=NS) and diastolic (12.9±3.4 vs 12.2±2.9 mmHg, P=NS) or day/night BP difference. In hypertensive men, plasma TT is independently associated with increased risk of major cardiovascular events in middle-aged hypertensive men. Central (aortic) blood pressures predict cardiovascular mortality with equal sensitivity compared to peripheral (brachial) blood pressures. The aim of the present study was to assess the relationship of plasma total testosterone (TT) with peripheral and central haemodynamics in hypertensive men.

**Methods:** We studied 70 non-diabetic, hypertensive men (mean age = 60 years old) for 10 yrs. At the 1st PAMELA examination carried out 10 yrs before. For similar heart rate, office and home blood pressures, and blood pressure variability (Fourier spectral analysis).

**Results:** In the PAMELA study cognitive function was assessed via minimental score (C, 24–30). For similar heart rate, office and home blood pressures, and blood pressure variability (Fourier spectral analysis).

**Conclusions:** The relation between blood pressure (BP) and cognitive function has received growing interest in recent years. Some cross-sectional studies have shown an inverse association between BP and cognitive dysfunction, while longitudinal studies yield mixed results.
Results: Subjects were 56.6±8.5 years old. 36% were male and 49.3% had hypertension. Mean (SD) baseline eGFR was 101.2±10.6 ml/min/1.73 m². Mean (SD) baseline cSBP was 133.1±18.5 mmHg. After 2.2 years follow-up, the incidence of rapid decline and CKD was 7.3% and 0.7%, respectively. In multivariable logistic-regression analyses, cSBP was associated with both rapid decline (odds ratio [OR] 95% confidence interval [CI] 1.02, 1.01–1.02) and incident CKD (OR, 95% CI, 1.03, 1.00–1.05) after adjustment for demographic variables, comorbidities, antihypertensive medications and baseline eGFR. This relationship remained (rapid decline, OR, 95% CI, 1.02, 1.01–1.02; incident CKD, OR, 95% CI, 1.00–1.03) even after further adjustment for peripheral SBP. However, peripheral SBP was not associated with either rapid decline or incident CKD after adjustment for confounders including cSBP.

Conclusion(s): cSBP is an independent risk factor related to early kidney function decline in a Chinese community-based population with normal kidney function. Future research should focus on the mechanisms of central as opposed to peripheral haemodynamics on kidney function decline.

4123 | BEDSIDE
Associations between serum uric acid levels and the incidence of hypertension and atrial fibrillation

Objective: Serum uric acid (SUa) is associated with many traditional cardiovascular risk factors as well as hypertension (HTN). Our aim was to investigate the relationship of SUA with HTN and atrial fibrillation as also the correlation of SUA with pulse wave velocity and specific diastolic echocardiographic parameters in hypertensive patients.

Design and methods: We prospectively enrolled 678 hypertensive patients (mean age 61.9) and 143 controls (mean age 68.3). In all subjects routine blood chemistry, including SUA determination, echocardiographic examination and 24 h ambulatory blood pressure (BP) monitoring were obtained. The group of hypertensives was divided into two subgroups: subgroup A (N=47): hypertensives with atrial fibrillation and subgroup B (N=631): hypertensives in sinus rhythm. We investigated the differences of SUA levels among group A, group B and the control group. In the second part we studied the correlation of SUA with left atrial diameter (LA), left ventricular mass (LVM) and pulse wave velocity (PWV) in the overall hypertensive population (N=678).

Results: Logistic regression analysis showed that increased SUA levels were significantly and positively associated with the incidence of hypertension and atrial fibrillation. The group A: 9.3±1.8 mg/dl vs group B: 5.2±0.9 mg/dl vs control group: 4.8±1.8 mg/dl, p<0.001). Furthermore the ANOVA regression analysis revealed that SUA levels are significantly associated with LVM (p<0.001) and LA (p<0.001), while there was no significant correlation between SUA and PWV (p=NS). For a 100 mg and 10 mm increase in the LVM and LA respectively, an 0.4 and 0.6 mg/dl increase in biomarkers of myocardial injury and fibrosis in patients with breast cancer.

Conclusion: Increased SUA levels were significantly associated with the incidence of hypertension and atrial fibrillation, while there was also a strong positive association between SUA, LVM and LA, implicating that hyperuricemia might be a novel risk factor for the LA and LV remodelling and finally for the development of atrial fibrillation.

KILLING THE HEART

4149 | BEDSIDE
Can we predict which patients are at risk of florourouracil cardiotoxicity?

Objective: Serum uric acid (SUa) is associated with many traditional cardiovascular risk factors as well as hypertension (HTN). Our aim was to investigate the relationship of SUA with HTN and atrial fibrillation as also the correlation of SUA with pulse wave velocity and specific diastolic echocardiographic parameters in hypertensive patients.

Design and methods: We prospectively enrolled 678 hypertensive patients (mean age 61.9) and 143 controls (mean age 68.3). In all subjects routine blood chemistry, including SUA determination, echocardiographic examination and 24 h ambulatory blood pressure (BP) monitoring were obtained. The group of hypertensives was divided into two subgroups: subgroup A (N=47): hypertensives with atrial fibrillation and subgroup B (N=631): hypertensives in sinus rhythm. We investigated the differences of SUA levels among group A, group B and the control group. In the second part we studied the correlation of SUA with left atrial diameter (LA), left ventricular mass (LVM) and pulse wave velocity (PWV) in the overall hypertensive population (N=678).

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Conclusion: Increased SUA levels were significantly associated with the incidence of hypertension and atrial fibrillation, while there was also a strong positive association between SUA, LVM and LA, implicating that hyperuricemia might be a novel risk factor for the LA and LV remodelling and finally for the development of atrial fibrillation.

4150 | BEDSIDE
Trimetazidine prevents doxorubicin cardiotoxicity: echo and biomarker study
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Background: Anthracyclines are highly effective for treatment of breast cancer but associated with irreversible cardiotoxicity. Trimetazidine is a metabolic agent proved to be effective in stable angina and heart failure.

Hypothesis: The aim of the study was to investigate the effectiveness of primary prevention of anthracycline cardiotoxicity with trimetazidine in patients with breast cancer.

Methods: 41 breast cancer patients with indications to anthracyline therapy and without history of cardiovascular disease or previous exposure to anticancer treatment were prospectively evaluated with echocardiography within one week before first treatment and 6 months after inclusion. Ejection fraction (EF) was calculated from biplane method of discs and peak global longitudinal systolic strain (S) was calculated from apical views with Echopac, GE software. Biomarkers of myocardial injury and fibrosis were additionally tested before chemotherapy and 6 months after the treatment (high sensitive troponin T [hsT], Roche; myeloperoxidase [MPO], Hybutek biocyt; Galectin-3 [Ga3], Elioscience; ST2, Critical diagnostics. Patients were randomized to receive trimetazidine 35 mg bid (20 patients) or standard chemotherapy only (21 patients – control group).

Results: None of the patients developed symptoms of heart failure. No significant decrease of EF was observed 6 months after chemotherapy in control (61.4±3.0 vs 60.1±2.7, p=0.08) and trimetazidine group (61.3±3.5 vs 61.2±3.5, p=0.28). At the same time 19% (4 patients) experienced decrease of EF -5% from baseline values was observed in control group only (S= -21.0±3.2 vs 20.6±3.6%, p=0.12 in trimetazidine group).

Control group experienced significant increase in hsT from 3.8±1.2 to 7.5±3.8 ng/L, p=0.008, and ST2 from 16.8±9.4 to 20.2±10.4 ng/ml p=0.038, MPO level significantly decreased from 10.0±3.8 to 7.8±2.2 ng/ml p=0.016, Ga3 values remained stable (from 5.5±1.8 to 4.7±5.9 ng/ml p=0.108). At the same time no significant changes of biomarkers were observed in trimetazidine group (hsT from 4.7±2.1 to 6.1±4.0 ng/ml p=0.105, ST2 from 14.6±4.2 to 16.4±4.1 ng/ml p=0.077, MPO 10.3±3.4 to 9.0±3.6 ng/ml p=0.385, Ga3 5.1±1.2 to 5.3±1.7 ng/ml p=0.629.

Conclusions: Trimetazidine prevented subclinical systolic dysfunction and increase in biomarkers of myocardial injury and fibrosis in patients with breast cancer treated with doxorubicin.

4151 | BENCH
Folic acid reduces doxorubicin-induced cardiomyopathy by modulating endothelial nitric oxide synthase and mitochondrial integrity
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Purpose: Endothelial nitric oxide synthase (eNOS) plays an important role in the pathogenesis of doxorubicin (DOXO)-induced cardiomyopathy. Here we tested the hypothesis that folic acid (FA), as an eNOS modulator, attenuates DOXO-induced cardiomyopathy and mitochondrial injury.

Methods: Male C57BL/6J mice (n=265) received DOXO (1x 20 mg/kg, i.p) or saline ( sham). (FA 10 mg/d po) or placebo was administered from 7 to 13 weeks after DOXO administration until the end of the experiment (10d). Left ventricular (LV)
function was measured by echocardiography; fibrosis and apoptosis by Picrosirius Red and TUNEL staining, respectively; eNOS uncoupling, activity and S-glutathionylation by co-immunoprecipitation and immunoblotting; superoxide (O2−) production by lucigenin-enhanced chemiluminescence; cardiac NO by Griess reaction. Mitochondrial oxygen consumption measurements and electron micro- 
scopy were performed at day 6.

**Results:** DOXO produced 70% mortality (P <0.01 vs sham), while mice receiv-
ing DOXO and FA (DOXOFA) had significantly lower mortality (45%; P <0.01). FA ameliorated DOXO-induced LV dysfunction, fibrosis, and apoptosis (Table). Uncoupling, activity and glutathionylation levels of eNOS were restored in DOX-
OFA, and subsequently lead to a reduction in O2− generation and an increase in 
cardiac NO. Furthermore, FA attenuated mitochondrial dysfunction and morpho-
logical changes.

**Folic acid effects after doxorubicin**

<table>
<thead>
<tr>
<th>Group</th>
<th>Stroke volume/tibia length (µl/cm)</th>
<th>Collagen content (%)</th>
<th>Apoptosis (%)</th>
<th>eNOS uncoupling (AU)</th>
<th>eNOS activity (AU)</th>
<th>eNOS S-glutathionylation (AU)</th>
<th>Superoxide production (RLU/sec/mg)</th>
<th>Caspase-3 (%)</th>
<th>Caspase-9 (%)</th>
<th>State 3 mitochondria (AU)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sham</td>
<td>20.0±3.8</td>
<td>1.6±0.2</td>
<td>0.16±0.03</td>
<td>0.00±0.04</td>
<td>0.00±0.03</td>
<td>0.00±0.09</td>
<td>188±141</td>
<td>0.15±0.04</td>
<td>9.1±1.1</td>
<td>33.9±2.7</td>
</tr>
<tr>
<td>DOXO</td>
<td>19.2±2.1</td>
<td>13.2±8.6*</td>
<td>0.15±0.04</td>
<td>0.98±0.01</td>
<td>1.24±0.08</td>
<td>1.00±0.06</td>
<td>206±181</td>
<td>0.15±0.04</td>
<td>14.0±1.7</td>
<td>21.7±2.1*</td>
</tr>
<tr>
<td>DOXOFA</td>
<td>20.2±1.8</td>
<td>9.4±1.9*</td>
<td>1.10±0.16</td>
<td>1.68±0.14*</td>
<td>6.63±0.06*</td>
<td>1.93±0.26*</td>
<td>683±79*</td>
<td>5.0±0.8</td>
<td>5.0±0.8*</td>
<td>39.6±3.1*</td>
</tr>
<tr>
<td>DOXOFA</td>
<td>20.2±1.8</td>
<td>9.4±1.9*</td>
<td>1.10±0.16</td>
<td>1.68±0.14*</td>
<td>6.63±0.06*</td>
<td>1.93±0.26*</td>
<td>683±79*</td>
<td>5.0±0.8</td>
<td>5.0±0.8*</td>
<td>39.6±3.1*</td>
</tr>
</tbody>
</table>

Data are mean ± SEM. eNOS, endothelial nitric oxide synthase; RLU, relative light unit; AU, arbitrary unit. n=4−10/group. *P<0.05 vs corr. sham; §P<0.05 vs corr. DOXO.

**Conclusion:** Targeting eNOS with FA might be a new and immediate therapeutic approach to reduce DOXO-induced cardiomyopathy.

### 4152 | BENCH

**Cardio-Oncology: the cardioprotective role of NACA in reducing oxidative stress due to doxorubicin and trastuzumab**


**Introduction:** Despite the clear therapeutic benefits of the anti-cancer drugs Doxorubicin (DOX) and Trastuzumab (TRZ) on improving the overall survival in women with breast cancer, the risk of developing heart failure cannot be ig-
ored. Amongst the potential mechanisms of DOX+TRZ mediated cardiotoxicity, increased oxidative stress (OS) and apoptosis has gained recent attention.

**Purpose:** To investigate whether a novel anti-oxidant, N-acetylcysteine amide (NACA), can attenuate DOX+TRZ mediated cardiac dysfunction in a murine model.

**Methods:** A total of 65 wild-type C57Bl/6 female mice received one of the following drug regimens: i) 0.9% saline (n=5); ii) DOX (20 mg/kg; n=15); iii) DOX+TRZ (20 mg/kg; 10 mg/kg; n=15); iv) NACA+DOX (250 mg/kg; n=15); or v) NACA+DOX+TRZ (n=15) and were followed for 10 days. In vivo cardiac function was assessed daily. At day 10, cardiac tissue was used to measure superoxide (O2−) production by lucigenin-enhanced chemiluminescence; cardiac NO by Griess reaction. Mitochondrial oxygen consumption measurements and electron mi-

croscopy were performed at day 6.

**Results:** Left ventricular ejection fraction significantly decreased and the left ven-
tricular end diastolic/systolic dimension and LV mass index significantly increased in single doxorubicin group compared to high dose seapolynol plus doxorubicin group. Also, electron microscopic finding showed less impaired myocardial and mi-

tochondria in high dose seapolynol plus doxorubicin group than in single dox-

**Conclusions:** Our data showed that high dose seapolynol had cardioprotective effects against doxorubicin-induced cardiotoxicity in a murine animal model with the evidence of electron microscopic finding in addition to echocardiographic results.

### 4154 | BEDSIDE

**Galectin-3 and longitudinal global strain predict drug-related cardiotoxicity in patients with breast cancer**

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**Background:** The methods currently available to identify patients (pts) at risk for cardiotoxicity (CTX) after chemotherapy (CT) are insufficient.

**Methods:** Prospective study of pts newly diagnosed with BC. Clinical, echocar-
diographic and biomarker (Troponin I, NT-proBNP and Galectin-3 (Gal3)) evalua-
tions were performed before and 1, 3, 6, 9 and 12 months after CT. The echocar-
diographic assessment included measurement of left ventricular ejection fraction (EF) and myocardial deformation analysis by speckle tracking. CTX was defined as a decline in initial EF of at least 5% to an absolute value <55%.

**Purpose:** To assess the role of biomarkers and myocardial deformation analysis in early detection of CTX in pts with breast cancer (BC).

**Results:** The pts who developed CTX had lower longitudinal global strain at 3 months (<15.6±0.9 vs. −19.4±2.7; P=0.009) and this parameter showed high accuracy in predicting the endpoint (AUC 0.92; P=0.016). Gal3 was significantly elevated 3 months after CT (11.9±4.3 vs. 14.3±5.6 ng/mL; P<0.001), especially in those pts who developed CTX (19.5±5.2 vs. 13.8±5.5 ng/mL; P=0.023). This biomarker was an accurate predictor of CTX (AUC 0.84; P=0.027 – figure). The cut-off value of 17.8 ng/mL showed the best specificity- 

**Conclusions:** Longitudinal global strain and Gal3 measured 3 months after CT were strong predictors of CTX in pts with BC.
4157 | BEDSIDE
New mechanisms of taxanes-related cardiotoxicity in women with breast cancer
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Data about mechanisms of taxanes-related cardiotoxicity, frequently detected in breast cancer, is lacking.

Aim: To describe the mechanisms and the outcome of taxanes-related LV dysfunction.

Methods: 35 women with HER2- breast cancer (45±7 years) were evaluated at baseline, after the 1st cycle, immediately after taxanes, and 2 years after therapy, in order to assess LVEF and deformation (by 4D echo): radial (RS), longitudinal (LS), circumferential (CS), and area strain (AS); p index for arterial stiffness; oxidative stress from carboxyl concentration into the plasma proteins (CCPP); and genetic variation from genotypes rs28371759, rs2032582, and rs1056836.

Results: 13 patients developed cardiotoxicity (group I), recovered 2 years after therapy, whereas 22 patients did not (group II) (table). LV systolic and oxidative stress were increased in group I (p: 11.6±4 vs 8.1±3). CCPP: 0.54±0.120 vs 0.320±0.099 mmol/mg, both p<0.01. Homozygote of genotype rs1056836 was related to the decrease of LVEF (r=0.45, p<0.05). A reduction of AS by 16% after the 1st cycle of taxanes was the most powerful predictor of LVEF reduction after therapy.

Acknowledgement/Funding: PN-II-ID-PCE-2011-3-0791, no. 112/2011 and POSDRU/159.1.5/S/141531

4158 | BEDSIDE
Detection of early and late left and right ventricular dysfunction in patients treated with anthracyclines
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Introduction: Cardiotoxicity can be a side effect of chemotherapy (CT) with anthracyclines and other drugs used in oncological therapy. Echocardiographic monitoring is recommended for timely detection of left ventricular dysfunction. Myocardial deformation imaging has been suggested to have higher reproducibility and sensitivity compared to conventional echocardiography. The effects of CT in right ventricular function are poorly studied.

Methods: Prospective echocardiographic study of a cohort of patients (pts) referred for CT with anthracyclines. Echocardiography done one week before the beginning of CT (T0), one week after the first cycle (T1), one week after the third cycle (T2), one week after the conclusion of CT (6-8 cycles, T3) and 1 year after the conclusion of CT (T4). In each moment, a conventional echocardiographic study was performed (M-mode, 2D and Doppler assessment of the dimensions and systolic and diastolic function of the left and right ventricles), as well as 2D-speckle tracking strain of the left ventricle.

Results: Fifty-one pts (breast cancer, n=32, from which 5 c-erbB2-positive; lymphoma, n=14; gastric cancer, n=5). Treated with doxorubicin, n=26 or epirubicin, n=25. Age 51±12.4 years, forty (78.4%) females. A significant and progressive decrease of global longitudinal strain (GLS) was noticed, throughout and after CT. T0: −22.5±2.6% T1: −19.3±3.0% T2: −17.3±2.0% and at T4: −16.2±2.7% (p<0.0005). Left ventricular ejection fraction (LVEF) also decreased significantly throughout CT (66.7±4.0% at T0; 64.1±3.3% at T1; 62.2±2.9% at T3, p<0.0005), but partially recovered in the long term (62.6±4.6% at T4, p=0.005 vs T0 but p=NS vs T1 or T2). At T4, GLS was −19% in 72.4% of the pts and −15% in 10.3%. All pts except one had FE >55% at T4 and in 10.3% a >10% decrease in LVEF was observed between T0 and T4. A GLS at T2 >−17.5% had a sensitivity of 80% and a specificity of 91.5% to predict a >10% decrease of LVEF between T0 and T3 (AUROC=0.95; p<0.02), but no absolute value or relative change in strain was able to predict a >10% decrease in LVEF between T0 and T4. Right ventricular systolic function decreased significantly throughout and after CT (TAPSE 23.3±2.9 mm at T0; 23.6±3.7 mm at T1; 22.3±3.8 mm at T2; 21.2±2.7 mm at T4, p=0.001).

Acknowledgement/Funding: PN-II-ID-PCE-2011-3-0791, no. 112/2011 and POSDRU/159.1.5/S/141531
Conclusions: Anthracyclines provoke a significant and progressive decrease of left ventricular function, during and after CT. GLS is a sensitive and early marker of myocardial lesion and was still decreased in the long-term. Right ventricular function also progressively decreases and should be monitored.

**RISK STRATIFICATION IN PULMONARY EMBOLISM AND IN PULMONARY HYPERTENSION**

### 4174 | BEDSIDE

**Acute pulmonary embolism: external validation of the 2014 risk stratification model of the European Society of Cardiology**

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**Background:** In patients with acute pulmonary embolism (PE), risk stratification for short-term mortality is crucial to drive clinical management. The European Society of Cardiology (ESC) has recently proposed an updated model for risk stratification based on clinical features, right ventricle dysfunction (RVD) and/or elevated troponin (2014-ESC model).

**Methods:** The aim of this study was to provide an external validation of the 2014-ESC model. Consecutive patients with symptomatic, objectively confirmed PE were included in prospective cohorts that were subsequently merged in a collaborative database. Patients were included in the analysis if full information about their sPESI score, RVD (by either echocardiography or computed tomography) and troponin levels were available. Study outcomes were 30-day death and PE-related death (as adjudicated by the local investigator).

**Results:** Among 906 patients (mean age 68±16, 489 females), 801 were hemodynamically stable. Death and PE-related death occurred in 7.2% and 4.1% of the patients. Death rates according to risk stratification (2014 and 2008-ESC models) are reported in the Table. Of the 196 low-risk patients died (0.5%). The 2014 and the 2008 ESC models showed similar discriminatory powers for death (c-statistics 0.71; 95% CI 0.65–0.77 versus 0.71; 95% CI 0.65–0.78) as well as for PE-related death (c-statistics 0.77; 95% CI 0.70–0.85 versus 0.79; 95% CI 0.72–0.85).

**Conclusions:** The 2014-ESC model avoids further testing in about 20% of the cases. The 2014-ESC model and the 2008 ESC models showed similar discriminatory powers for death (c-statistics). Further studies are required to improve the clinical profile of patients at intermediate-risk to justify a treatment upgrading.

**Acknowledgement/Funding:** this study was performed without any external support.

### 4175 | BEDSIDE

**BNP testing performed after triaging patients with acute PE by standard Hestia decision rule is not needed - a randomized trial**

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**Background:** Traditionally, patients with acute pulmonary embolism (PE) are hospitalised for initial anticoagulant treatment. Out of hospital treatment has in- creased but there is still great uncertainty as to what is the optimal triaging instrument. BNP testing is a promising simple bedside tool in acute PE, which has not been extensively investigated in this setting.

**Aims:** To investigate the efficacy and safety of selecting PE patients for outpatient treatment by NT-proBNP testing.

**Methods:** Randomized non-inferiority trial conducted in the Netherlands. Patients with CT pulmonary angiography proven acute PE were first screened for outpatient treatment eligibility based on the Hestia criteria (Zondag et al JTH 2011). Patients without any of the Hestia criteria were randomized to (1) discharge within 24 hours after diagnosis of acute PE, or (2) additional NT-proBNP testing. Patients in the BNP group were only discharged within 24 hours after diagnosis, if NT-proBNP was <500ng/L; they were admitted to the hospital if NT-proBNP was ≥500ng/L. Primary endpoint was 30-day adverse outcome defined as PE or bleeding-related mortality, cardiopulmonary resuscitation or ICU admission. Secondary endpoints were recurrent VTE, major bleeding and all-cause mortality.

**Results:** Between 2010 and 2013, 550 patients were randomized. In the NT-proBNP group, 34/275 (12%) had elevated NT-proBNP values and were managed as inpatients. The primary endpoint occurred in none of these 275 patients (0%; 95% CI 0–1.3%), versus in 3/275 (1.1%; 95% CI 0.2–3.2%) of the patients in the direct discharge group (p=0.08). These 3 patients had normal NT-proBNP levels measured post-hoc. During 3-month follow-up, recurrent VTE occurred in 2 patients (0.73%; 95% CI 0.1–2.6%) in the NT-proBNP group versus 3 patients (1.1%; 95% CI 0.2–3.3%) in the direct discharge group (p=0.65). The rates of major bleeding were 0.4% vs 1.1% (p=0.62) and of all-cause mortality 1.5% vs 1.1% (p=0.70), respectively.

**Conclusion:** Prognostic assessment, based on NT-proBNP levels does not affect 3-month outcomes. It changes the routine in the mortality of patients. It is concluded that additional BNP testing is not needed after applying the Hestia decision rule.

### 4176 | BEDSIDE

**Crossing of a clinical score, cardiac troponin, and echocardiography testing algorithm for risk stratification of normotensive patients with acute symptomatic pulmonary embolism**

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**Background:** For risk stratification of normotensive patients with acute symptomatic pulmonary embolism (PE), the updated guidelines of the European Society of Cardiology (ESC) recommend use of an algorithm that sequentially applies risk stratification of normotensive patients based on a clinical score, imaging testing assessing right ventricle (RV) function, and cardiac biomarkers. This study aimed to validate the ESC prognostic algorithm.

**Methods:** We retrospectively examined the cohort of normotensive patients that had acute symptomatic PE and enrolled in the multicenter prospective protect study. Using the baseline dataset collected at the time of PE diagnosis, the central coordinating center prospectively determined the simplified Pulmonary Embolism Severity Index (sPESI). Patients underwent transthoracic echocardiography within 24 hours after diagnosis of PE, and the core laboratory personnel measured cardiac troponin I levels. This study used a complicated course (i.e., death from any cause, hemodynamic collapse, or adjudicated recurrent PE) through 30 days after the PE diagnosis as the primary outcome.

**Results:** Of 848 patients, 313 (37%; 95% confidence interval [CI], 34–40%) had a sPESI score >1 (low-risk ESC group), and 5 (1.6%; 95% CI, 0.5–3.7%) of these patients experienced a complicated course. Of the 63% (535/848) patients with a sPESI score ≤1 (intermediate-risk ESC group), 478 (89%) had normal RV function on echocardiography and/or normal troponin level (intermediate-low ESC group), and 48 (10%; 95% CI, 7.3–13%) experienced a complicated course. Fifty-seven (11%; 95% CI, 8.0–13%) of the 535 patients with a sPESI score >1 had both echocardiographic RV dysfunction and elevated troponin level (intermediate-high ESC group), and 10 (18%; 95% CI, 7.7–27%) experienced a complicated course. Of the 194 patients with tachycardia and/or mild hypotension, 164 (85%; 95% CI, 79–90%) had normal RV function on echocardiography and/or normal troponin level (intermediate-low ESC group), and 18 (11%; 95% CI, 6.2–16%) experienced a complicated course. Thirty-five (15%, 95% CI, 10–21%) of the 194 patients with tachycardia and/or mild hypotension had both echocardiographic RV dysfunction and elevated troponin level (intermediate-high ESC group), and 7 (23%; 95% CI, 8.2–38%) experienced a complicated course.

**Conclusions:** A prognostic strategy that uses a simple clinical rule, echocardio- graphy and cardiac troponin testing in a stepwise fashion effectively risk strati- fies normotensive patients with acute symptomatic PE. Compared to the sPESI, tachycardia and/or mild hypotension refine stratification of intermediate-risk PE.

### 4177 | BEDSIDE

**Acute not-high-risk pulmonary embolism: a comparison of risk assessment strategies**

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**Background and Introduction:** Based on numerous scores and models for risk
stratification of normotensive pulmonary embolism (PE) developed and validated during the past years, a new algorithm for risk assessment was introduced by the 2014 ESC guideline.

**Purpose:** To compare the performance of the new algorithm proposed by the 2014 ESC guideline with other scores for risk stratification of not-high-risk PE.

**Methods:** Not-high-risk patients with confirmed PE were included in an observational cohort study at our university medical center Germany between September 2008 and August 2014. Risk classes were assessed according to the algorithms proposed by the 2008 and 2014 ESC guideline, the sPESI, the Bova score and the FAST score. Age-adjusted cut-off value for hsTnT (>14 pg/ml for <75 years, ≥45 pg/ml for ≥75 years) was used for calculation of the Bova and the (modified) FAST score.

**Results:** During the first 30 days, 25 of 388 patients (6.4%) had an adverse outcome, defined as PE-related death or complications) and 14 patients (3.6%) died. The sPESI, the 2008 and the 2014 ESC guideline algorithms classified a greater number of patients in the higher risk classes while the Bova and the FAST score classified more patients in the low-risk classes. Regardless of the score or algorithm used, the risk of an adverse 30-day outcome was highest in the high-risk classes while all patients classified in low-risk classes had a favourable 30-day outcome (no PE-related deaths, rate of an adverse outcome 0 to 1.4%). The c-index for prediction of an adverse 30-day outcome was higher for the ESC 2014 algorithm (AUC, 0.71 [0.64–0.79]) compared to the ESC 2008 algorithm (AUC, 0.63 [0.57–0.74]) and highest for the FAST score (AUC, 0.82 [0.75–0.86]). Regardless of the score used, increase in risk classes was associated with an elevated risk of an adverse 30-day outcome with the highest OR for patients classified as "high-risk" in the FAST score (compared to "low-risk"; OR, 15.9 [5.3–47.4]) and in the FAST score compared to "low-" and "intermediate-risk"; OR, 37.8 [5.1–282.4]; 19.3% adverse outcome).

**Conclusions:** The new algorithm proposed by the ESC 2014 guideline is more suitable for risk stratification of normotensive PE patients compared to the only tool currently available, the 2008 ESC guideline algorithm. Good prognostic performance was observed for the FAST score if an age-adjusted hsTnT cut-off value was used for calculation instead H-FABP. All available scores and algorithms safely identify low-risk patients while the FAST and the Bova score most reliably identify patients at elevated risk.

4179 | BEDSIDE

Investigation of a new pathophysiological axis for risk stratification of normotensive pulmonary embolism: prognostic impact of copeptin

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**Background:** Vasopressin plays a key role in cardiovascular homeostasis and is released upon stress and hypotension. While previous studies emphasize the value of the vasopressin surrogate marker copeptin in myocardial infarction, heart failure or pulmonary hypertension, the prognostic value of copeptin in pulmonary embolism (PE) is unknown.

**Purpose:** To assess the prognostic impact of copeptin in normotensive patients with PE.

**Methods:** We prospectively studied 268 consecutively normotensive patients with acute PE at our University Hospital between 09/2008 and 08/2014. Copeptin plasma levels were measured on admission using a commercial sandwich immunoluminometric assay.

**Results:** Copeptin levels ranged between 0.9 and 705.0 pg/ml with a median concentration of 13.8 (IQR, 5.9–44.5) pg/ml. Patients with copeptin levels above the median were older (p < 0.001), had more often cardiopulmonary diseases (p = 0.002) or renal insufficiency (p = 0.001), and presented more frequently with tachycardia (p = 0.001) or hypoxemia (p = 0.034). Overall, 15 patients (5.6%) had an adverse 30-day outcome defined as PE-related death, resuscitation, catecholamine administration or intubation. These patients classified more patients in the low-risk classes. Regardless of the score or algorithm used, the risk of an adverse 30-day outcome was highest in the high-risk classes while all patients classified in low-risk classes had a favourable 30-day outcome (no PE-related deaths, rate of an adverse outcome 0 to 1.4%). The c-index for prediction of an adverse 30-day outcome was higher for the ESC 2014 algorithm (AUC, 0.71 [0.64–0.79]) compared to the ESC 2008 algorithm (AUC, 0.63 [0.57–0.74]) and highest for the FAST score (AUC, 0.82 [0.75–0.86]). Regardless of the score used, increase in risk classes was associated with an elevated risk of an adverse 30-day outcome with the highest OR for patients classified as "high-risk" in the FAST score (compared to "low-risk"; OR, 15.9 [5.3–47.4]) and in the FAST score compared to "low-" and "intermediate-risk"; OR, 37.8 [5.1–282.4]; 19.3% adverse outcome).

**Conclusions:** The new algorithm proposed by the ESC 2014 guideline is more suitable for risk stratification of normotensive PE patients compared to the only tool currently available, the 2008 ESC guideline algorithm. Good prognostic performance was observed for the FAST score if an age-adjusted hsTnT cut-off value was used for calculation instead H-FABP. All available scores and algorithms safely identify low-risk patients while the FAST and the Bova score most reliably identify patients at elevated risk.

4180 | BEDSIDE

RV dysynchrony predicts clinical outcomes after balloon pulmonary angioplasty in patients with chronic thromboembolic pulmonary hypertension

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**Background:** Balloon pulmonary angioplasty (BPA) may improve hemodynamics and exercise tolerance in patients with chronic thromboembolic pulmonary hypertension (CTEPH). Recently, we reported a significant correlation between echocardiographic right ventricle (RV) parameters and right heart catheterization (RHC) in patients with CTEPH, and that BPA could ameliorate RV function. However, long-term follow up of RV function after BPA has not been fully established.

**Purpose:** The objectives of this study were to follow up the RV hemodynamics and function after BPA, using RHC and echocardiography.

**Methods:** We studied 23 consecutive patients with CTEPH who underwent BPA and assessed RV hemodynamics and function before, immediately after, and at 6 months after the procedure. RV hemodynamic parameters, including mean pulmonary artery pressure (mPAP), pulmonary vascular resistance (PVR), and cardiac output were recorded by RHC. RV function was assessed using two-dimensional echocardiographic parameters such as RV diameter (RVD), tricuspid annular plane systolic excursion (TAPSE), RV S', RV index of myocardial performance (RIMP), and RV fractional area change (RVFAC). We also used two-dimensional speckle-tracking echocardiography (2DSTE) and three-dimensional transaxial echocardiography (3DTE) to investigate RV strain and RV volumetric parameters including RV ejection fraction (RVEF), RV end diastolic volume (RVEDV), and RV end systolic volume (RVESV). RV dysynchrony was also assessed by
the standard deviation (SD) of the intervals from QRS onset to peak systolic strain for 6 segments of the RV (SDTTP). Finally, exercise capacity was assessed by the 6-minute walk distance (6MWD) test.

**Results:** Hemodynamic parameters such as mPAP, PVR, and cardiac index were significantly improved immediately after BPA, and the effects of BPA were maintained at 6-month follow-up. RVD, RVEDV, and RVEF were significantly reduced after BPA. TAPSE, RVFAC, RVEF, and RV mid free wall longitudinal strain (MFWSL) were significantly improved after BPA, implicating that RV systolic function was ameliorated. RV dysynchrony was also improved after BPA. Receiver operating characteristic analysis revealed that SDTTP was a good predictor for improvement of 6MWD (sensitivity of 86% and specificity of 56%, area under the curve: 0.78, P<0.03).

**Conclusions:** BPA induced RV reverse remodeling and improved RV function, as assessed successfully by echocardiography. RV dyssynchrony could be a useful parameter for assessing exercise tolerance after BPA.

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**4181 | BEDSIDE**

**Reduction in NT-proBNP and its correlation with survival in patients with PAH treated with riocigaut:** 2-year results from the PATENT-2 long-term extension study


**Purpose:** Increased levels of N-terminal prohormone of brain natriuretic peptide (NT-proBNP), a biomarker of right ventricular dysfunction, are associated with poorer outcomes in pts with pulmonary arterial hypertension (PAH). Riociguat reduced NT-proBNP levels compared with placebo in pts with PAH during the 12-wk PATENT-1 study.

**Background:** Increased levels of N-terminal prohormone of brain natriuretic peptide (NT-proBNP), a biomarker of right ventricular dysfunction, are associated with poorer outcomes in pts with pulmonary arterial hypertension (PAH). Riociguat reduced NT-proBNP levels compared with placebo in pts with PAH during the 12-wk PATENT-1 study. Pts with PAH who were treatment-naive or pretreated with ERAs or prostanooids entered PATENT-2 after completing PATENT-1 without ongoing drug therapy during the 6-month follow up. RVD, RVEDV, and RVEF were significantly reduced after BPA. TAPSE, RVFAC, RVEF, and RV mid free wall longitudinal strain (MFWSL) were significantly improved after BPA, implicating that RV systolic function was ameliorated. RV dysynchrony was also improved after BPA. Receiver operating characteristic analysis revealed that SDTTP was a good predictor for improvement of 6MWD (sensitivity of 86% and specificity of 56%, area under the curve: 0.78, P<0.03).

**Conclusions:** BPA induced RV reverse remodeling and improved RV function, as assessed successfully by echocardiography. RV dyssynchrony could be a useful parameter for assessing exercise tolerance after BPA.

**Survival by NT-proBNP levels**

**Figure 1. Survival by NT-proBNP levels**

**Conclusion:** Reduction in NT-proBNP in pts with PAH treated with riocigaut was sustained for up to 2 yrs in PATENT-2. Change from baseline in NT-proBNP correlated with survival and clinical worsening-free survival.

**Acknowledgement/Funding:** Editorial assistance was provided by Adelphi Communications Ltd (Bollington, UK), supported by Bayer Pharma AG.

**4182 | BEDSIDE**

**Outcome comparison of patients with idiopathic/heritable pulmonary arterial hypertension, pulmonary hypertension due to heart disease and pulmonary hypertension due to lung disease**


**Purpose:** Despite therapeutic advances for idiopathic/heritable pulmonary arterial hypertension (iPAH) the most common forms of pulmonary hypertension (PH) are due to heart disease (PH-LHD) and lung disease (PH-LD). The actual lack of effective medications for the underlying LD may explain the worse prognosis of patients with PH-LD in comparison with PH-HAP.

**Background:** Increased levels of N-terminal prohormone of brain natriuretic peptide (NT-proBNP), a biomarker of right ventricular dysfunction, are associated with poorer outcomes in pts with pulmonary arterial hypertension (PAH). Riociguat reduced NT-proBNP levels compared with placebo in pts with PAH during the 12-wk PATENT-1 study. Pts with PAH who were treatment-naive or pretreated with ERAs or prostanooids entered PATENT-2 after completing PATENT-1 without ongoing drug therapy during the 6-month follow up. RVD, RVEDV, and RVEF were significantly reduced after BPA. TAPSE, RVFAC, RVEF, and RV mid free wall longitudinal strain (MFWSL) were significantly improved after BPA, implicating that RV systolic function was ameliorated. RV dysynchrony was also improved after BPA. Receiver operating characteristic analysis revealed that SDTTP was a good predictor for improvement of 6MWD (sensitivity of 86% and specificity of 56%, area under the curve: 0.78, P<0.03).

**Conclusions:** BPA induced RV reverse remodeling and improved RV function, as assessed successfully by echocardiography. RV dyssynchrony could be a useful parameter for assessing exercise tolerance after BPA.

**Survival by NT-proBNP vs PH-LD**

**Figure 1. Survival by NT-proBNP levels**

**Conclusion:** Reduction in NT-proBNP in pts with PAH treated with riocigaut was sustained for up to 2 yrs in PATENT-2. Change from baseline in NT-proBNP correlated with survival and clinical worsening-free survival.

**Acknowledgement/Funding:** Editorial assistance was provided by Adelphi Communications Ltd (Bollington, UK), supported by Bayer Pharma AG.

**4183 | BEDSIDE**

**Prognostic value of right heart adaptation to pulmonary arterial hypertension: a prospective cohort study**


**Purpose:** In this study we employed 3D motion analysis of cardiac magnetic resonance (CMR) imaging to understand how RV contraction changes in the re-modeled hearts of PAH patients, what features of systolic dysfunction are most strongly related to outcome and whether this enables better discrimination of ventricles which are destined to fail.

**Methods:** A cohort of 271 patients diagnosed with PAH underwent conventional CMR imaging. We used automated segmentation to construct a 3D representation of RV systolic motion. For machine-learning the patients were randomly allocated to training (50%) and testing (50%) cohorts. Patterns of 3D contraction of survival were learnt from the training cohort using supervised principal component analysis (SPCA), and compared with RV ejection fraction (RVEF), pulmonary vascular resistance (PVR) and six-minute walk distance (6MWD) as predictors of survival in the test cohort. Analysis was repeated 1,000 times using randomly allocated cohorts.

**Results:** Patients were followed-up for a mean of 3.8 years and 99 (36.5%) patients died. Baseline 3D systolic motion predicted mortality significantly better than RVEF, PVR or 6MWD (all p<0.001) and predicted 5-year mortality significantly better than RVEF (receiver operating characteristics' area under curve: 0.58 vs 0.41, p<0.001). Deterioration in the longitudinal component of function was most strongly related to survival (longitudinal: 60%, circumferential: 24%, radial 16%) whereas all three components of function reflected a deterioration of
RVEF (longitudinal 39%, circumferential 33%, radial 28%; difference: p<0.001). RV basal freewall and septal function provided the most informative functional changes.

Conclusions: The failing RV in PAH is manifest by independently prognostic adaptations in septal/freewall mechanics and long axis dysfunction. Analysis of RV contraction in the pressure overloaded heart is facilitated by machine learning techniques and provides greater prognostic power than global measures of loss of function irrespective of hemodynamic parameters. We propose this as a new technique for predicting outcome from functional cardiovascular phenotypes.

ADVANCES IN CARDIAC REGENERATION

4189 | BENCH
Leukemia inhibitory factor enhances cardiomyocyte regeneration after myocardial infarction from endogenous stem cells and not from circulating bone marrow-derived cells.

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Purpose: Cardiac stem cells or precursor cells can regenerate cardiomyocytes, but the mechanisms underlying this effect remain unclear. Using a genetic fate-mapping model, we tested the hypothesis that leukemia inhibitory factor (LIF) influences cardiac stem cells and stimulates endogenous cardiomyocyte renewal after myocardial infarction (MI).

Methods: We generated CreLacZ mice in which the cardiomyocytes in the left ventricular field showed positive 5-bromo-4-chloro-3-indolyl-β-d-galactoside (X-gal) staining immediately after tamoxifen injection. We counted the number of X-gal-negative (newly generated) cardiomyocytes in the mice after various interventions, including the administration of the LIF plasmid. Combining this with a label-retaining strategy and a EGFP-bone marrow transplantation technique, we also analyzed the origin of cardiac regeneration. Results: More than 99.9% of the cardiomyocytes in the CreLacZ mice heart field showed positive X-gal staining after tamoxifen injection. Three months after MI, the MI mice had more X-gal-negative controls than the control mice (3.0±1.38/mm², MI; 0.47±0.16/mm², sham; p<0.05). The cardiac side population (CSP) cell fraction contained label-retaining cells, which differentiated into X-gal-negative cardiomyocytes after MI. We injected the LIF plasmid at the time of MI and found significant functional improvement in the LIF-treated group. At 1 month after MI, in the MI border, and MI scar area, the LIF-injected mice had 31.4±5.83 X-gal-negative cardiomyocytes/mm², while control mice had 12.3±2.56 X-gal-negative cardiomyocytes/mm² (p<0.05). On 5-ethyl-2'-deoxyuridine (EdU) administration after MI, the percentages of EdU-positive GSP cells in LIF-treated and control mice were 29.4±2.7% and 10.6±3.7%, respectively, suggesting that LIF influenced CSP proliferation. We also showed that LIF activated the JAK-STAT pathway in CSPs, in vivo and in vitro. The results observed in EGFP-bone marrow chimeric CreLacZ mice indicated that LIF did not stimulate cardiomyogenesis via circulating bone marrow-derived cells during the 4 weeks following MI.

Conclusions: LIF stimulates, in part, stem cell-derived cardiomyocyte regeneration by activating cardiac stem or precursor cells, but not circulating bone marrow-derived cells.

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4190 | BENCH
Epigenetic modulation of cardiac progenitor cells through miR-29a/Dnmt3a axis promotes their cardiac differentiation

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Epigenetic programming within the cardiac progenitor cell (CPC) niche controls CPC specification and differentiation, but the identity of putative mediators is poorly characterized.

To dissect these mechanisms, we used primary expanded Sca-1+ CPC from murine adult hearts and stimulated cardiomyocyte differentiation upon culture in a differentiation medium (DIFF) containing 5'-Azacytidine and TGFβ1 or co-cultured with rat cardiomyocytes. With this model, we previously showed that inducing deletion of β-catenin enhanced CPC differentiation in vitro and in vivo. Accordingly, we detected a constitutive activity of Wnt/β-catenin pathway in undifferentiated CPC (Axin2: 36±4%; Snai2: 46±7%: p<0.01) together with a reduced β-catenin protein level (62.80±7.5%; p<0.05) in DIFF-treated CPC, associated with an upregulation of Wnt antagonist Noggin (2.6±0.8; p<0.05). Several Wnt/β-catenin repressor genes, Wnt-1 expression is DNA methylation sensitive and susceptible to be regulated by the de novo DNA methyltransferases Dnmt3. Indeed, Dnmt3a was downregulated in CPC treated with DIFF, while siRNA targeting Dnmt3a decreased Wnt-1 promoter methylation (34.2±1.99%; p<0.05) and increased Wnt-1 gene expression in non-differentiated cells (425±254%; p<0.05). Dnmt3a silencing promoted CPC cardiac differentiation in co-culture assay (assessed by quantitative expression of cTnT: 162±7% vs. siRNA-ct; p<0.001). In parallel, we found an early upregulation of miR-29a (44±3%; p<0.01), a well-known regulator of Dnmt3a, in DIFF-treated CPC. Indeed, modulation of miR-29a using mimic or anti-miR affected Dnmt3a protein level, promoter methylation of Wnt-1 and Wnt-1 expression (mimic: 839±257%; LNA: 51±9%; p<0.05). Importantly, LNA treatment also significantly decreased CPC differentiation in co-culture assay (63±4% vs. ct: p<0.001). Altogether, this suggests that miR-29a controls CPC differentiation through Dnmt3a-dependent regulation of Wnt-1.

We conclude that CPC differentiation involves the epigenetic regulation of canonical Wnt/β-catenin activity through miR-29a/Dnmt3a axis, possibly amenable to therapeutic modulation for cardiac repair.
sensus on daily temperature, lag time and snowfall on ST segment elevation myoccardial infarction (STEMI).

Methods: A retrospective audit of all patients with STEMI within the coldest Canadian city was completed (January 1, 2009 to December 31, 2014). Temperature and snowfall data was collected from Environment Canada. Poisson regression modelling was used to identify the relationship between weather and STEMI. Weather characteristics tested included daily high (DH), low and average temperature on the same day, previous day, and two days before, along with the average temperature for the combined current and previous days, and the current and previous two days. Daily snowfall was analyzed similarly.

Results: Over the 6 year study period, there were 1817 STEMI. The DH was the strongest predictor of STEMI. Of days with a DH < 0°C, STEMI event rates were 0.94/day, compared to 0.79/day when DH = 0°C. Despite yearly variation, the average STEMI rate over the study period has a statistically significant linear trend across temperature (p < 0.0001). Temperature (DH) in the preceding 1 or 2 days was also predictive (p < 0.001). Higher temperature groups were not associated with higher STEMI rates. With every drop of 1°C in DH, the risk of STEMI increased by 0.7% (p < 0.001). Snowfall was a univariate predictor but showed no independent association after adjusting for temperature.

Conclusion: There is a clear association between daily temperature and STEMI risk with predictability seen 1 to 2 days prior to STEMI. Increased public awareness and or reallocation of health care resources should be considered to respond to the seasonal increased incidence of STEMI.

4196 | BEDSIDE

Particulate matter and NO2 air pollution trigger ST-elevation myocardial infarction: a case cross over study of Belgian STEMI registry

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Background: Previous studies have shown that air pollution particulate material (PM) is associated with increased risk of myocardial infarction. Effects of air pollution on the particular subset of transmural myocardial infarction (STEMI), the role of gaseous air pollutants such as NO2 and O3 and the susceptibility of specific populations are still under debate.

Methods: From 2009 to 2013 all patients of the Belgian prospective STEMI registry were included. National air pollution parameters were extracted from the Belgian Environment Agency and adjusted for population density using a validated spatial interpolation model. A case cross-over analysis of the risk of STEMI was performed and all risks were adjusted for ambient temperature, day of the week and season.

Results: 11428 STEMI patients were included in the study. According to WHO air quality guidelines, PM2.5 air quality standard was exceeded in 17.5% of days. Each 10 μg/m3 increase in PM10, PM2.5 and NO2 were respectively associated with an increased relative risk (RR) of STEMI of 1.026 (IC 95%; 1.001–1.054), 1.021 (IC 95%; 1.003–1.049) and 1.017 (IC 95%; 1.018–1.084). No effect of O3 was found (fig.1). These associations between air pollutants and STEMI were only observed in men (all p < 0.05). STEMI were associated with PM10 exposure in ≥ 75 μg/m3 patient (RR: 1.046, IC 95%; 1.002–1.092), and with NO2 in ≤ 54 μg/m3 (RR: 1.071, IC 95%; 1.010–1.136). No effect of air pollution on cardiac arrest and in-hospital STEMI mortality was found.

Conclusion: In Belgium, 10 μg/m3 increase in PM2.5 and NO2 increase the risk of STEMI of respectively 2.8 and 5.1%. This relation is observed only in men. Older population develop more STEMI in relation to PM exposure, whereas younger population appears more susceptible to NO2.

PREDICTING THE FUTURE: THE ACCURACY OF RISK SCORES

4203 | BEDSIDE

External validation of the biomarker-based ABC-stroke risk score for atrial fibrillation


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Background: The ABC-stroke score is a novel biomarker-based stroke risk score including the variables Age, Biomarkers (troponin-T high sensitivity [TnT] and N-terminal pro-B-type natriuretic peptide [NT-proBNP]), and Cardiovascular disease history (prior stroke). In the derivation cohort of 14701 pts with AF from the ARRITOTLE trial the ABC-stroke score outperformed the traditional CHA2DS2-VASc score (C index 0.67 vs. 0.62, p < 0.001). Purpose: To externally validate the ABC-stroke risk score in pts with AF and compare with the CHA2DS2-VASc score.

Methods: The STABILITY trial, randomising 15828 pts with stable coronary heart disease to darapladib or placebo showed no significant effect on cardiovascular outcomes. 1400 pts had a history of AF (689 on oral anticoagulation) and qualified for external validation of a stroke risk score in AF. Blood was collected at randomisation, and TnT and NT-proBNP were centrally analysed with high-sensitivity assays.

Results: In the external validation, based on 4751 person-years of follow-up and 48 adjudicated stroke events, ABC-stroke score achieved a C index of 0.66 in
Comparison to 0.58 for the CHA2DS2-VASc score (p = 0.001). The incidence rates (events per 100 person-years) were similar in the derivation and validation data within each predefined risk class: 0.69 vs. 0.72, 1.66 vs. 1.58, and 3.31 vs. 3.81. Kaplan-Meier curves within risk classes (Fig) for both the derivation and validation data illustrate that the ABC-stroke score was well-calibrated in different cohorts of AF-pts.

Conclusions: The ABC-stroke score was successfully validated and performed better than the CHA2DS2-VASc score in several populations with AF. The ABC-stroke score should thereby be ready for implementation as a decision support tool in routine clinical care.

4204 | BEDSIDE
Exercise capacity can significantly improve SCORE risk prediction model in low risk asymptomatic adults

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Background: The SCORE estimation system is used for cardiovascular risk stratification in apparently healthy adults. The purpose of the current study was to evaluate whether exercise capacity can be used to improve the accuracy of the SCORE cardiovascular risk estimation.

Methods: We investigated 21,301 asymptomatic men and women who were annually screened in a tertiary medical centre. All subjects were free of ischemic heart disease or diabetes, and had completed maximal exercise stress test according to the Bruce protocol at their first visit. The SCORE risk estimation system was used to evaluate individual cardiovascular risk for all subjects. The primary endpoint of the current analysis was all-cause mortality. The incremental contribution of exercise capacity in predicting the risk of death was evaluated by net reclassification improvement (NRI) and area under the receiver operating curve (AUROC).

Results: Mean age of the study population was 47±10 and 71% were men. There were 384 (1.80%) deaths during a mean follow up of 9.2±4.0 years. Kaplan Mayer survival analysis showed that both high SCORE and low exercise capacity are associated with poor survival (FIGURE). When added to the SCORE risk prediction, exercise capacity allowed improved risk stratification: NRI analysis showed a significant improvement (NRI) and area under the receiver operating curve (0.69 vs. 0.72, 1.66 vs. 1.58, and 3.31 vs. 3.81) in men and women. These observations were also present in the calibration plot of the ACC/AHA risk score. Discrimination analysis showed area under the curves of 0.78 in KORA and 0.73 in HNR.

Conclusion: Our results are in line with recently published reports documenting an overestimation of the true risk for ASCVD by the new AHA/ACC risk score. Nevertheless, results from the ROC analysis indicate reasonable discriminative power. We therefore recommend a re-calibration of the ACC/AHA risk score for the German population.

ECHO STRAIN IMAGING: WHAT DOES IT TELL EARLY AFTER MYOCARDIAL INFARCTION?

4237 | BEDSIDE
Two-dimensional diastolic speckle tracking echocardiography in the triage of patients with acute chest pain department

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Background: Two-dimensional diastolic speckle tracking echocardiography (2D-STE) has been reported to be useful for the diagnosis of myocardial ischemia by detecting delay in regional myocardial expansion after an episode of angina. The hypothesis is that 2D-STE is useful in the triage of patients with possible acute coronary syndrome (ACS) who visit emergency department (ED) complaining of chest pain.

Methods: 101 consecutive patients with acute chest pain and without wall motion abnormality were enrolled and underwent 2D-STE at ED. Left ventricular (LV) longitudinal, circumferential, transverse and radial strain values at aortic valve closure and one-third of diastolic duration were measured, and strain imaging diastolic index (SI-DI) was assessed to analyze regional LV delayed relaxation (Figure).

Results: After comprehensive clinical evaluations, ACS was diagnosed in 8 patients. 2D-STE was obtained at a mean of 7.5 hours after chest pain episode. SI-DI of longitudinal, circumferential, transverse and radial strain of ischemic segments were significantly lower than those of non-ischemic segments (44.6±24.2 vs. 59.3±37.0, 51.5±19.5 vs. 69.5±20.1, 56.3±20.5 vs. 81.6±20.6, 59.0±21.3 vs. 83.1±16.5, p < 0.001, respectively). Analysis of strain imaging diastolic index (SI-DI) was categorized to be useful for the diagnosis of myocardial ischemia by detecting delay in regional myocardial expansion after an episode of angina. The hypothesis is that 2D-STE is useful in the triage of patients with possible acute coronary syndrome (ACS) who visit emergency department (ED) complaining of chest pain.

Conclusions: 2D-STE has been reported to be useful for the diagnosis of myocardial ischemia by detecting delay in regional myocardial expansion after an episode of angina. The hypothesis is that 2D-STE is useful in the triage of patients with possible acute coronary syndrome (ACS) who visit emergency department (ED) complaining of chest pain.
The timeline of changes in regional systolic and diastolic function in patients with stunned myocardium

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Background: The purpose of this study was to evaluate the timeline of changes in regional systolic and diastolic left ventricular function within six months after successful reperfusion therapy of acute myocardial infarction (AMI).

Methods: 97 consecutive patients admitted with AMI and treated with successful percutaneous coronary intervention were included in this study. On days 1, 2, 3, 7, 30 and 180 following admission patients underwent transthoracic echocardiography with subsequent measurement of systolic longitudinal strain (SLS), systolic longitudinal strain rate (SLSR) and early diastolic longitudinal strain rate (DLISR) in left ventricular segments by speckle-tracking technique. 379 segments with systolic dysfunction at baseline, which recovered function after 180 days, were analyzed.

Results: The largest increase in regional SLS and SLSR was observed between days 1 and 2 (from −8.06±3.03 to −15.48±4.29, p<0.0001 and from −0.67±0.22 s⁻¹ to −1.24±0.33 s⁻¹, p<0.0001, respectively). On days 3, 7, 30 and 180 further improvement was noticeable, but the changes were less significant. The most significant improvement in regional DLISR was evenly distributed between days 1, 2, 3, 7 (0.71±0.24, 0.96±0.26, 1.16±0.30 and 1.42±0.35, respectively with p<0.0001 for all differences). The increase observed on days 30 and 180 was less significant.

Conclusion: The most of regional systolic function recovery after successful reperfusion therapy in patients with AMI occurs within the first 2 days. However, the recovery of regional diastolic function takes longer – the most significant part of improvement occurs within the first 7 days. These observations have clinical implications for diagnosis and treatment of patients with myocardial stunning.

MANAGEMENT OF CARDIGENIC SHOCK

Temporal trends in the epidemiology, management and outcome of patients with cardiogenic shock complicating acute coronary syndromes

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Background: Despite advances in the management of patients with an acute coronary syndrome (ACS), cardiogenic shock (CS) remains the leading cause of death in these patients.

Purpose: We sought to describe the evolution of clinical characteristics, in-hospital management and outcome of patients with CS complicating ACS.

Methods: We analysed data from five Italian nationwide prospective registries, conducted between 2001 and 2014, including consecutive patients with ACS.

Results: Out of 28,217 patients with ACS enrolled in the 5 registries, 1209 (4.3%) had CS during admission. Over the years, the proportions of CS patients with a history of heart failure declined, whereas those with hypertension, renal dysfunction, previous percutaneous coronary intervention (PCI) and atrial fibrillation significantly increased. The use of PCI considerably increased from 2001 to 2014 (19% to 60%; percentage change, 41 [95% CI 29 to 51]); while the rate of bypass surgery remained unchanged (2.3% to 3.3%; percentage change, 1 [95% CI –4 to 6]). In-hospital mortality of CS patients decreased from 68% (95% CI, 59–76) in 2001 to 38% (95% CI, 29–47) in 2014 (percentage change, −30 [95% CI –41 to −18]). After adjustment for the changing baseline characteristics, compared with 2001, the risk of death was significantly lower in all of the following registries with reductions in adjusted mortality between 45% and 66%.

Conclusions: Over the last 14 years, substantial changes occurred in the clinical characteristics and management of patients with CS complicating ACS, with a greater use of PCI and a significant reduction in adjusted mortality rate.
comes. The weaning and survival rates were dependent on the aetologies of shock or cardiac arrest.

UNDERSTANDING POST INFARCTION RISK FOR A BETTER LONG TERM SURVIVAL

4260 | BEDSIDE
Chronology of events after hospital discharge following acute myocardial infarction is not uniform. Five-year follow-up of the FAST-MI 2005 registry


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Background: Contemporary data on chronology of events after acute myocardial infarction (AMI) are scarce.

Aim and methods: We analysed the chronology of 5-year mortality post hospital discharge in the nationwide French FAST-MI 2005 registry of STEMI and NSTEMI patients admitted in 223 institutions over one month in 2005; 5-year mortality follow-up was 97%. We determined splines in event curves and sought optimal curve fitting according to time elapsed since the acute event.

Results: In 2894 patients discharged alive, 5-year mortality was 34% in NSTEMI (n=1377) and 16% in STEMI (n=1517). In NSTEMI patients, the best spline points were found at 5 months and 18 months, with declining event rates and near-perfect linear correlations for each time interval. Slope coefficients were: 29.0 (r²=0.999, P<0.0001) from discharge to 5 months; 10.3 (r²=0.999, P<0.0001) from 5 to 18 months; and 7.5 (r²=0.999, P<0.0001) from 18 months to 5 years.

In STEMI patients, the optimal spline points were found at 6 weeks and 5 months. Slope coefficients were: 29.0 (r²=0.999, P<0.0001) from discharge to 6 weeks; 10.9 (r²=0.992, P<0.0001) from 6 weeks to 5 months; and 4.1 (r²=0.998, P<0.0001) from 5 months to 5 years.

Conclusion: Mortality following discharge after AMI is not uniform with time. Event curves can be modelled with 3 slopes of declining steepness; a first period with a high event rate up to 5 months (NSTEMI) or 6 weeks (STEMI), a second period from 5 months to 18 months (NSTEMI) and 6 weeks to 5 months (STEMI) with an intermediate event rate and a third period corresponding to fully stabilized disease (from 18 months onward in NSTEMI and 5 months onward for STEMI). The chronology of events suggests that different therapeutic strategies might be considered for each of the three periods.

Acknowledgement/Funding: Pfizer, Servier, CNAM-TS

4261 | BEDSIDE
Long term relative survival and excess mortality after acute myocardial infarction, 2003-2010: a national cohort study


Background: Survival after AMI is high, however there are no whole-country studies of survival after STEMI and NSTEMI which account for background mortality.

Methods: Nationwide population-based cohort (247 hospitals, 583,466 patients, England and Wales, 2003–10), using data from the Myocardial Ischaemia National Audit Project (MINAP). Age, sex, and calendar year-specific population mortality rates for England and Wales were matched to calculate expected survival, and 5-year cumulative relative survival using the Ederer II approach and Poisson regression to estimate excess mortality rate ratios (EMRR).

Results: Excess mortality increased significantly with age. For STEMI, EMRRs were 1.91 (95% CI: 1.80 to 2.03), 4.22 (CI: 4.00 to 4.46), 9.34 (CI: 8.90 to 9.86) and 17.67 (CI: 16.70 to 18.71) for 56–65yrs, 66 to 75 yrs, 76–85 yrs and >85 yrs respectively compared with patients matched background counterparts – suggesting that these groups be targeted for enhanced and persistent cardiovascular care.

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logistic EuroSCORE2 was 28.4±13.3%. NYHA class III/IV was reported in 92.5%. At 5 years, the mean effective orifice area (EOA) was 1.6±0.6 cm² (n=34), mean gradient was 11.7±5.4 mmHg (n=39), and peak gradient was 21.2±9.8 mmHg (n=40). In paired patient data, the difference between discharge and 5-year EOA was 0.1±0.7 cm² (p=0.0596) and mean gradient was 2.2±5.7 mmHg (p=0.0060).

Left ventricular ejection fraction (LVEF) at 5 years was 55.7±16.1% (n=26). At discharge and 5 years, respectively, aortic regurgitation (AR) was evaluated as none/trace in 65.9% (n=172/261) and 57.5% (n=23/40), mild in 28.4% (n=74/261) and 37.5% (n=15/40), and moderate in 5.7% (n=15/261) and 5.0% (n=20). No severe AR was reported at any follow-up. Valve thrombosis was observed in 2 patients and occurred within 30 days. No valve-related explants after 30 days and no case of structural valve deterioration have been reported.

**Conclusions:** Long-term echocardiographic outcomes in high-risk patients with severe symptomatic aortic stenosis and haemodynamic function of first-generation balloon-expandable THVs at 5 years, with no worsening of AR severity over time. Data gained from these early feasibility studies may help evolve treatment options for intermediate-risk patients.

**Acknowledgement/Funding:** Edwards Lifesciences

### 4269 | BEDSIDE

**Comparative survival after trans-apical, direct aortic, and subclavian transcatheter aortic valve implantation**


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**Background:** Many patients have ilio-femoral anatomy unsuitable for conventional trans-femoral (TF) trans-catheter aortic valve implantation (TAVI). Safe and practical alternatives to the TF approach are therefore needed.

**Objective:** To compare survival outcomes of alternative non-femoral routes, transapical (TA), direct aortic (DA) and subclavian (SC), with standard femoral access.

**Methods:** In this retrospective study conducted at 33 sites in the United Kingdom, data from 3,962 patients in the UK TAVI registry were analysed. All patients who received TAVI via a femoral, subclavian, transapical or direct aortic approach were eligible for inclusion. The primary outcome measure was survival up to two years. Secondary endpoints included safety and morality.

**Results:** Median Logistic EuroSCORE was similar for SC, DA, and TA, but significantly lower in the TF cohort (22.1% vs 20.3% vs 21.2% vs 17.0% respectively). Median Logistic EuroSCORE was similar for SC, DA, and TA, but significantly lower in the TF cohort (22.1% vs 20.3% vs 21.2% vs 17.0% respectively) cohorts was significantly lower in the TF cohort (22.1% vs 20.3% vs 21.2% vs 17.0% respectively). Survival in the SC group was not significantly different to the TF group (HR 1.22, 95% CI 1.05 to 1.43, p=0.24). In contrast, survival in the TA (HR 1.74, 95% CI 1.43 to 2.11; p<0.001) and DA (HR 1.74, 95% CI 1.43 to 2.11; p<0.001) cohorts was significantly reduced compared to TF.

**Table 1**

<table>
<thead>
<tr>
<th>Subclavian</th>
<th>Transapical</th>
<th>Direct aortic</th>
<th>Femoral</th>
</tr>
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<tbody>
<tr>
<td>(n=188)</td>
<td>(n=761)</td>
<td>(n=761)</td>
<td>(n=2828)</td>
</tr>
</tbody>
</table>
| 30-day mortality | 5 (2.7) | 8 (10.7) | 15 (4.4) | p=0.0001
| 12-months mortality | 33 (22.2) | 187 (27.4) | 42 (29.2) | p=0.0001
| Need for haemofiltration | 7 (4.0) | 54 (7.0) | 19 (10) | p<0.0001
| Pacemaker implantation post TAVI (n, %) | 43 (23) | 37 (5.0) | 13 (7.0) | p=0.001

**Conclusion:** Transapical and direct aortic TAVI were associated with similar survival, both significantly worse than with the trans-femoral route. In contrast, subclavian access was not significantly different to trans-femoral, and may represent the safest non-femoral access route for TAVI.

### 4270 | BEDSIDE

**TAVI in local anesthesia without general anesthesia or deep sedation**, a single center comparison of 30-day clinical outcome between balloon-expandable vs self-expandable THV


**Background:** Transcatheter aortic valve implantation (TAVI) is the treatment of choice for patients with severe symptomatic aortic stenosis with high surgical risk. Most centers perform TAVI under general anesthesia or deep sedation. TAVI under local anesthesia might result in less periprocedural episodes of hypotension, shorter procedure time and hospital stay.

**Purpose:** The purpose of this study was to compare feasibility and clinical outcome after TAVI under local anesthesia using the self-expandable 18-F-CoreValve prosthesis (MCV) versus the 14–20F-balloon expandable Edwards Sapien XT valve (ESV).

**Methods:** Between April 2010 and October 2014, 570 consecutive pts (age 81.0±3.0 years, 281 female) underwent successfully transfemoral TAVI in local anesthesia exclusively without general anesthesia or deep sedation. Patients were divided into the following groups: MCV and 209 pts (age 81.7±4.1 years, log Euroscore 0.68±0.2% mmHg, AVG 0.68±0.2% mmHg) underwent TAVI with the MCV and 209 pts.

**Results:** Patients: 361 pts (age 80.6±3.4 years) with severe aortic stenosis (p<0.0001). Survival in the MCV vs. ESV was 55.9±2.4% vs. 55.7±2.4%, p=0.4257). In contrast, survival in the TA (HR 1.74, 95% CI 1.43 to 2.11; p<0.001) and DA (HR 1.74, 95% CI 1.43 to 2.11; p<0.001) cohorts was significantly lower in the TF cohort (22.1% vs 20.3% vs 21.2% vs 17.0% respectively). Survival in the SC group was not significantly different to the TF group (HR 1.22, 95% CI 1.05 to 1.43, p=0.24). In contrast, survival in the TA (HR 1.74, 95% CI 1.43 to 2.11; p<0.001) and DA (HR 1.74, 95% CI 1.43 to 2.11; p<0.001) cohorts was significantly reduced compared to TF.

**Conclusion:** Transfemoral TAVI using local anesthesia only is feasible and safe in an all-comer TAVI population using either self-expandable or balloon-expandable transcatheter heart valves.

**BIOMARKERS: PRESENT AND FUTURE**

### 4277 | BEDSIDE

**Soluble Neprilysin compared to NT-proBNP for heart failure risk stratification in ambulatory patients**

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**Introduction:** Neprilysin (NEP) breaks down numerous vasoactive peptides. NEP has been studied as a therapeutic target and its inhibition has proven to improve outcomes in patients with chronic heart failure (HF). The soluble form of NEP (sNEP), recently identified in heart failure (HF), is associated with cardiovascular (CV) outcomes.

**Objective:** We directly compared sNEP vs NT-proBNP as risk stratifiers.

**Methods:** sNEP and NT-proBNP levels were measured in 1030 consecutive ambulatory HF patients from May 2006 to May 2013. Patients were followed for 4.2 years. Comprehensive multivariable analyses and head-to-head assessments of performance were performed. The composite endpoint of CV death or HF hospitalization and CV death alone were explored.

**Results:** Median sNEP and NT-proBNP concentrations were 0.64 ng/mL and 1302 ng/L, respectively. Both biomarkers significantly correlated with age (both p<0.001), but only NT-proBNP significantly correlated with eGFR and BMI. In multivariable Cox regression analyses, both sNEP and NT-proBNP were significantly associated with the composite endpoint (hazard ratio [HR] 1.18, 95% confidence interval [CI] 1.07 to 1.30, p<0.001; HR 1.30, 95% CI 1.15 to 1.48, p<0.001) and CV death (HR 1.17, 95% CI 1.05 to 1.32, p=0.007; HR 1.41, 95% CI 1.21 to 1.65, p<0.001). Only sNEP remained independently associated with the composite endpoint and CV death when hs-TNT and ST2 were incorporated in the analysis. The head-to-head sNEP vs. NT-proBNP comparison showed good calibration and similar discrimination (figure) and reclassification for both endpoints in all models.
Conclusions: sNEP performed similarly to NTproBNP as a risk stratifier in ambulatory patients with HF, though it was less influenced by comorbidities and retained its prognostic value in multimer analysis.

4278 | BEDSIDE
Cardiac injury in neoplasia and association with cardiovascular hormones
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Objectives: Patients with malignancies display elevated levels of B-type natriuretic peptide (BNP) and hs-TnT without clinical manifestation of cardiac disease. This study evaluated circulating cardiovascular hormones and hs-TnT and their association with mortality in neoplastic disease.

Methods: We prospectively enrolled 555 consecutive patients with primary diagnosis of neoplastic disease without prior cardiotoxic anticancer therapy. NTproBNP, MR-proANP, MR-proADM, CT-proET-1, Copeptin, hs-TnT, IL-6 and CRP were measured. Cox regression analysis was performed to investigate the prognostic values of cardiovascular hormones and hs-TnT on survival. Correlation with inflammatory markers was tested.

Results: During a median follow-up of 25 (IQR 16–31) months 186 (34%) patients died. All cardiovascular hormones and hs-TnT levels rose with progressing tumor stage. All markers were significant predictors of mortality with hazard ratios per IQR of 1.21 (95% CI 1.14–1.30; p<0.001) for NTproBNP, 1.31 (95% CI 1.19–1.44; p<0.001) for MR-proANP, 1.21 (95% CI 1.14–1.30; p<0.001) for MR-proADM, 1.29 (95% CI 1.19–1.39; p<0.001) for CT-proET-1, 1.21 (95% CI 1.14–1.30; p<0.001) for Copeptin, 1.29 (95% CI 1.19–1.39; p<0.001) for hs-TnT, independent of age, gender, entity of neoplastic disease, tumor stage, and prevalence of cardiac comorbidities. Kaplan-Meier analysis confirmed the discriminatory power of the hormones and hs-TnT (Fig.). NTproBNP, MR-proANP, MR-proADM and hs-TnT displayed significant correlation with IL-6 and CRP.

Conclusions: Circulating cardiovascular peptides like NTproBNP, MR-proANP, MR-proADM, CT-proET-1, Copeptin and hs-TnT are elevated in an unselected population of patients with neoplastic disease and strongly related to all-cause mortality suggesting the presence of subclinical myocardial damage.

4279 | BEDSIDE
Soluble neprilysin in acute heart failure: prognostic value and kinetics. A pilot study
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Introduction: The soluble form of neprilysin (sNEP) was recently identified in acute heart failure (HF) and associated with cardiovascular outcomes. Purpose: To examine the prognostic value of sNEP in acute HF (AHF) and sNEP kinetics during hospital admission.

Methods: A total of 350 patients (53% women, mean age 72.6±10.7 years) were included in the study. Primary endpoints were a composite of cardiovascular death or heart failure hospitalizations at short-term (2 months) and long-term (mean 1.8±1.2 years) follow-up. sNEP was measured using an ad hoc modified ELISA assay and its prognostic value assessed using Cox regression analyses. In a subgroup of patients sNEP was measured both at admission and discharge (n=92).

Results: Median admission sNEP levels were 0.67 ng/ml (Q1-Q3 0.37–1.29), and sNEP was significantly associated, in age-adjusted Cox regression analyses, with the composite endpoint at short-term (hazard ratio [HR] 1.29, 95% confidence interval [CI] 1.04–1.61, p=0.02) and long-term follow-up (HR 1.23, 95% CI 1.01–1.05, p=0.003). In multivariable Cox analyses that included clinical variables and NTproBNP, admission sNEP showed a clear trend towards significance for the composite endpoint at 2 months (HR 1.22, 95% CI 0.97–1.53, p=0.09) and remained significant at the end of follow-up (HR 1.21, 95% CI 1.04–1.40, p=0.01). At discharge, sNEP levels decreased from 0.70 to 0.52 ng/ml (p=0.06).

Conclusions: Admission sNEP was associated with short- and long-term outcomes in AHF and dynamic sNEP concentrations were observed during hospital admission. These preliminary data may be proof-of-principle for the use of NEP inhibitors in AHF.

MODERN DRUG THERAPY IN HEART FAILURE

4282 | BEDSIDE
One-year mortality in diuretic treated patients with heart failure. A report from the Swedish Heart Failure registry based on a cohort of 27,374 patients
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Background and introduction: Diuretics are recommended in international guidelines for relief of symptoms related to heart failure (HF). However, the prognostic impact of diuretics in HF is unclear. Hospitalization for HF is associated with a poor prognosis. Previous observational data have indicated a worsened prognosis associated with diuretics irrespective of hospitalization or not. Purpose: To analyze the association between diuretics and one year all-cause mortality in HF patients at hospital discharge and in HF outpatients respectively with data from a nationwide HF registry.

Methods: The Swedish Heart Failure Registry was introduced in 2003. Inclusion criteria are clinician-judged HF. Approximately 80 variables are recorded. Of 45,174 unique patient baseline registrations between 2003 and 2011 27,374 had information on diuretic medication, ejection fraction (EF) and the Heart Association (NYHA) class and were included in this study. Of the included cohort 13,424 were registered at hospital discharge and 13,950 as outpatients. Propensity score (PS) for diuretic treatment was estimated with logistic regression using 44 clinically relevant baseline variables. Matching was made 1:1 on diuretic medication versus no diuretic medication. An age difference of 5 years and a PS difference of less than 0.01 were accepted. This resulted in a 1:1 matched population of 3,252 patients at hospital discharge and a 1:1 matched outpatient population of 5,490 patients. Hazard ratio (HR) for all-cause one-year mortality was estimated.

Results: See Table 1.

Table 1

<table>
<thead>
<tr>
<th>One-year mortality %</th>
<th>n deaths/total</th>
<th>HR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital discharge</td>
<td>No diuretics</td>
<td>19.5</td>
<td>317/1626</td>
</tr>
<tr>
<td>Diuretics</td>
<td>18.1</td>
<td>294/1626</td>
<td>0.898 (0.766–1.053)</td>
</tr>
<tr>
<td>Outpatients</td>
<td>No diuretics</td>
<td>4.7</td>
<td>128/2745</td>
</tr>
<tr>
<td>Diuretics</td>
<td>6.6</td>
<td>181/2745</td>
<td>1.432 (1.142–1.795)</td>
</tr>
</tbody>
</table>

Conclusion(s): In this observational report we found that in clinically stable outpatients with HF diuretics are associated with increased risk of one-year all-cause mortality. In contrast, diuretics in HF patients at hospital discharge are not associated with increased one-year mortality. The clinical implications of these findings are that diuretics should be discontinued when symptomatically feasible in outpatients.

Acknowledgement/Funding: The Swedish Heart-Lung Foundation, Region Vastra Gotaland
**4283** | BEDSIDE
Low-dose aspirin therapy is not associated with reduced cardiovascular morbidity or mortality in heart failure with sinus rhythm: a nationwide propensity score matched study
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Background: Chronic low dose aspirin (75 mg/day) therapy has never been evaluated against placebo in a randomized clinical trial in heart failure (HF). However, aspirin is widely used in HF with sinus rhythm regardless of the etiology of the disease.

Purpose: We aimed to assess safety and efficacy of aspirin therapy in a nationwide cohort of HF patients with sinus rhythm.

Methods: Patients with a first diagnosis of HF in the period 2007–2012 and with sinus rhythm were identified from Danish administrative registries and classified according to ischemic or non-ischemic etiology. Aspirin-users and non-users were compared in propensity score matched Cox regression models with respect to a primary composite outcome of all-cause mortality, myocardial infarction and ischemic stroke, and the secondary outcomes all-cause bleeding and HF readmission.

Results: In patients with ischemic HF (3,931 aspirin users and 3,931 non-users; median follow-up 23 months), aspirin therapy was not associated with a significantly altered risk of the primary composite outcome, (hazard ratio [HR]: 0.99, 95% CI: 0.92–1.06). Aspirin therapy was, however, associated with an increased risk of bleeding (HR: 1.29, 95%-CI: 1.08–1.53). In the non-ischemic HF population (3,744 aspirin users and 3,744 non-users; median follow-up 22 months), aspirin therapy was not associated with significantly altered risk of the primary composite outcome, (HR: 0.95, 95%-CI: 0.89–1.02), nor bleeding (HR: 1.01, 95%-CI: 0.84–1.22).

Conclusion: In patients with HF and sinus rhythm, we found no benefit of aspirin therapy, regardless of ischemic or non-ischemic etiology, but aspirin was associated with increased risk of bleeding in patients with ischemic HF. Routine use of aspirin in HF might cause more harm than benefit.

**4284** | BEDSIDE
Use of digoxin is safe in patients with atrial fibrillation and heart failure: a nationwide propensity matched study
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Background: The treatment of atrial fibrillation (AF) in heart failure (HF) is complex, and the optimal strategy for rhythm or rate control is not fully elucidated. Therefore, we evaluated the role of digoxin in patients admitted with HF and AF.

Purpose: We aimed to assess safety and efficacy of digoxin in a nationwide cohort of patients admitted with HF and AF.

Methods: From Danish nationwide registries, digoxin-naïve HF patients with co-existing AF from 1996–2012 were identified and included if they were in sinus rhythm. The study population comprised 4,868 digoxin users, and 4,868 non-users with a median age of 75 years. Over a median follow-up of 38 months, 3,693 (37.9%) patients died and 5,838 (60.0%) patients were readmitted due to HF and/or AF. Use of digoxin was associated with a reduced risk of death (hazard ratio [HR]: 0.92, 95%-CI: 0.86–0.98), but a slightly increased risk of readmission (HR: 1.07, 95%-CI: 1.01–1.12). However, considering death as a competing risk, the cumulative incidences of readmission were close to similar (64.9% for digoxin users and 64.4% for non-users).

Conclusion: In digoxin-naïve HF patients with AF use of digoxin was safe and associated with a slightly reduced risk of death, whereas no difference was observed regarding HF AF readmission.

**4286** | BEDSIDE
How to make a diagnosis of microvascular angina; the diagnostic potency of rest-stress myocardial perfusion magnetic resonance imaging
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Background: Microvascular Angina (MVA) causes chest pain without significant stenosis and spasm in epicardial coronary artery. Its diagnosis is very difficult because few efficient diagnostic modalities have been reported in the past studies.

Purpose: The purpose of this study is to make a diagnosis of MVA using rest-stress myocardial perfusion magnetic resonance imaging (MRI).

Methods: Clinically suspected patients of MVA with chest pain were examined after coronary angiography revealed no significant stenosis in their epicardial coronary arteries and coronary spasm provocation test by ergometrine maleate turned out to be negative. Subsequently, contrast-enhanced myocardial perfusion MRI was performed under the rest conditions and the stress conditions with adenosine triphosphate (ATP). ATP dose was 140 μg/kg/min for 6 minutes. Contrast media was injected 3 minutes after starting ATP-stress. The semi-quantitative analysis of the rest-to-stress ratio index of the maximal slope of the myocardial 12 segments was adopted. The patients were diagnosed as MVA when MRI showed localized endocardial perfusion defect only under ATP-stress and the rest-to-stress index of the endocardial segment in question showed ischemic pattern.

Results: Thirty-nine patients were included in this study. Thirty patients were diagnosed as MVA, rest of the patients were diagnosed as non-MVA. Twenty-five patients showed localized endocardial perfusion defect only under ATP-stress in anterior segment, 27 patients in anterolateral, 27 patients in inferolateral, 20 patients in inferior, 21 patients in interoseptal, and 26 patients in anteroseptal. The average of the rest-to-stress ratio index of the endocardial segment in question and not in question of MVA were 0.81±0.16 and 1.52±0.54, respectively. That of non-MVA was 1.56±0.44. Sensitivity was 89.7%. Supplementarily, rest-stress myocardial perfusion scintigraphy was performed to 24 patients of 35 MVA, and only 1 patient showed ischemia.

Conclusion: This study showed efficacy of rest-stress myocardial perfusion MRI in the diagnosis of MVA. Rest-stress myocardial perfusion MRI could cast new light on the problem of diagnostic difficulty of MVA.
Coronary flow reserve (CFR) is impaired in patients with aortic stenosis (AS) and that impaired CFR has a prognostic value in patients with asymptomatic AS. We investigated whether the diabetes mellitus type II (DM) additionally impairs microvascular circulation assessed with asymptomatic AS, normal left ventricular ejection fraction (LVEF) and nonobstructed coronary arteries.

Methods: A total of 127 patients, mean age 66.14±11.02 (59.52% males), with DM and non-DM were prospectively evaluated. CFR was measured during adenosine infusion (0.84 mg/kg) and CAC was obtained by the method described by Agatston.

Results: CFR and CAC were measured in 110 women, mean age (SD) 62.4 years (8.8), 51% (n=56) had a CAC of zero. Median (IQR) CFR was 2.67 (2.29–3.10). No significant correlation between CFR and CAC was found (R2=0.001; p=0.911 for all patients, and R2=0.015; p=0.379 for patients with CAC above 0. CAC and CFR were correlated to the presence of hypertension and CFR was correlated to diabetes. Furthermore, increasing age and atheromatosis on CAG were associated with a higher CAC (Table 1).

Conclusions: In patients with angiographic preejection and NO-CAD suspected for CMD, there is no association between CAC and CFR, suggesting that CFR and CAC provide different information regarding cardiovascular risk and the atherosclerotic process. Therefore CAC score cannot be used to identify CMD.

Background: Women with angiographic preejection and NO-CAD suspected for CMD, have a higher cardiovascular risk. CFR is impaired in patients with aortic stenosis (AS) and that impaired CFR has a prognostic value in patients with asymptomatic AS. We investigated whether the diabetes mellitus type II (DM) additionally impairs microvascular circulation assessed with asymptomatic AS, normal left ventricular ejection fraction (LVEF) and nonobstructed coronary arteries.

Methods: A total of 127 patients, mean age 66.14±11.02 (59.52% males), with DM and non-DM were prospectively evaluated. CFR was measured during adenosine infusion (0.84 mg/kg) and CAC was obtained by the method described by Agatston.

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Conclusions: In patients with angiographic preejection and NO-CAD suspected for CMD, there is no association between CAC and CFR, suggesting that CFR and CAC provide different information regarding cardiovascular risk and the atherosclerotic process. Therefore CAC score cannot be used to identify CMD.
Methods: Sixty-four patients with STEMI undergoing primary PCI were randomly assigned to receive either placebo (Control group, n=32) or intracoronary nicorandil (Nicorandil group, n=32). Coronary flow reserve (CFR) as an established marker of microvascular injury was assessed by 1.5T contrast enhanced CMR in a population of patients with ST segment resolution between Nicorandil and Control group (5.3±3.2mm vs. 2.03±0.41, p<0.001). In multivariable regression IMR was assessed 2 days post-MI, mean LV ejection fraction was 54.9±9.6%, mean infarct size (%LVmass) 17.9±13.4%. Mean RRR 2.07±1.07 and CFR 1.74±0.84. There was a strong correlation between CFR and RRR (R=0.33, p<0.001). There was a weak correlation between the T2 AAR and RRR (r=-0.21, p=0.002 and also CFR (r=-0.17, p=0.004). There was a weak correlation between RRR and the LV ejection fraction at 6 months (r=0.13, p=0.05) but not with CFR.

Conclusion: The RRR predicts acute infarct characteristics and was more closely associated with myocardial injury in acute STEMI than CFR.
CFR > 2.0. In a survival analysis adjusting for cardiovascular risk factors CFR above 2.0 independently predicted cardiovascular event free survival (HR: 2.8, p=0.028). In a multivariate linear regression analysis adjusting for cardiovascular risk factors, high Homeostatic model assessment for insulin resistance (HOMA-IR) was independently associated with low CFR (β=-0.018, p=0.026). In gender specific analysis, the relation was statistically significant in women (β=-0.034, p=0.016) but not in men (β=-0.004, p=0.685). Also, women with CFR below 2.0 displayed increased HOMA-IR as compared to women with CFR equal or above 2.0 (β=0.05).

Conclusions: In non-diabetic patients with angina symptoms but no MPS-verified ischemia, abnormal CFR is of prognostic value. Insulin resistance determined by HOMA-IR is associated with impaired CFR, especially in women and could potentially add value in risk stratification in this relevant patient group.

Acknowledgement/Funding: Agreement concerning research and education of doctors

BEST POSTERS SESSION 5
BEST POSTERS IN IMPLANTABLE AND SUBCUTANEOUS DEFIBRILLATOR THERAPY

P4297 | BEDSIDE
The evolution of ICD programming practice: What is the relative impact of clinical evidence on clinical practice?
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Introduction: Numerous clinical trials have evaluated ICD detection programming primarily as a means to reduce shocks. However, the factors that influence compliance with evidence-based programming in clinical practice are largely unknown. This retrospective evaluation was designed to understand the impact of single manufacturer’s “out-of-box” ICD settings on initial device programming.

Methods: Data from 105,462 single and dual chamber ICDs and CRT-Ds in the de-identified CareLink Data Warehouse were queried from 2008–2014. Initial programming was based on the earliest transmission post-implant. Initial programming over time was investigated in reference to programming evidence publications and changes in out-of-box settings. Programming variables of interest included ventricular fibrillation number of intervals to detect (VFVFD) and supraventricular tachycardia discrimination limit (SVTMAX).

Results: Mean age 66±12 years. 73% male. The figure shows an example of progression in programming of VFVFD. The “up arrows” reflect clinical evidence publications supporting VFVFD = 30/40: PREPARE (2008), ADVANCE III (2013). The “down arrows” reflect change in out-of-box VFVFD settings: 24/02 (2013) and 30/40 (2014). The largest changes in initial VFVFD programming occurred following changes in out-of-box settings. Similar findings were also found for initial SVTMAX programming. Compliance with current evidence for VFVFD and SVTMAX is greater than 50% now that these have become nominal values.

Conclusion: Clinical trials have demonstrated that shocks can be significantly reduced and patient quality of life preserved by careful programming of detection and therapy parameters. Yet, utilization of evidence-based programming appears to be principally driven by manufacturer changes to nominal settings.

P4298 | BEDSIDE
Efficacy and safety of the implantable cardioverter defibrillator in pediatric patients with channelopathies
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Purpose: Cardiac channelopathies induce risk of Sudden Cardiac Death (SCD), that may require an Implantable Cardioverter Defibrillator (ICD) in pediatric patients. Limited information exists for the long-term outcome of young patients affected by channelopathies and carriers of an ICD.

Methods: We studied patients diagnosed with inherited arrhythmias in structurally normal hearts who received an ICD by age 18.

Results: N=83 pediatric patients (36 males,43%) received an ICD for the following diagnoses: 49 (59%) Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT), 26 (31%) Long QT Syndrome (LQTS). 3 (4%) Brugada Syndrome (BrS), 2 (2%) Short QT Syndrome (SQTS). N=3 (4%) patients had an aborted SCD (aSCD) without diagnosis (Idiopathic Ventricular Fibrillation, IVF). N=67 (81%) patients carried a pathogenic mutation and 27 (33%) had a family history of SCD within 40 years. N=76 (92%) patients had symptoms before ICD implant. N=37 (45%) patients were implanted for “secondary prevention”, post aSCD (n=34) or documented polymorphic ventricular tachycardia (n=3); n=46 (55%) patients were implanted for “primary prevention”. Age at implant was 12±4 years. Follow-up: 3 months was available for 76 patients (median 78, IQR 38–131; months); 39 (51%) patients received 131 appropriate shocks (median 2, IQR 1–4, per patient) in separate arrhythmic episodes; the first shock was delivered 29 (IQR 3–48) months post-implant. Appropriate shocks occurred in 29/46 CPVT patients, 8/23 LQTS, 0 BrS, 1/2 SQTS and 1/3 IVF. No statistically significant difference was observed in the occurrence of appropriate shocks between “primary” or “secondary prevention” patients (p=0.489). A boy with LQT3 died at 18 months during an arrhythmic storm, despite several appropriate shocks. A patient had a pulmonary oxymoronic during ICD placement and 26 (34%) patients had major complications, 14 (IQR 4–76) months post-operatively. Of these, 21 subjects had device dysfunction or lead fracture and 5 had significant infections. Inappropriate shocks occurred in 14 (18%) patients due to T-wave over-sensing and supraventricular arrhythmias or sinus tachycardia, in one third of cases respectively. Overall 35 (46%) patients had documented complications.

Conclusions: Half of our pediatric patients affected by inherited arrhythmias with an ICD experienced appropriate shocks regardless of whether the ICD was placed for “primary” or “secondary prevention” of SCD. The high incidence of major complications (36%) requires solid justifications for use of the ICD in children. Accurate programming of the ICD is essential to reduce inappropriate shocks.

P4299 | BEDSIDE
Learning curve associated with inappropriate shocks of the subcutaneous implantable defibrillator: results from a pooled analysis of 882 patients from the IDE study and EFFORTLESS Registry
T.F. Brouwer1, R.E. Knops1, C.S. Bar2, D.A. Theuns3, R. Weiss4, P.D. Lamblin2, A.R. Leon1, P. Jones2, N. Carter2, M.C. Burke2, 1 Academic Medical Center of Amsterdam, Cardiology, Amsterdam, Netherlands; 2 Dudley Group of Hospitals NHS Trust, Cardiology Department, Dudley, United Kingdom; 3 Erasmus Medical Center, Rotterdam, Netherlands; 4 The Ohio State University, Columbus, United States of America; 5 University College London, Cardiology Department, London, United Kingdom; 6 Emory University, Atlanta, United States of America; 7 The University of Chicago, Heart Rhythm Center, Chicago, United States of America

Introduction: The subcutaneous ICD (S-ICD) uses a morphology based discrimination algorithm that requires a unique programming strategy. We evaluated the occurrence of appropriate shocks between “primary” or “secondary” prevention patients (p=0.489). A boy with LQT3 died at 18 months during an arrhythmic storm, despite several appropriate shocks. A patient had a pulmonary oxymoronic during ICD placement and 26 (34%) patients had major complications, 14 (IQR 4–76) months post-operatively. Of these, 21 subjects had device dysfunction or lead fracture and 5 had significant infections. Inappropriate shocks occurred in 14 (18%) patients due to T-wave over-sensing and supraventricular arrhythmias or sinus tachycardia, in one third of cases respectively. Overall 35 (46%) patients had documented complications.

Conclusions: Half of our pediatric patients affected by inherited arrhythmias with an ICD experienced appropriate shocks regardless of whether the ICD was placed for “primary” or “secondary prevention” of SCD. The high incidence of major complications (36%) requires solid justifications for use of the ICD in children. Accurate programming of the ICD is essential to reduce inappropriate shocks.

Figure 1

Conclusion: Clinical trials have demonstrated that shocks can be significantly reduced and patient quality of life preserved by careful programming of detection and therapy parameters. Yet, utilization of evidence-based programming appears to be principally driven by manufacturer changes to nominal settings.
Gensini, (relative importance 16%, p < 0.0001), compared to those without depression (63%). In a multivariable linear model, both the independent predictor of AF even in the subset of patients without significant CAD. Whether treatment of underlying depression improves AP needs to be further studied.

**BEST POSTERS IN CARDIOVASCULAR DISEASE**

**P4301 | BEDSIDE**

**Depression is the strongest predictor of angina and is independent of underlying coronary artery disease severity in patients with cardiovascular disease**

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**Introduction:** Angina pectoris (AP) is a hallmark of obstructive coronary artery disease (CAD). Depression is three times more frequently in patients with CAD and is associated with worse morbidity and mortality. While patients with CAD and depression tend to experience chest pain more frequently than those without depression, it is unclear whether this is due to differences in underlying CAD severity.

**Purpose:** To determine whether depression is associated with AP independently of underlying CAD severity.

**Methods:** 5825 patients underwent left heart catheterization (LHC) between 2004 and 2013 at Emory Healthcare sites and were recruited into the Emory Cardiovascular Biobank. Patients completed the Seattle Angina Questionnaire (SAQ) to assess angina frequency (AF) and the Patient Health Questionnaire-9 (PHQ-9) to screen for depression. A lower AF score is indicative of more frequent chest pain.

**Results:** Mean age was 63±12 years, 64% male, 76% white, 65% with CAD severity >50% in at least one coronary artery. There was a significant negative correlation between PHQ-9 and AF (r = −0.284, p < 0.0001) scores, indicating that angina was more frequent with more severe depression. Patients with even mild depression (22%) had significantly lower AF score (73 vs. 84, p < 0.0001) compared to those without depression (83%). In a multivariable linear model, both the PHQ-9 (relative importance 16%, p < 0.0001), and Gensini score (10–14), indicated that moderate depression (score of 5 to 9), moderately depressed (score of 5 to 19), and severely depressed (score of 20 to 27). Angiographic CAD severity was estimated using the Gensini score. Multivariable analysis using linear regression was performed with the AF score as dependent variable and the PHQ-9 and Gensini scores in addition to demographics and clinical characteristics as independent variables.

**Conclusions:** Depressive comorbidities appear to be significant independent predictors of AP. Multivariable analysis using linear regression was performed with the AF score as dependent variable and the PHQ-9 and Gensini scores in addition to demographics and clinical characteristics as independent variables.

**P4302 | BEDSIDE**

**Role of CHA2DS2-VASc score in evaluating patients with atrial fibrillation (AF) undergoing percutaneous coronary intervention (PCI)**

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**Purpose:** AF is an independent predictor of mortality in those with coronary artery disease. These represent a particularly challenging group with optimal antithrombotic therapy remaining controversial. The CHA2DS2-VASc score has been validated in predicting stroke risk in AF and is used to guide management with oral anticoagulation. We aimed to evaluate the CHA2DS2-VASc score in predicting adverse outcomes in patients with AF undergoing PCI.

**Methods:** CHA2DS2-VASc score was calculated in 584 consecutive patients with AF undergoing PCI in a large Australian multicentre registry between May 2007 and November 2013. Patients were divided into categories of low (score 1–2), intermediate (3–4) and high (4 or >4) risk. Clinical and procedural data, 30-day, 12-month and long-term outcomes were compared between the 3 groups. Patients with out-of-hospital arrest, cardiac shock and incomplete data to calculate scores were excluded.

**Results:** Mean CHA2DS2-VASc score was 4.4±1.6. By definition, the high-risk group were significantly more likely to be older and female, have more diabetes, hypertension, vascular disease, cerebrovascular disease and congestive cardiac failure. Renal impairment and multivessel disease were also significantly higher within the higher risk groups. The high-risk group were less likely to receive Gp2b3a inhibitors; surprisingly the use of drug eluting stents was not different between the groups (30%, 30% and 25% respectively). Anticoagulation use in intermediate and high-risk patients was 43% and 44% at 30 days, and 48% and 47% at 1 year.

**Conclusions:** When compared with the low-risk group, intermediate CHA2DS2-VASc scores (HR 3.57, 95% CI 1.28–9.92, p=0.015) and high CHA2DS2-VASc scores (HR 7.82, 95% CI 2.88–21.24, p<0.001) were strong predictors of long-term mortality.

**30-day, 1-year and long-term outcomes**

<table>
<thead>
<tr>
<th>Low</th>
<th>Intermediate</th>
<th>High</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n=633)</td>
<td>(n=226)</td>
<td>(n=275)</td>
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<tr>
<td>30-day death, %</td>
<td>0</td>
<td>2.65</td>
<td>6.55</td>
</tr>
<tr>
<td>Stroke, %</td>
<td>0</td>
<td>1.33</td>
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<tr>
<td>MACCE, %</td>
<td>3.17</td>
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<td>1-year death, %</td>
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<td>7.52</td>
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<tr>
<td>Stroke, %</td>
<td>0</td>
<td>2.21</td>
<td>5.82</td>
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<tr>
<td>MACCE, %</td>
<td>11.17</td>
<td>19.03</td>
<td>25.45</td>
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<tr>
<td>Long-term mortality, % (3.44±1.97 yrs)</td>
<td>6.35</td>
<td>20.09</td>
<td>37.5</td>
</tr>
</tbody>
</table>

**MACCE, Major Adverse Cardiovascular and Cerebrovascular Events.**

**Conclusions:** Higher CHA2DS2-VASc scores, in patients with AF undergoing PCI, are associated with significantly worse outcomes. Despite being high risk, these patients are undertreated with anticoagulation. CHA2DS2-VASc score may be a useful tool in identifying those patients at high risk who need aggressive therapy.
P4304 | BEDSIDE
Persistence to secondary prevention drugs in ACS patients with reduced renal function and long-term outcome
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Purpose: The high risk of recurrent events in patients with reduced renal function following an acute coronary syndrome (ACS) may in part be due to suboptimal secondary prevention. We aimed to i) describe the association between renal dysfunction and persistent use of established secondary prevention drugs after an ACS, and ii) to determine whether persistence was associated with improved outcome also in patients with reduced renal function.

Methods: We used the SWEDHEART registry to identify all patients admitted to any Swedish coronary care unit for ACS between 2005–10, and whom survived >1 year (N=3254). In 6324 patients, creatinine levels were available to estimate glomerular filtration rate (eGFR by CKD-EPI). Data on drug use was extracted from the Prescription registry recording all dispensed drugs in Sweden. Persistence was measured for 1 year and patients with a gap >30 days between end of dispensed supply and next dispensed prescription were considered to have discontinued treatment.

Results: Loss to follow up 0%. Compared with patients with eGFR <60 ml/min, after adjustment for age, patients with eGFR 30–59 ml/min that initiated treatment with 30 days, were more likely to discontinue ASA (HR 1.22, CI 95% 1.16–1.28), ACE/ARB (HR 1.35, CI 95% 1.26–1.41), statins (HR 1.14, CI 95% 1.08–1.20) and beta-blockers (HR 1.07, CI 95% 1.01–1.13). After adjustment for age, sex, diabetes, hypertension, heart failure, stroke and drugs on admission, performed PCI or CABG during hospitalization, being persistent on each of the four drugs at 1 year was associated with an improved 3-year outcome (combined death and reinfarction) also in patients with eGFR 30–59 ml/min. The associations in the smaller group of patients with eGFR <30 did not reach significance.

Conclusion: Patients with moderately reduced kidney function are less likely to be persistent on secondary prevention drugs. However, persistent use is associated with improved prognosis.

BEST POSTERS IN EARLY DETECTION OF CARDIAC DISEASE
P4306 | BEDSIDE
Subclinical left ventricular systolic dysfunction by strain imaging in chronic kidney disease subjects with preserved ejection fraction: The use of biochemical parameters (Coeffecient, −0.03; 95% CI, −0.05 to −0.01; P=0.001). Further- more, both treatment groups had reduced LV GLS compared with controls (LV GLS <20.9 ± 2.1% vs 22.9 ± 3.1%, P=0.001)

P4307 | BEDSIDE
Normal range of LV global longitudinal strain in asymptomatic lymphoma survivors
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Background: LV global longitudinal strain (GLS) has emerged as a sensitive marker of LV systolic function and is included in the latest guidelines for detecting cardiac toxicity during administration of chemotherapy. However, little is known about the normal range of LV GLS in asymptomatic cancer survivors years after chemotherapy.

Purpose: To determine the normal range of LV GLS after cardiototoxic treatment including anthracyclines (AC) and radiotherapy involving the heart (RT), assessed in asymptomatic lymphoma survivors (LS).

Methods: All LS treated with autologous hematopoietic stem cell transplantation (auto-HCT) in Norway from 1987–2007 and aged >18 years at auto-HCT were eligible, but only asymptomatic LS are included in this report. LV GLS was estimated by two-dimensional speckle tracking echocardiography (Vivid 7 or E9, GE Vingmed Norway) in a 16–segment model, and stratified according to age and lymphoma treatment (AC alone vs AC+RT). Results in the LS were compared with those found in a healthy control group, matched in a 1:1 fashion based on age, gender, systolic blood pressure and body mass index.

Results: In total, 274 LS (69% of all eligible) participated, of whom 245 were asymptomatic. The feasibility of LV GLS was 85%. Median observation time since lymphoma diagnosis was 12 years (range 4–34) and 61% were males. Mean doxorubicin exposure in LS treated with AC and AC+RT was 298±104 vs 325±147 mg/m² (p<0.010), respectively. LV GLS was reduced in LS after AC+RT compared with AC alone (−17.8±1.8 vs −19.2±2.4, p<0.001). Furthermore, both treatment groups had reduced LV GLS compared with controls (LV GLS <−20.9±1.9%, p<0.001 for both). LV GLS according to age in the two treatment groups and controls are presented in the table.

P4308 | BEDSIDE
Usefulness of 2D strain parameters to rule out acute rejection after heart transplantation
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Background: AR is a limiting factor of survival after HT. The only validated method to detect AR is endomyocardial biopsy (EB). Recent advances in 2D-strain imaging may allow early detection of AR.
Objective: To analyze the usefulness of conventional and new echocardiographic parameters to exclude acute rejection (AR) after heart transplantation (HT).

Methods: We prospectively included 55 consecutive adult recipients admitted at our center for an OHT. A total of 383 pairs of EMB and echocardiograms were performed. A median of 7 (IQR 6–8) studies per patient were performed along the first year of follow-up. We analyzed classic echocardiographic parameters, speckle-tracking derived left ventricular global longitudinal strain (LV GLS), and global and free wall right ventricular longitudinal strain (Free wall RVLS).

Results: AAR was detected in 33% of EMBs (n=128), 8% (n=31) required specific treatment (AAR≥2R). Lower absolute values of LV GLS and Free Wall RVLS were observed in patients with AAR≥2R (14.9±3.4% vs 18.2±3.1% and 17.0±4.8% vs. 20.8±5.2%). An average LV longitudinal strain <15.5% presented 67.7% sensitivity (Se), 74.1% specificity (Sp), 96.1% negative predictive value (NPV), 19.8% positive predictive value (PPV), and 73.6% accuracy (Acc) for the presence of AAR≥2R. Free wall RV longitudinal strain <17% presented 60.0% Se, 80.0% Sp, 95.1% NPV, 23.4% PPV and 78.1% Acc for AAR≥2R. Both variables were normal in 193 echocardiograms (50.4%), only 2.6% of them presented with AAR ≥2R.

Conclusions: We propose the combination of two new parameters, namely global LV and free wall RV Long-strain to detect AAR after OHT. In case of external validation of these findings, its routine measure could be a reliable tool to diagnose AAR and to alleviate the burden of repeated EMB.

P4309 | BEDSIDE
Early detection of abnormal left atrial and left ventricular coupling using two-dimensional speckle tracking echocardiography in patients with preserved left ventricular ejection fraction

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Background: Left atrial (LA) structural remodeling is reflecting the duration and severity of diastolic left ventricular (LV) dysfunction. An accurate examination of alternations in not only LA structure but also function is an important and necessary step forward to early diagnosis of abnormal LA-LV coupling.

Purpose: The aim of this study was to detect the abnormalities of LA-LV coupling using two-dimensional speckle tracking echocardiography in patient with preserved LV ejection fraction.

Methods: A total of 177 asymptomatic patients with preserved LV ejection fraction were studied. Global LV longitudinal peak strain (GLS) and global LA longitudinal strain during systole (S-LAs) were measured. The ratio of E/Ea to S-LAs was used as an index of LA stiffness.

Results: The patients were classified into 2 groups: impaired group (n=81; 46.3%), and non-impaired group (n=96; 53.7%). The impaired group showed significant alternations in not only LA structure but also function. LA-LV coupling was impaired in 80% of patients in the impaired group, compared to 28% in the non-impaired group (p<0.001). Moreover, the ratio of E/Ea to S-LAs was significantly higher in the impaired group (1.78±0.54 vs 1.25±0.37, p<0.001).

Conclusions: The optimal ratio of E/Ea/S-LAs to detect the impaired LA-LV coupling was ≥1.75. This ratio could be a useful method to detect the abnormalities of LA-LV coupling.

P4312 | BEDSIDE
Exercise training is associated with favourable cardiovascular effects on endothelial function and arterial stiffness in healthy subjects.

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Background: Exercise training is associated with favourable cardiovascular effects on endothelial function and arterial stiffness in healthy subjects.

Methods: Twenty healthy men (mean aged 23.3±3 yr) were recruited in this cross over study. They participated in two exercise sessions: a) CAE: volume at 50% of maximum aerobic work on a cycle ergometer for 30 min and b) IRE: 3 sets of 15 repetitions, volume at 50% of 1 repetition maximum on leg press. Endothelial function was evaluated by flow-mediated dilation (FMD) in the brachial artery. Carotid femoral pulse wave velocity (PWV) was measured as an index of arterial stiffness.

Results: There was no significant difference in baseline measurements of the study group before CAE and IRE, concerning FMD measurements (6.3±1.48% vs. 6.4±1.97%, p=0.89), and PWV measurements (5.87±0.82mm/sec vs. 5.65±0.67mm/sec, p=0.11). Importantly, both CAE (6.67±2.33% vs. 6.37±1.48%, p<0.05) and IRE (6.72±1.97% vs. 6.44±1.97%, p=0.005) caused a significant improvement in FMD compared to baseline measurements. Interestingly, CAE has no significant impact on PWV (5.76±0.63mm/sec vs. 5.87±0.62mm/sec, p=0.28) while IRE caused an increase in PWV (6.05±0.77mm/sec vs. 5.65±0.67mm/sec, p<0.001) compared to baseline measurements.

Conclusion: Moderate intensity aerobic exercise and moderate interval resistant exercise can favourably affect endothelial function while interval resistant exercise can adversely affect central aortic stiffness. The diverse effects of different types of exercise on arterial wall properties highlighted the need to further evaluate their impact on cardiovascular health.
P4314 | BENCH
Inhibition of ROCK1 activity by calcium channel blocker suppresses angiotensin-II-induced endothelial dysfunction
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Introduction: Rho-associated kinase 1 (ROCK1) is involved in endothelial dysfunction, a key variable in the pathogenesis of atherosclerosis. Calcium channel blocker (amlodipine) has been used for atherosclerotic cardiovascular diseases treatment. However, whether amlodipine could inhibit ROCK1 activity is unclearly.

Purpose: The aims of present research are to explore: (1) whether amlodipine could inhibit up-regulation of endothelial p53 significantly enhanced neovascularization upon hyperglycemic stress. Mechanistically, p53 negatively regulated the phosphorylation of p-eNOS, Bcl-2 and Bax, and phosphorylated-ROCK1 were detected by western blot. Nicotin oxide (NO) concentration within HUVECs was quantitatively assessed by 4-aminomethyl-2,7-difluorescein (DAF-FM) diacetate was stained in green colour. Flow cytometry with Annexin V-fluorescein isothiocyanate (FITC)/propidium iodide (PI) staining was performed to quantitatively evaluate the apoptotic index of HUVECs.

Results: As compared to blank control group, expressions of eNOS and p-eNOS and concentration of NO were profoundly reduced in Ang-II group. Nonetheless, endothelial dysfunction was reversed by each enantiomer of amlodipine therapy. ROCK1 activity (as indicated by phosphorylated-ROCK1 expression) was significantly enhanced in Ang-II group, while was offset by each enantiomer of amlodipine. Moreover, amlodipine could revert Ang-II-induced acetylcholine-induced vasodilatation was significantly impaired in a murine model of diabetes.

Conclusion: Our findings demonstrated that amlodipine could suppress Ang-II-induced endothelial dysfunction and apoptosis, and dextrorotary and racemic amlodipine seem to be more potent than levorotatory amlodipine. The benefits may be associated with ROCK1 activity diminishment.

P4314 | BENCH
Endothelial p53 is crucially involved in regulating vascular function
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p53 is known as a guardian of genome that protects against genomic instability induced upon cellular stresses. Recently, accumulating evidence has shown that p53 has undesirable effects on aging and age-associated diseases. Here we show that endothelial p53 is crucially involved in the pathologies of vascular dysfunction, metabolic dysfunction, and cardiovascular diseases. We found that acetylcholine-induced vasodilatation was significantly impaired in a murine model of type 2 diabetes, which was associated with up-regulation of endothelial p53 expression. Endothelial deletion of p53 markedly improved endothelial dysfunction upon hyperglycemic stress. Mechanistically, p53 negatively regulated the phosphorylation of eNOS by up-regulating PTEN expression. We also found that p53 expression was markedly increased in vessels of ischemic tissues and that inhibiting up-regulation of endothelial p53 significantly enhanced neovascularization in ischemic tissues. To further investigate the role of endothelial p53, we generated a gain-of-function model of endothelial p53 by deleting Mdm4, a negative regulator of p53, from endothelial cells. Endothelial deletion of Mdm4 led to an increase in p53 expression and a decrease of phospho-eNOS level, causing endothelial dysfunction as well as reducing blood flow recovery in ischemic tissues. These results indicate that endothelial p53 is critically involved in regulating vascular function under hyperglycemic and hypoxic conditions. Inhibition of endothelial p53 would become a novel therapeutic target in patients with systemic metabolic dysfunction.

BEST POSTERS IN PROSTHETIC VALVE DISEASE

P4316 | BEDSIDE
Antithrombotic strategy after bioprosthetic aortic valve replacement in patients with sinus rhythm: evaluation of guideline implementation
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Background: Patients undergoing aortic valve replacement are at risk of developing valve thrombosis and systemic thromboembolism. Current guidelines recommend antithrombotic therapy with aspirin or vitamin K antagonists (VKA) during the first three months after the procedure. As a consequence, the most appropriate antithrombotic therapy is still a matter of debate. This retrospective work aimed to analyse thromboembolic and bleeding complications in patients with either anticoagulation or antiaggregation therapy one year after bioprosthetic aortic valve replacement.

Methods: A total of 402 patients undergoing bioprosthetic aortic valve implantation at the University Medical Centre and subsequently treated at three regional hospitals were included. The individual duration of either vitamin K antagonists (acenocoumarol) or aspirin was determined and related to thrombotic and bleeding events. Patients were followed and censored at 1 year postoperatively for survival, cerebral ischemia, myocardial infarction, peripheral arterial embolism and minor and major haemorrhages.

Results: A total of 24 thromboembolic complications and 31 bleeding episodes occurred. Multivariate analyses revealed that acenocoumarol caused more bleedings (relative risk (RR): 8.41; 95% CI: 0.36–19.79) and a similar amount of thromboembolic events (RR: 1.2; 95% CI: 0.47–3.02) compared to aspirin after one year of follow up. Prior use of acenocoumarol was found to be a predictive risk factor for thromboembolic events (RR: 3.1; 95% CI: 1.31 to 7.19). For bleeding events, gender, dyslipidemia, prior percutaneous coronary intervention and prior use of acenocoumarol and concomitant coronary artery bypass grafting were found to be predictors.

Conclusion: In patients one year following bioprosthetic aortic valve replacement, acenocoumarol therapy was associated with a significant increase in bleeding events and no reduction of thromboembolic events compared to antiplatelet therapy. These findings support the recommendations of aspirin over VKA as post-operative thromboprophylaxis during three months.

P4316 | BEDSIDE
Postoperative lipids management among patients with bioprosthetic heart valves: mid-term follow-up analysis
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Background: Lipids have been claimed to affect outcomes in many clinical settings, including heart valve surgery. No definite data are available on the effect of different lipid management strategies over the postoperative course of patients receiving bioprosthetic heart valves.

Purpose: To investigate whether lipid management affects mid-term outcomes after heart valve replacement with bioprosthetic valves.

Methods: A total of 1346 patients who underwent heart valve replacement with bioprosthesis from 2004 to 2010 were reviewed, and only those patients for whom 5-year clinical follow-up (FU) was available were included in the analysis. The outcomes examined were major and minor haemorrhages. Patients were followed and censored at 1 year postoperatively for survival, cerebral ischemia, myocardial infarction, peripheral arterial embolism and minor and major haemorrhages.

Results: A total of 24 thromboembolic complications and 31 bleeding episodes occurred. Multivariate analyses revealed that the use of acenocoumarol caused more bleedings (relative risk (RR): 8.41; 95% CI: 0.36–19.79) and a similar amount of thromboembolic events (RR: 1.2; 95% CI: 0.47–3.02) compared to aspirin after one year of follow up. Prior use of acenocoumarol was found to be a predictive risk factor for thromboembolic events (RR: 3.1; 95% CI: 1.31 to 7.19). For bleeding events, gender, dyslipidemia, prior percutaneous coronary intervention and prior use of acenocoumarol and concomitant coronary artery bypass grafting were found to be predictors.

Conclusion: In patients one year following bioprosthetic aortic valve replacement, acenocoumarol therapy was associated with a significant increase in bleeding events and no reduction of thromboembolic events compared to antiplatelet therapy. These findings support the recommendations of aspirin over VKA as post-operative thromboprophylaxis during three months.

P4318 | BEDSIDE
Thrombolytic therapy for left side prosthetic valve thrombosis short and long term follow up study
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Background: Prosthetic valve thrombosis is a devastating complication. Urgent
valve replacement has been the treatment of choice in left side prosthetic valve thrombosis (PVT) in critically ill NYHA Class III-IV patients. Thrombolytic therapy is normally recommended for NYHA III patients with small thrombus burden.

**Purpose:** We have analyzed the results of thrombolytic therapy in left sided prosthetic valve thrombosis in critically ill NYHA III/IV patients where surgery was either refused due to financial constraints or by the surgical team.

**Methods:** 11 patients with left sided prosthetic valve thrombosis (8 mitral and 3 aortic) in NYHA III/IV were studied. Patients belonged to small villages/towns and had poor financial background without any insurance support. They were administered intravenous streptokinase (STK) in dose of 500,000 units bolus over 15–20 minutes and followed by infusion of 100,000 units/hour for 3 days. Results were assessed clinically, 2DECHO and by fluoroscopy.

**Results:** 11 patients, 35–65yrs, female 4 and male 7 had mechanical bileaflet prosthetic valves implanted: mitral (8) and aortic (3). One patient had both mitral and aortic prosthetic valves. One patient had diabetes and had undergone prior PCI with DES implantation to ostial left main. The interval between prosthetic valve implantation and thrombosis varied between 2–11 years. Three had associated atrial fibrillation and one had multiple VPCs. All had significant cardiomegaly and LVH. EF varied between 30–50%. Mean gradient across valves was increased on 2DECHO in all patients. All had only one mobile leaflet of prosthetic valve on fluoroscopy. INR varied between 1.0–1.8 at the time of diagnosis of PVT. 4 patients were in severe hypotensive shock and 6 presented with pulmonary hypertension.

**Conclusion:** The success rate was 81%. For successful cases, the mean t-PA dose and UFH treatment duration were 46±19 mg and 14±6 days, respectively. p=0.003). The only univariate predictor of an unsuccessful result was being non-obstructive PVT. The TT regimen was increased on 2DECHO in all patients. All had only one mobile leaflet of prosthetic valve on fluoroscopy. INR varied between 1.0–1.8 at the time of diagnosis of PVT. 4 patients were in severe hypotensive shock and 6 presented with pulmonary hypertension.

**P4319 | BEDSIDE**

**Thrombolysis versus unfractionated heparin as first-line strategy for non-obstructive prosthetic valve thrombosis**

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**Background:** Thrombolytic therapy (TT) is efficient and relatively safe in patients with prosthetic valve thrombosis (PVT). However, current guidelines recommend optimized anticoagulation as an initial approach and thrombolysis is restricted to very high risk surgical candidates in patients with non-obstructive PVT with a valve thrombus diameter ≥10 mm.

**Purpose:** To compare the short term efficacy and safety of optimized anticoagulation with unfractionated heparin (UFH) versus TT with recombinant tissue plasminogen activator (t-PA) in patients with PVT.

**Methods:** Overall 58 patients (38 female, age 49±10 years) with non-obstructive PVT and a thrombus diameter of <10 mm assessed by transesophageal echocardiography (TEE) and without a contraindication to TT were prospectively included between 2011 and 2014 in a single center. Patients were assigned to either TT (29 patients) or anticoagulation (29 patients) strategies. The TT regimen was ultra-low (25-h) infusion of low dose (25 mg) t-PA with repetition (maximum total dose 200 mg). The anticoagulation regimen was continuous infusion of UFH with optimized partial thromboplastin time until treatment success or for maximum 28 days. The treatment efficacy was assessed by serial TEE. The end-points were in-hospital treatment success, mortality and complication rates.

**Results:** There were no difference between the two groups in terms of baseline clinical and TEE characteristics including age (p=0.89), gender (p=1), heart rhythm (p=0.43), functional capacity (p=0.63), elapsed time since valve surgery (p=0.3), thrombosed valve position (p=0.7), thrombus area (p=0.86), baseline stroke area (p=0.63), history of stroke or transient ischemic attack (p=0.54). The overall success rate was 81%. For successful cases, the mean t-PA dose and UFH treatment duration were 46±19 mg and 14±6 days, respectively. Success rate was significantly higher in t-PA group compared to UFH group (96.6% vs 85.5%, respectively, p=0.003). The only univariate predictor of an unsuccessful result was being non-obstructive PVT in the UFH treatment group (RR: 9.0, 95% CI: 2.65–p=0.003). Overall 6 (10.3%) patients suffered from complications. There were one intrabdominal bleeding requiring transfusion and 2 minor bleedings in t-PA group. There were one death and 3 cases of recurrent thrombus in the UFH group. The thrombosis was observed relatively lower incidence of major complications (3.3% vs 10.3%, p=0.35) was observed in the t-PA group compared with UFH group.

**Conclusion:** Ultra-low (25 hours) infusion of low dose (25 mg) t-PA is superior to UFH as first-line treatment strategy in patients with non-obstructive PVT.
expressed in quintiles ALA intake was not associated with incident MI neither among men nor women (Table). No effect modification was observed when a cross-product term was added in between analyses including tertiles of energy-adjusted dietary intake of ALA and LC-n3 acid or linoleic acid. Conclusion: Dietary intake of ALA was not significantly associated with incident MI neither among men nor women.

**P4323 | BEDSIDE**
Association between persistent psychological distress and 12 year cardiovascular and total mortality in patients with stable coronary artery disease

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Background: Psychological distress has been associated with higher mortality, but the importance of persistence of symptoms over time is not known. Aim: To determine whether persistent or intermittent psychological distress is associated with cardiovascular and total mortality in patients with stable coronary artery disease.

Methods: 940 participants enrolled in the Long Term Intervention with Pravastatin in Ischemic Disease (LIPID) trial completed ≥4 General Health Questionnaires (GHQ-30) at baseline and after 6 months, 1, 2 and 4 years. The hazard ratio (HR) for cardiovascular (CV) and total mortality were determined after follow-up for the next 121, (IGR 8.6,12.5) years for subjects who reported mild (GHQ score ≥5 and more severe (GHQ score ≥10) psychological distress which was either intermittent (on one or two occasions), or persistent (on 3 or more occasions) compared with those reporting no distress. HR’s were adjusted for baseline variables.

Results: Moderate to severe psychological stress was reported –60% of the time by 35% (4%) subjects. These patients had higher CV (adjusted HR 2.50, 95% CI 1.44 to 4.36, p=0.0012), and all-cause mortality (adjusted HR 2.02, 95% CI 1.32 to 3.14, p=0.0013). In contrast, 188 (18%) patients who reported moderate-severe distress once or twice did not have higher CV (adjusted HR 0.93, 95% CI 0.64 to 1.34, p=0.69) or all-cause mortality (adjusted HR 0.94, 95% CI 0.73 to 1.22, p=0.65). The associations between lower severe psychological distress (GHQ-5) present >60% of the time and CV (adjusted HR 1.17, 95% CI 0.76 to 1.82, p=0.47) and total mortality (HR 1.30, 95% CI 0.96 to 1.76, p=0.08) were not statistically significant, and there was no association with mortality if present <50% of the time.

Conclusion: In patients with stable coronary artery disease, persistent moderate-severe psychological distress was associated with a substantially higher risk of long-term CV and total mortality, but distress that was not persistent was not associated with mortality. Further research is needed to determine whether reducing persistent psychological distress improves outcomes in this high risk group.

**P4324 | BEDSIDE**
European HeartQoL reference values in patients with coronary heart disease

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Background and introduction: In comparison with the general population, Health Related Quality of Life (HRQoL) outcomes are significantly impaired in coronary heart disease (CHD) patients. Recently, the HeartQoL instrument was developed, from which a global HeartQoL score and two subscale scores (physical and emotional subscale), each ranging between 0 (worst) and 3 (best), can be calculated.

Purpose: The aim of this study was to set HeartQoL reference values in a population of stable coronary patients stratified by age, gender, diabetes and educational level. Additionally, we aimed to investigate the association between HeartQoL and the patients coronary risk profile.

Methods: Analyses are based on the EUROASPIRE IV (EUROpean Action on Secondary and Primary prevention through Intervention to Reduce Events) survey. Patients eligible for inclusion were males and females, who had been hospitalised for a first or recurrent coronary event. HeartQoL scores were available for 7261 patients.

Results: Significantly worse outcomes were observed in higher risk patient groups, with lower scores in females, older patients and lower educated patients.

**P4326 | BEDSIDE**
Differential impact of diabetes on platelet reactivity and stent thrombosis in women and men: insights from the ADAPT-DES study

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Introduction: Diabetes mellitus (DM) has been reported to be a strong risk factor for stent thrombosis (ST) after DES implantation. Previous data have shown that the clinical impact of DM is greater for women than for men.

Objectives: To examine differences in the prevalence of high platelet reactivity (HPR) on clopidogrel between sexes according to DM status and to assess the sex-specific impact of DM on cumulative definite/probable ST at 2 years, adjusting for baseline clinical confounders and HPR.

Methods: Patients from the prospective, multicenter ADAPT-DES study were stratified by sex and the DM status. HPR was defined as a P2Y12 reactivity units >228.

Results: Of 8,582 patients included in ADAPT-DES, 9.6% were women with DM and 16.2% were women with no DM, while 22.8% were men with DM and 51.3% were men with no DM. Women with DM had higher BMI and prevalence of insulin-treated DM. Conversely, men with DM had more comorbidities and more severe CAD. Presence of DM was associated with a higher prevalence of HPR irrespective of sex (Figure), with the highest values observed in women with DM (p < 0.01). The unadjusted risk for ST associated with DM was higher in both men (0.8% vs. 1.6%, p=0.01) and women (0.8% vs. 1.7%, p=0.03); however, after multivariable adjustment for baseline clinical confounders, including HPR, these associations were no longer significant in women (adjHR: 0.84; 95% CI: 0.22–3.29) or men (adjHR: 1.57; 95% CI: 0.89–2.77), with no interaction between DM status and sex (p=0.05).

Conclusions: DM is associated with a higher prevalence of HPR in both sexes, particularly in women. The unadjusted risk for ST associated with DM is attenuated after adjusting for HPR across sexes, suggesting that modulation of platelet function may affect long-term ST risk in DM patients.

**BEST POSTERS IN RISK FACTORS AND OUTCOMES AFTER PCI**
P4327 | BEDSIDE
Mortality trends after unprotected left main stem PCI in England and Wales, 2005-2014: Analysis of 10,825 cases from the British Cardiovascular Intervention Society (BCIS) national registry
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Background: High platelet reactivity (HPR) on clopidogrel predicts major adverse cardiovascular events (MACE) post PCI. Anemia is also known to be strongly associated with adverse prognosis and bleeding risk.

Methods: Prospective population-based linked cohort study of 10,825 patients from the BCIS database, 1st Jan 2005 through 31st March 2014.

Results: Compared with 2005, in 2013 the annual numbers of cases increased from 348 to 2,122. Between 2005 and 2014 the proportion of cases treated as STEMI increased (10.4% vs. 19.4%). Overall, baseline risk increased; cardiogenic shock 7.9% to 13.1%, P < 0.001; severe left ventricular systolic dysfunction, 9.0% to 12.5%, P = 0.002; age > 80 years, 20.7% to 24.2%, P = 0.046. Radical PCI increased from 18.4% in 2005–6 to 61.2% in 2013–14. Compared with 2005–6, 30-day mortality in 2013–14 was stable (STEMI: adjusted odds ratio (aOR), 95% CI 0.3–0.5; 1.6–4.3; NSTEACS 0.9, 0.6 to 1.4; CSA 1.2, 0.2 to 6.4). Likewise, 1-year mortality remained stable (STEMI aOR 1.2, 95% CI 0.7 to 2.3; NSTEACS 1.6, 1.1 to 2.2; CSA 1.8, 0.9 to 3.8). By 2013–14, for STEMI with cardiogenic shock, 30-day mortality rates decreased by 13.4% (95% CI 10.9% to 16.0%) and 1-year mortality rate increased by 2.5% (1.5% to 4.0%).

Conclusions: Between 2005 and 2014, the number of cases of UPLMS PCI in England and Wales increased by over 6-fold. Although baseline risk increased, mortality was stable across all clinical presentations. Early mortality rate for STEMI with cardiogenic shock declined, however late mortality rate remained high.

P4328 | BEDSIDE
Impact of platelet reactivity in anemic and non-anemic patients with coronary artery disease undergoing percutaneous coronary intervention: insights from the adapt-des study
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Background: Combined HPR and anemia has a synergistic effect on thrombotic risk after PCI, whereas anemia in the absence of HPR is associated with a higher risk for bleeding. The independent impact of HPR on both ischemic risk and freedom from bleeding appears uniform irrespective of baseline anemia status.

Methods: Randomized comparison of 9-month stent struts coverage of biolimus and everolimus drug-eluting stents assessed by OCT in patients with STEMI
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Aim: The aim of this trial was to compare healing (assessed by optical coherence tomography-OCT) of biolimus A9 and everolimus drug-eluting stents at 9-month follow-up in patients with ST-segment elevation myocardial infarction (STEMI) treated by primary PCI (pPCI). 9-month clinical and angiographic data were also compared in both groups.

Methods: 201 patients with STEMI treated by primary PCI were randomly enrolled in the trial. 101 patients were randomized to the biolimus A9 stent group and 100 patients to the everolimus group. All patients were pre-treated with a standard triple therapy (unfractionated heparin, aspirin and clopidogrel). The use of inhibitors of GP IIb/IIIa and thrombus-ascilation were left at the discretion of physicians, however both were strongly recommended. Stent implantation was carried out according to the standard clinical practice employing low pressure stent deployment with high-pressure postdilatation using shorter, non-compliant balloon.

Results: All patients were scheduled for 9-month clinical, angiographic and OCT follow-up. Primary end-point of this study were the number of uncovered struts.

Results: All procedures were carried out without complications in both groups. Baseline demographic and procedural characteristic were well balanced in both groups. The rate of MACE did not differ significantly at 30 days between both groups. There was one acute stent thrombosis requiring immediate re-PCI in the everolimus stent group and one asymptomatic stent thrombosis in the biolimus group (revealed during stage PCI of non-culprit lesion). Furthermore, there was one non-cardiac death in the biolimus group. 9-month angiographic and OCT follow-up underwent 87% patients in everolimus and 90% patients in biolimus group respectively. At 9-month follow, the rate of MACE and angiographic restenosis were comparable and very low in both groups (2 vs. 1% and 1 vs 1% respectively; P=NS). All in-segment and in-stent angiographic data (reference diameter, minimal diameter, mean diameter, % stenosis) were comparable at 9-month in both groups. OCT data presents Table. The rate of uncovered struts were significantly higher in biolimus group (19.67±16.52 vs. 9.99±10.38; P < 0.0001). On the other hand, there was a trend to higher mean and minimal lumen diameter (3.35mm±0.56 vs. 3.2mm±0.43; p=0.06 and 2.88mm±0.55 vs. 2.74mm±0.49; p=0.09).

Conclusions: Combined HPR and anemia has a synergistic effect on thrombotic risk after PCI, whereas anemia in the absence of HPR is associated with a higher risk for bleeding. The independent impact of HPR on both ischemic risk and freedom from bleeding appears uniform irrespective of baseline anemia status.
BEST POSTERS IN VENTRICULAR FUNCTION / HAEMODYNAMICS

P4331 | BEDSIDE
Effect of high-intensity interval training combined with strength exercise on aortic-ventricular coupling in patients with chronic heart failure. A randomized phase III clinical trial

Background: It is known that heart failure causes changes in cardiac mechanics, like an unfavorable alteration of ventricular/vascular coupling is associated with increased arterial stiffness and has been linked directly to the subsequent development of adverse cardiovascular outcomes. Aim of this work was to evaluate the effect of high-intensity interval exercise (i.e., 30 sec at 100% of max workload, followed by 30 sec at rest, on 3 days/week 45 minutes working-out schedule for 12 weeks), on left ventricular function and aortic elastic properties among chronic heart failure (CHF) patients.

Methods: A phase III clinical trial. Of the 100 consecutive CHF patients (NYHA class II-IV, ejection fraction <50%) that were randomly allocated, 72 completed the study (exercise training group, n=33, 63±9 years, 88% men, and control group, n=39, 56±11 years, 82% men). All patients underwent cardiopulmonary stress test, non-invasive high-fidelity tonometry of the radial artery, pulse wave velocity measurement using a SphygmoCor device and echocardiography before and after completion of the training program.

Results: Both groups reported similar medical characteristics and physical activity status. General mixed effects models revealed that the intervention group reduced pulse wave velocity by 9% (p<0.05); Emv/Vp by 14% (p<0.06); E to A ratio by 24% (p<0.004), E to Emv ratio by 8% (p<0.05), MLHFG score by 66% (p<0.001), glutathione peroxidase score by 19% (p<0.05), increased aortic rigidity index by 29%; VTI by 4% (p<0.05), 6-minutes-walk distance up to 13% (p<0.05), peak oxygen uptake by 28% (p<0.001) and peak power by 25% (p<0.005). There were no significant changes in the control group.

Conclusions: Intensive high-intensity aerobic training, combined with strength exercise, seems to benefit aortic dilatation capacity and augmented systolic pressure in parallel with improvement in left ventricular diastolic function and quality of life. Those findings reflect a beneficial impact of exercise on arterial-ventricular coupling that creates boost of systolic pressure and the wave reflection of the aorta regains a positive influence on pressure.

P4332 | BEDSIDE
Lung function in relation to cardiac dysfunction and heart failure in the general population
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Background: Lung and heart diseases share common risk factors and dyspnea as main clinical symptom. Impairment of lung function may cause symptoms of heart failure, although no overt cardiovascular or structural heart disease is present. The association between pulmonary hypertension (PH) and left ventricular impairment in the general population remains to be investigated.

Methods: In 5000 individuals from the general population (mean age 55±11 years, age range 46–65 years, 50.8% men) in the Gutenberg Health Study we performed spirometry with the micromedical siro USB and multimodal echocardiography with an iE33 echocardiography system with an 5S–1 sector array transducer, a phased array with 80 elements and a 5- to 1-MHz operating frequency range. Lung function parameters (FEV1, FVC, FEV1/FVC) were associated with echocardiographic measures of cardiac structure and systolic and diastolic function.

Results: The mean left ventricular ejection fraction (EF) was 64±7% (current smoking 19.2%, COPD 4.8%). The common cardiovascular risk factors age, male gender, BMI, diabetes, current smoking and hypertension were associated with FEV1 and FVC. Diabetes and hypertension showed no association with FEV1/FVC. The linear regression analysis showed significant associations (p<0.001) both for FEV1 and FVC with IVST, LVEDD, E/E’, EDV, SV and EF, whereas FEV1/FVC was significantly related to LVEDD (p<0.0017), ESV (p<0.006), LVESD and EF. Increased age (p<0.005), increased augmentative left ventricular impairment in the general population remains to be investigated.

Conclusions: The associations may indicate early stages of hypertension, reduction of left ventricular filling and cardiac output, whereas the relation with diastolic function may be explained by subclinical changes with a shortened diastolic filling, hypoxemia and reduced preload. Such associations have been suggested in COPD patients and were confirmed in our sample.

P4333 | BEDSIDE
A single-centre experience in the hemodynamic improvement and prognosis of heart transplantation candidates with group 2 reactive pulmonary hypertension treated with sildenafil
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Background: The post-capillary reactive form of pulmonary hypertension (PH) due to left heart disease (group 2 PH) is characterized by increased transpulmonary pressure gradient (TPG) and pulmonary vascular resistance (PVR). Pulmonary arterial vasodilator treatment with phosphodiesterase 5 inhibitors is sometimes used in order to meet eligibility criteria for heart transplantation (HTx). We aimed to study the hemodynamic and clinical effects of sildenafil in a reactive group 2 PH cohort and the prognostic implications of the hemodynamic response.

Methods: Retrospective analysis of 107 patients with reactive group 2 PH (TPG > 12 mmHg) referred for HTx, on optimal medical therapy, treated with sildenafil 20 mg tid, at a single centre (2004–2014). We studied clinical and hemodynamic data before and after treatment. Clinical endpoints: time to all-cause death, HTx and first hospitalization after sildenafil initiation. Hemodynamic positive response was defined as lowering of PVR to 3.5 Wood units, provided that the cardiac index (CI) was not reduced. Statistical analysis: Wilcoxon/McNemar tests, Kaplan Maier and Cox regression methods.

Results: Mean age was 55±11 years, 73% were male. Half of the patients were in NYHA class IV, with median BNP 605 (IQR 665) pg/dL and peak VO2 15.6 ± 6.8 ml/kg/min. Hemodynamic baseline parameters: mean pulmonary artery pressure (mPAP) 45 (IQR 14) mmHg, pulmonary capillary wedge pressure (PCWP) 27 (IQR 13) mmHg, CI 1.8 (IQR 0.7) mL/min/m², PVR 5.5 (IQR 3.2) Wood units, TPG 17 (IQR 8) mmHg. For 56 patients, data from a follow-up visit after cardiac catheterization were available. After a mean of 24 (IQR 20) days of treatment the NYHA class improved, with lowering of BNP, mPAP and PCW, and increase of VO2 max and CI (p<0.05) and mean systemic arterial pressure did not change (p=0.07). Half of the group had at least one hospitalization, 74% underwent HTx and 20% died (median 1658 days to follow-up). There was a positive hemodynamic response in 36%; this group had a numerically higher HTx rate (50%) than those without hemodynamic response (22%). We found no significant difference in death (20 vs. 14%) nor in first hospitalization (80 vs. 80%) when comparing patients with and without positive hemodynamic response.

Conclusion: There was improvement of clinical and hemodynamic parameters in reactive group 2 PH patients referred for HTx after sildenafil treatment. There was no significant difference in the outcomes of patients with positive hemodynamic response though there was a trend to higher HTx performance, eventually signaling achieving of eligibility.

P4334 | BEDSIDE
Percutaneous ventricular restoration (PVR) therapy using the parachute device in subjects with ischemic heart failure: one year meta-analysis and bad nauheim experience
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Background: Left ventricle (LV) remodeling after anterior wall myocardial infarction (AWMI) leads to increased LV volumes, myocardial stress, and ultimately heart failure (HF). Treatment options are limited for these high-risk HF patients.

Aims: The primary objective is to assess one year safety and efficacy of the CardioKinetic Parachute Implant System in the partitioning of the left ventricle in subjects with heart failure due to ischemic heart disease across trials completed to date (PARACHUTE Cohort A, PARACHUTE US Feasibility, and PARACHUTE III) and compare these results to the observations from recent cases performed in Germany.

Methods: One hundred thirty-four subjects with NYHA class II-IV HF secondary to AWMI, with akinetic or dyskinetic wall motion abnormality, and LV ejection fraction <40%, were enrolled in Europe and the United States. The major endpoints evaluated at one year will be stroke, all-cause death, and the combination of all-cause death and repeat hospitalization for worsening HF. Hemodynamic assessments will be evaluated with echo, and functional capacity assessed by NYHA and 6MWT.

Results: Of the 134 subjects enrolled, 128 were successfully treated (96%). The rates of stroke, all-cause death, and the combination of all-cause death and repeat hospitalization for worsening HF were 2.4%, 8.8%, and 23.8%, respectively. Improvement of systolic cardiac function (p<0.05) was noted in LV volume indices, EF%, stroke work, and contractility index, along with a trend in fractional shortening, at 1-year follow-up relative to baseline values. This was accompanied by a significant reduction in left atrial volume suggesting improved diastolic function. The 1-year mean NYHA Class of subjects (1.9±0.7) was significantly reduced (p<0.0001) from baseline NYHA Class (2.5±0.5) reflecting functional improvement. Performance on 6-minute walk test with also improved from...
369 meters at baseline to 391 at 1 year (p=0.01). The longer term data on the Bad Nauheim patients will be collected prior to the ESC meeting in late August 2015.

Conclusions: The meta-analysis of the Parachute data confirms the safety and efficacy of the Parachute device in treating HF. The additional Bad Nauheim data will be available prior to ESC 2015.

BEST POSTERS IN AUTONOMIC NERVOUS SYSTEM IN HYPERTENSION

P4336 | BEDSIDE
Cardiac pacemaker stimulates the brain as well as the heart in humans - a PET functional study
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Purpose: Cardiac pacemaker implantation is a standard therapy for patients with clinically significant bradyarrhythmia. After cardiac pacemaker implantation, some patients complain of palpitation, implying possible activation of cortical receptive fields of afferent nerves such as anterior cingulate cortex (ACC). ACC also modulates autonomic nervous system in collaboration with hypothalamus and brainstem. We thus examined brain activity and plasma catecholamine levels in response to cardiac electrical stimulation in humans.

Methods: We studied 10 patients (74.7±1.9 yrs, M/F 5/5) with cardiac pacemaker implantation. Before the measurement, mode of cardiac pacemaker was changed to VVI 80–90 bpm with 1.5V intensity. Cerebral blood flow (CBF) was measured during sham stimulation (1.5V) and intense stimulation (7.5–8V) using [15O]H2O PET. The CBF images of intense stimulation were compared with those of sham stimulation using SPM8, a common analysis tool for neuroimages. Blood samples were obtained from the cubital vein before and after CBF measurements for plasma catecholamine levels (one patient was excluded for the analysis due to clinical significant bradyarrhythmia. After cardiac pacemaker implantation, some patients presented with palpitation, implying possible activation of cortical receptive fields of afferent nerves such as anterior cingulate cortex (ACC). ACC also modulates autonomic nervous system in collaboration with hypothalamus and brainstem. We thus examined brain activity and plasma catecholamine levels in response to cardiac electrical stimulation in humans.

Results: Intense stimulation significantly increased CBF in ACC as compared with sham stimulation (intense, 64±6.7 vs. sham, 61±1±3 ml/100g/min, P=0.008, n=10 each) (Figure, yellow arrowhead). Plasma adrenaline level was significantly increased in response to intense stimulation as compared with sham stimulation (intense, 64.6±0.7 vs. sham, 61.0±1.3 ml/100g/min, P=0.008, n=10 each).

Conclusion: This study demonstrates for the first time that electrical stimulation of cardiac pacemaker activates ACC with increased plasma adrenaline level.

Figure 1

P4337 | BEDSIDE
Increased cardiovascular sympathetic modulation as a predictor of death in patients with amyotrophic lateral sclerosis
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Background: Amyotrophic Lateral Sclerosis (ALS) is one of the most devastating of adult-onset neurodegenerative disorders, characterized by a marked heterogeneity in both presentation and rate of progression, and by motor and extramotor neuron loss. There is increasing evidence that the autonomic nervous system (ANS) is also affected as part of the complex degenerative process. ALS has a progressive course with death occurring as a mean in 3 ys, but with some variability among patients. The predominant cause of death is respiratory failure, but sudden death has also been reported.

Purpose: Aim of this study was to investigate the cardiovascular neural regulation in ALS.

Methods: We enrolled 31 ALS patients (14 F, 17 M, age 61±13 ys), ECG, arterial pressure and respiration activity signals were continuously recorded at rest and during a 75° head-up tilt. Autoregressive spectral analysis provided the indices of the baroreflex and catecholaminergic modulation (LF_RR and HF_RR, respectively) and the sympathetic vasomotor control (LF_SAP). Data are expressed as mean±SD. Discriminant analysis was applied to spectral indices and all clinical characteristics.

Results: All the patients were characterized by low RR variance both at rest and during tilt (73±1746 and 490±467 ms²) and by an altered response to orthostasis, as reflected by the absence of increase of LF_RR, LF_SAP and LF/HF ratio during tilt. Disease duration (DD) significantly separated our population in Group 1 (15 pts, DD=36 mo) and Group 2 (16 pts, DD=36 mo). At rest, sympathetic cardiac indices were higher in Group 1 than Group 2 (LF_RR 64±19 vs 44±30 ns). At follow-up, 8 patients died, 7 of Group 1 (31±14 mo from disease onset) and 1 of Group 2 (56 mo from disease onset).

Conclusions: Our study outlined that ANS is invariably impaired in ALS, and patients can present with different patterns that can be relevant in terms of prognosis. At rest, patients with high or low sympathetic activity directed to the heart differed for disease duration. The cut-off corresponded to the mean survival time in ALS, and might have clinical relevance in separating slow versus fast progressive ALS. Accordingly, different ANS patterns are significantly higher in the group with high sympathetic modulation. These findings support the new concept of ALS as a multisystem disorder with phenotypic heterogeneity, and suggest that the patient’s sympathovagal profile could provide prognostic indices. A comprehensive ANS evaluation is needed for a better understanding of the physiopathology of this complex neurodegenerative and multisystem disorder and to confirm our hypothesis.

P4338 | BEDSIDE
Sympathetic nerve activity and arterial baroreflex function in rheumatoid arthritis
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Background: Rheumatoid Arthritis (RA) is a chronic, systemic inflammatory disorder associated with elevated cardiovascular mortality. Heightened sympathetic nerve activity (SNA) and/or arterial baroreflex dysfunction are potentially important contributory factors. Experimental elevations in pro-inflammatory cytokine concentration robustly increase SNA and reduce cardiac baroreflex sensitivity in rats. However, the clinical relevance of positive correlations between RA and sympathetic activation remains unknown.

Methods: Seventeen rheumatoid RA patients (RA, 8 women, mean age ± standard deviation 56±12 yr), 17 RA patients with hypertension (RA-HTN, 12 women, 61±10 yr), 16 patients with hypertension (HTN, 11 women, 60±10 yrs) and 17 healthy normotensive control subjects (HC, 10 women, 54±13 yr) were studied. Efferent SNA to the skeletal muscle vasculature (MSNA, peroneal microneurography) was recorded with blood pressure (BP) and heart rate (HR) while subjects rested supine. Arterial baroreflex control of HR (slope of systolic BP vs. R-R Interval) and MSNA (slope of diastolic BP vs. MSNA) was determined from sequential infusion of sodium nitroprusside (100 μg) and phenylephrine (150 μg; modified Oxford method).

Results: Mean BP was elevated in RA-HTN and HTN groups (geometric mean 109, 95% confidence interval 104–114 vs. 105, 98–112 mmHg, respectively) compared to RA (95, 91–100 mmHg, p=0.05) and HC (89, 82–95 mmHg, P<0.001). MSNA was also higher in RA and RA-HTN (86±10 vs. 65±10 b.min-1 respectively) than HTN and HC (60±7, HC 57±7 b.min-1; P<0.001). MSNA was higher in the RA, RA-HTN and HTN groups compared to HC (32±9, 35±14, 37±8 vs 22±8 bursts/min, respectively; P<0.004). Arterial baroreflex control of MSNA was not different between groups (p=0.927), whereas cardiac baroreflex sensitivity was higher in HC (5.3, 3.4–8.3 ms/mmHg) than RA, RA-HTN and HTN (5.3, 3.4–8.3; 4.0, 2.4–6.9; and 6.0, 4.0–8.9 ms/mmHg respectively; p=0.002).

Conclusion: These findings provide the first evidence that MSNA is elevated in RA patients, despite the sensitivity of arterial baroreflex control of MSNA being preserved. Furthermore, cardiac baroreflex sensitivity is reduced in RA and heart rate is elevated. This apparent imbalance in the autonomic neural control of the heart and peripheral vasculature in patients with RA, appears independent of hypertension, and may partly explain the elevated cardiovascular mortality and occurrence of cardiac arrhythmias.

P4339 | BEDSIDE
Cerebral blood flow to the brain stem is reduced in humans with hypertension
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Background: The total cerebral blood flow (CBF) is reduced in hypertensive humans. The reduction in brain blood flow may play a role in hypertension via the so-called “Cushing’s mechanism”. This hypothesis states that a reduction in blood flow to the brain stem will trigger a compensatory increase in sympathetic nervous activity, which in turn drives an increase in blood
pressure. This is the first study to assess the regional cerebral blood flow to the brain stem in hypertensive patients.

**Purpose:** To investigate the regional CBF to the brain stem in hypertensive humans. We also sought to study how brain stem blood flow may relate to muscle sympathetic nerve activity (MSNA).

**Methods:** 36 hypertensive and 20 normotensive participants were included in the study (aged 19–76 years). Hypertension was defined as systolic blood pressure > 140mmHg and diastolic blood pressure > 90mmHg. The mean ± SD for the hypertensive subjects was 148±9/89.5±14.0/10.8 mmHg, and 120±7/4.5/12.7.7±2.2 mmHg for normotensive subjects. Resting blood flow to the brain stem was measured by pseudo-continuous arterial spin labelling (pCASL). The pCASL images were analysed using FSL software to obtain the averaged flow measure in ml/100g/min for the brain stem. Flow was compared between hypertensive and normotensive subjects by independent t-test. MSNA was recorded from the peroneal nerve at rest. MSNA burst activity was analysed per 100 heartbeats and per minute.

**Results:** There was a significant reduction in brain stem blood flow in the hypertensive population compared to the normotensive participants (mean ± SEM: normotensive 29.7±0.8 ml/100g/min, hypertensive 25.4±1.3 ml/100g/min, p=0.01). MSNA analysed as bursts per 100 heartbeats did not differ between the hypertensive and normotensive subjects (mean ± SEM: normotensive 48±3.9 versus hypertensive 57±3.4 bursts per 100 heartbeats, p=0.08) although a trend towards higher MSNA in hypertensive subjects was seen. However, MSNA burst data were comparable to the results in the 1st generation PVAC patients (mean ± SEM: normotensive 27±2.1 versus hypertensive 37±2.2 p=0.02).

**Conclusion:** We have shown for the first time that regional cerebral blood flow to the brain stem is reduced in hypertensive patients. We have also shown that in these patients the sympathetic driving to the brain stem blood flow, MSNA is increased. These data supports our hypothesis that a reduction in brain blood flow and increased sympathetic nervous activity may contribute to hypertension via the Cushing’s mechanism.

**POSTER SESSION 5 ABLATION OF ATRIAL FIBRILLATION I**

**P4340 | BEDSIDE**

Initial results of a second-generation multielectrode mapping and ablation catheter for pulmonary vein isolation (PVAC GOLD)

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**Background:** Antral pulmonary vein isolation (PVI) with radiofrequency energy is widely used as a strategy for catheter ablation of atrial fibrillation (AF). With the increasing demand for ablation procedures, new circular mapping and ablation catheters have been especially developed for AF ablation.

**Purpose:** The purpose of this study was to investigate the acute efficacy of the 2nd generation PVAC catheter (PVAC GOLD) in patients with AF. Performance data were compared with the results in the 1st generation PVAC catheters that have been especially developed for AF ablation.

**Methods:** We consecutively enrolled 40 patients (60±11 years) with highly symptomatic, drug refractory AF for PVI using phased RF ablation technique. Patients were subdivided into two groups (PVAC and PVAC GOLD). The first 20 patients were treated with the PVAC. The subsequent 20 patients were treated with the PVAC GOLD.

**Results:** All 164 targeted PVs could be isolated successfully. There were 23 patients with paroxysmal AF and 17 patients with persistent AF. The primary endpoint was defined as arrhythmia recurrence during follow-up. The mean follow-up was 15 months. Thirty-six eligible paroxysmal (n=27) or persistent (n=9) AF patients were consecutively enrolled. Twelve patients underwent PVI with the non-CF- catheter (CF- group) in a recall period and 24 with the CF-catheter (CF+ group). After the first circumferential lesion set the number of PV pairs requiring additional RF ablations needed for PVI (34.7±7.0 vs. 27.0±6.5), fluoroscopy time (29.5±9.5 vs. 16.0±5.5 min) and procedure time (93.8±18.9 vs. 83.1±10.6) were significantly lower in the CF+ group (n=24) compared to the CF- group (n=48). The mean ± SD for the hemodynamic efficiency may have been a result of reduction of low power ablations from 23.4±7.0 to 14.0±14.7 (p=0.006). There were no adverse events in either group.

**Conclusions:** The PVAC GOLD system allows a reduction in radiofrequency ablation time, higher effective energy delivery, fewer low power ablations and improved biophysical efficiency when compared to the first generation PVAC system. Further studies are needed to rule out if the improved acute parameters result in increased efficacy for PVI and freedom from AF.

**P4341 | BEDSIDE**

First in man evaluation of a new ablation catheter Thermocool smarttouch sf in atrial fibrillation ablation


**Background:** A sufficient tissue contact and an effective cooling of ablation catheters seems to be important for the success rate of complex ablation procedures.

**Hypothesis:** “First in man” evaluation of the new ablation catheter Thermcool SmartTouch SF, which combines a new highly effective open irrigated cooling system with a real time monitoring of tissue contact force. Three important properties of the catheter were evaluated: 1. the reproducibility of electroanatomic substrate maps (EAM). 2. The proportion of effective tissue contact during ablation. 3. Thrombogenicity during ablation.

**Methods:** For the evaluation of the mapping accuracy three independent operators generated a substrate map of the left atrium (low voltage areas were defined as voltage < 0.5mV) in the same patient. Subsequently the reproducibility of the low voltage areas was analyzed. For the evaluation of the tissue contact the mean tissue contact force and the percentage of ablation time within a predefined contact force (40−50g) were quantified. For the evaluation of the thrombogenicity high intensive ultrasound signals (HITS) in transcranial doppler flow sonography were counted during ablation.

**Results:** In total 12 patients suffering from atrial fibrillation were treated with the new ablation catheter (9 male, age 61±13 years, LA diameter 46±9mm). The low voltage areas had a matching of 92% in all 3 physicians. The mean tissue contact force during ablation was 28±8g. Ablation time in the predefined tissue contact force range. Under ablation within this contact force range almost no HIT could be counted. No catheter associated complication occurred.

**Conclusions:** The new ablation catheter Thermcool smart touch SF has very good mapping properties. Additionally, a high degree of predefined tissue contact force was reached during ablation. This fact together with the highly effective cooling tip of the catheter lead to an optimal prevention of thromboembolic events during ablation.

**P4342 | BEDSIDE**

Superior efficacy of pulmonary vein isolation with online contact force measurement persists after the learning period: a prospective case control study

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**Background and purpose:** Use of online contact force (CF)-measurement during circumferential pulmonary vein (PV) isolation (CPVI) for atrial fibrillation (AF) has demonstrated improvements in procedural parameters and mid-term clinical outcome. However it is unknown if experience gained with CPVI in patients performing CPVI with online contact force measurement to maintain this advantage.

**Methods and results:** This prospective trial compared procedural results of CPVI performed without a CF-measuring catheter to a control group performed with CF-measuring catheter, by an operator with prior experience with CF-technology. Thirty-six eligible paroxysmal (n=27) or persistent (n=9) AF patients were consecutively enrolled. Twelve patients underwent CPVI with the non-CF- catheter (CF- group) in a recall period and 24 with the CF-catheter (CF+ group). After the first circumferential lesion set the number of PV pairs requiring additional touch-up lesions to achieve adenosine-proof electrical isolation was significantly less in the CF+ group (2 of 48 (4.2%) vs. 7 of 24 (29.2%) in the CF+ and CF- group respectively, p=0.005). The procedure time was significantly lower in the CF+ group (117.9±23.3 min vs. 134.1±25.3 min, p=0.033), RF and fluoroscopy time did not differ between groups (31.5±7.1 min vs. 31.8±7.0 min and 11±5.6 min vs. 11±5.8 min in the CF+ and the CF- group, respectively).

**Procedural results**

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<td>Number of PV pairs requiring touch-up (n, %)</td>
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<td>2/24 (4.2)</td>
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<tr>
<td>Number of patients requiring touch-up (n, %)</td>
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<td>2/24 (8.3)</td>
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<td>Fluoroscopy time (min)</td>
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</tbody>
</table>

Data are presented as mean ± standard deviation or absolute number (n) + percentage (%). CF−: group in which CPVI is performed with the Navistar® Thermocool® ablation catheter: CF+: control group in which CPVI is performed with the Thermocool® SmartTouchTM catheter.

**Conclusion:** With the use of online CF-measurement PV isolation is more frequently completed following the first circumferential lesion set. A previous learning period with direct CF-feedback is not a substitute for real-time direct CF-measurement to maintain this advantage.

**P4343 | BEDSIDE**

Pulmonary vein isolation for paroxysmal atrial fibrillation using a novel gold multi-electrode duty cycled radiofrequency ablation catheter.


**Purpose:** Pulmonary vein isolation (PVI) is the cornerstone of ablation in paroxysmal atrial fibrillation (P-AF). With the multi-electrode ablation approach PVI isolation can be performed with less RF-energy applications and without additional 3D-mapping. The aim of this study was to investigate procedural characteristics and efficacy of the novel gold multi-electrode duty cycled radiofrequency ablation catheter (PVAC Gold).

**Methods:** A total of 91 consecutive patients (65±9 years old, 49 male) with P-AF undergoing PVI with PVAC Gold were studied. All procedures were performed with use of a non-steerable transseptal sheath. The primary endpoint was defined...
as documented recurrent AF or atrial tachycardia >30 seconds considering a blanking period of 3 months after the procedure. 52 patients had completed more than 3 months follow-up.

Results: Mean procedure and fluoroscopy times were 68±20 minutes (35–139) and 13.8±2.1 (7.4–27.3) minutes, respectively. The mean number of applications was 20±9 (10–31). The mean energy delivery time was 1084±235 (600–1902) seconds. Complete acute PVI was achieved in 89/91 patients (98%). 36/52 patients (69%) were in stable sinus rhythm after one procedure during a follow-up of 7.5±1.8 months. 5 patients with recurrence of AF underwent a redo-procedure. One patient developed TIA with complete neurological remission within 24 hours of the procedure.

Conclusion: In patients with PAF, stable sinus rhythm could be achieved in 69% of patients after PVI using the novel PVAC Gold catheter. The PVAC Gold procedure is associated with very short procedure and fluoroscopy times.

P4344 | BEDSIDE
Do patients and doctors differ in their perception of the patients symptom relief after ablation of atrial fibrillation?
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Introduction: Success of atrial fibrillation (AF) ablation is usually defined as freedom of AF, although symptomatic relief often is what patients' desires. The symptom relief after an intervention may be perceived differently by the patient and the physician.

Purpose: To assess symptom relief after AF ablation as perceived by the patient using AF-specific symptom questionnaire AF6 and as classified by the physician using the EHRA score.

Methods: 57 patients, who underwent AF ablation, filled out the validated AF-specific symptom questionnaire AF6 and were classified by their physician using the EHRA classification at baseline, 6, 12 and 24 months. The AF6 items were “breathing difficulties at rest”, “breathing difficulties upon exertion”, “limitations in day-to-day life due to atrial fibrillation”, “feeling of discomfort due to atrial fibrillation”, “tiredness due to atrial fibrillation” and “worry/anxiety due to atrial fibrillation”. Each item could score 0 to 10. Symptom relief was documented by continuous ECG monitoring (implantable loop recorder). The generic health-related quality of life was measured by SF-36.

Results: In total 55 patients completed the forms at baseline and 52 at 24 months. The AF6 symptom score decreased in 77% of the patients, and the EHRA class improved in 56%. The mean AF6 score improved from baseline to 6 months (27.14±19±16) and further at 12 months (12±13), but stayed at this level at 24 months (13±14). All six items in AF6 improved. The physician-assessed EHRA class also improved over time, also from 12 to 24 months. The number of patients in EHRA I increased (20–42–38–44 at baseline, 6, 12 and 24 months) and decreased in EHRA II (23–10–15–7), III (13–4–2–1) and IV (1–0–1–0). EHRA classes most often improved by one class (II to I, n=20), (III to II, n=1), (IV to III, n=1) and (V to IV, n=1).

Conclusions: Not only total contact force, but also the angle between CF-sensing and catheter tissue contact angles was associated with more shifting on the tissue.

P4345 | BEDSIDE
Ablation of atrial fibrillation
M. Moltrasio, G. Fassini, A. Dello Russo, M. Gawaz, J. Schreieck, University of Tübingen, Department of Cardiology, Tübingen, Germany

Background: Sufficient contact force (CF) during antral pulmonary vein isolation (PVI) with radiofrequency (RF) energy is associated with acutely durable PVI. All such reports concentrated on analysing total CF, however, the importance of lateral and axial contact force at the catheter tip has not been analysed. Axial CF enables the catheter tip to swing with the beating heart, whereas lateral CF is associated with more shifting on the tissue. The objective of this study was to determine the impact of ablation catheter-tissue angle on acute pulmonary vein reconnection (PVR) after PVI with CF-guided RF catheter ablation.

Methods: Contact force-controlled RF ablation (SmartTouch, CARTO 3, Biosense Webster) for circumferential PVI was performed in 14 consecutive patients (pts; 8 male) with paroxysmal atrial fibrillation. Acute PVR was defined as recovery of pulmonary vein (PV) conduction after a 20 min waiting period and unchanged CF during latest recording. The mean procedure and fluoroscopy times were 68±20 minutes (35–139) and 13.8±2.1 (7.4–27.3) minutes, respectively. The mean number of applications was 20±9 (10–31). The mean energy delivery time was 1084±235 (600–1902) seconds. Complete acute PVI was achieved in 89/91 patients (98%). 36/52 patients (69%) were in stable sinus rhythm after one procedure during a follow-up of 7.5±1.8 months. 5 patients with recurrence of AF underwent a redo-procedure. One patient developed TIA with complete neurological remission within 24 hours of the procedure.

Conclusion: In patients with persistent AF, stable sinus rhythm could be achieved in 41% of patients after single PVI using the novel PVAC Gold catheter. This is comparable to energy usage when using other ablation catheters performing only PVI in persistent AF. The PVAC Gold procedure is associated with very short procedure and fluoroscopy times.

P4346 | BEDSIDE
Comparison in Long-Term Efficacy between First and Second Generation Cryoballoon Ablation Catheter
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Introduction: Cryoballoon (CB) ablation has emerged as a novel treatment option for drug-refractory atrial fibrillation (AF). The second generation, CB Advance (ADV) catheter was redesigned with technical modifications resulting in a larger and more uniform zone of freezing on the balloon’s surface aiming at procedural outcome improvement in the setting of AF ablation. Aim of the study is to compare the efficacy of the two different technologies on a long-term follow-up.

Methods: A total of 120 patients were enrolled in this study. Sixty patients underwent CB using the first generation catheter and 60 patients with the ADV catheter. All patients enrolled completed 3 years of follow-up. All patients underwent regular recording and outpatient clinic evaluation every 3 months during the first year after ablation and annually thereafter.

Results: There was no significant difference between the two groups regarding patients' characteristics including the age (59.1±12.2 vs 57.2±10.9 years respectively; p=0.35), the left atrial areas (22.6±3 vs 22.5±4.7 cm² respectively; p=0.61) and the left ventricular ejection fraction (62.5±6.1 vs 60.9±7.4% respectively; p=0.23). Procedures performed with the old balloon showed longer fluoroscopy time (56.3±26.8 vs 32.2±15.3 min respectively; p=0.00016) and longer procedure times as well (193.1±52 vs 162±44.8 min respectively; p=0.019). The overall long-term success was significantly different between the two groups (68.3 vs 86.7% respectively; p=0.017). Interestingly, no difference were found in the lesion area of left and right pulmonary vein between the two groups (respectively; p=0.61 and 0.57). There was one case of cerebral embolization among patients treated with the old balloon and one case of reversible phrenic nerve palsy for each group.

Conclusion: The ADV catheter compared to the first generation balloon allows to obtain a significantly higher success rate after a single procedure during the long-term follow-up. Fluoroscopy and procedural times were significantly shorter in the first generation CB catheter group than in the ADV catheter group

P4347 | BEDSIDE
Acute recovery of pulmonary vein conduction in contact force-optimized circumferential pulmonary vein isolation is associated with minor catheter tissue contact angles
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Background: Sufficient contact force (CF) during antral pulmonary vein isolation (PVI) is associated with acutely durable PVI. All such reports concentrated on analysing total CF, however, the importance of lateral and axial contact force at the catheter tip has not been analysed. Axial CF enables the catheter tip to swing with the beating heart, whereas lateral CF is associated with more shifting on the tissue. The objective of this study was to determine the impact of ablation catheter-tissue angle on acute pulmonary vein reconnection (PVR) after PVI with CF-guided RF catheter ablation.

Methods: Contact force-controlled RF ablation (SmartTouch, CARTO 3, Biosense Webster) for circumferential PVI was performed in 14 consecutive patients (pts; 8 male) with paroxysmal atrial fibrillation. Acute PVR was defined as recovery of pulmonary vein (PV) conduction after a 20 min waiting period and unchanged CF during latest recording. The mean procedure and fluoroscopy times were 68±20 minutes (35–139) and 13.8±2.1 (7.4–27.3) minutes, respectively. The mean number of applications was 20±9 (10–31). The mean energy delivery time was 1084±235 (600–1902) seconds. Complete acute PVI was achieved in 89/91 patients (98%). 36/52 patients (69%) were in stable sinus rhythm after one procedure during a follow-up of 7.5±1.8 months. 5 patients with recurrence of AF underwent a redo-procedure. One patient developed TIA with complete neurological remission within 24 hours of the procedure.

Conclusion: In patients with persistent AF, stable sinus rhythm could be achieved in 41% of patients after single PVI using the novel PVAC Gold catheter. This is comparable to energy usage when using other ablation catheters performing only PVI in persistent AF. The PVAC Gold procedure is associated with very short procedure and fluoroscopy times.
Conclusions: The increase of LAVmaxI and the decrease of the LAAEF and Va correlation and regression analysis showed that Va and LAAEF correlated better. Specificity of 78.6%, positive predictive value of 67.5%, and a negative predictive value of 81.5% (area under ROC curve, 0.782; 95% CI, 0.576–0.772), specificity of 75.3% (area under ROC curve, 0.674; 95% CI, 0.573–0.769) for AF recurrence after catheter ablation. In a multivariate logistic regression model, LAVmaxI, LAAEF, Va showed the predictive power for recurrence after PFCA. In ROC curve analysis, the cutoff value of 32ml/m² for baseline LAVmaxI was associated with a sensitivity of 67.2%, specificity of 62.4%, positive predictive value of 47.5%, and a negative predictive value of 75.3% (area under ROC curve, 0.674; 95% CI, 0.573–0.769) for AF recurrence. The cutoff value of 25% for LAAEF was associated with a sensitivity of 76.4%, specificity of 67.5%, positive predictive value of 56.8%, and a negative predictive value of 81.5% (area under ROC curve, 0.782; 95% CI, 0.576–0.772). The cutoff value of 4.1cm/s for Va was associated with a sensitivity of 84.3%, specificity of 73.6%, positive predictive value of 67.5%, and a negative predictive value of 84.7% (area under ROC curve, 0.886; 95% CI, 0.555–0.755). Linear correlation and regression analysis showed that Va and LAAEF correlated better. The increase of LAVmaxI and the decrease of the LAAEF and Va were the risk factors of recurrence of PF after RFCA.

P4349 | BEDSIDE
Low flow velocities in the left atrial appendage can predict atrial fibrillation recurrence in patients undergoing ablation?
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Background: Atrial fibrillation (AF) is the most common arrhythmia and the catheter ablation is one of the strategies used in the treatment of these patients. The aim of this study is to test if left atrial appendage (LAA) peak flow velocity, assessed by transesophageal echocardiography (TEE), can predict AF recurrence after catheter ablation.

Methods: Retrospective study of single centre including 91 patients (mean age 57±12 years; 71.4% male) who underwent AF catheter ablation between July 2011 and December 2012 and who underwent TEE pre-procedure. We excluded patients with severe valvular heart disease or prosthetic heart valve. The primary endpoint was the recurrence of AF.

Results: During a follow up of 2.1 years, the AF recurrence was seen in 25 patients (27%). The LAA flow velocity was lower in patients who had relapsed compared to those who did not (48 cm/s versus 63 cm/s respectively, p=0.007). Using a ROC curve, the best cut-off to predict the recurrence of AF was ≤70.1 cm/s. There was a statistically significant difference in the primary endpoint between the 2 groups of patients divided by this cut-off (see chart 1).

Conclusion: Patients undergoing ablation of AF, the LAA flow peak velocity is a marker of risk of recurrence. These findings suggest that this echocardiographic parameter can be used in addition to clinical variables for better selection of these patients.

P4350 | SPOTLIGHT
Risk factors of recurrence of paroxysmal atrial fibrillation after radiofrequency catheter ablation
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Background: Looking for risk factors of recurrence after radiofrequency catheter ablation (RFCA) of paroxysmal atrial fibrillation (AF) is still the important goal

Purpose: To investigate the value of echocardiographic parameters of LA size and function in predicting the recurrence of AF after RFCA.

Methods: A cohort of 125 consecutive patients underwent PAF catheter ablation were included in our study. Real-time multi-plane echocardiography (RT-3PE) and quantitative tissue velocity imaging (QTVI) were used to evaluate the LA structure and function preoperatively (off-line EchoPac workstation). Patients were followed up 1, 3 and 6 months after RFCA. The symptoms, 12-lead ECG, 24hrs-Holter and echocardiography were followed up. The recurrence of PAF defined as that AF recurred 3 months after RFCA. According to the recurrence of PAF, the patients were divided into two groups: the AF-NR group with 81 patients and the AF-R group with 35 patients.

Results: Univariate analysis showed that LADlap, mitral peak A, E/A ratio, LAVmax, LVpVI, LVdmmin, LAAEF, LATEF, LAEpkl, Va, were related to the recurrence of AF. In a multivariate logistic regression model, LAVmax, LAAEF, Va showed the predictive power for recurrence after PFCA. In ROC curve analysis, the cutoff value of 32ml/m² for baseline LAVmax was associated with a sensitivity of 67.2%, specificity of 62.4%, positive predictive value of 47.5%, and a negative predictive value of 75.3% (area under ROC curve, 0.674; 95% CI, 0.573–0.769) for AF recurrence. The cutoff value of 25% for LAAEF was associated with a sensitivity of 76.4%, specificity of 67.5%, positive predictive value of 56.8%, and a negative predictive value of 81.5% (area under ROC curve, 0.782; 95% CI, 0.576–0.772). The cutoff value of 4.1cm/s for Va was associated with a sensitivity of 84.3%, specificity of 73.6%, positive predictive value of 67.5%, and a negative predictive value of 84.7% (area under ROC curve, 0.886; 95% CI, 0.555–0.755). Linear correlation and regression analysis showed that Va and LAAEF correlated better. The increase of LAVmaxI and the decrease of the LAAEF and Va were the risk factors of recurrence of PAF after RFCA.

P4351 | BEDSIDE
Effect of type of monitoring on verification of atrial fibrillation recurrence after catheter ablation: Comparison of the 7 Day Holter monitoring and implantable monitor with remote control
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Introduction: The intensity of monitoring of patients after catheter ablation (CA) does not have currently clear recommendations. It depends on the setting (clinical follow up, type of scientific study) and on clinical circumstances.

Methods: 187 patients without structural myocardial disease with documented symptomatic paroxysmal atrial fibrillation (AF) indicated to CA were randomized into two monitoring techniques. For the first group (90 patients) was used a standard 7-day Holter monitoring (3.2 and 12 M), a second group of patients (97) underwent ≥7±3 days before ablation implantation of a SQ monitor in combination with remote control. As a recurrence of atrial fibrillation was defined each episode with a duration ≥30 seconds. All antiarrhythmic drugs except betablockers were stopped before ablation. CA was performed in a centre with a long experience with AF ablation using 3D technology. Wide Antral pulmonary veins isolation, point by point ablation, intracardiac echocardiography, steerable sheaths were used.

Results: Results of monitoring after AF ablation FS are presented in Table 1.

Conclusion: Reliable detection of AF recurrence after ablation depends on the intensity of monitoring and recurrence characteristics (burden, temporal pattern, symptoms). Intensive monitoring using SQ monitor and remote control leads to more accurate detection of AF recurrence compared to standard 7-day Holter monitoring. It detects multiple atrial fibrillation episodes and in relation to the risk of thromboembolism in patients after ablation of AF. Using of SQ monitoring against 7-day Holter is still characterized by a higher percentage invalid episodes (23.1% vs 11.2%) due to the detection myopotentials.
Left atrial surface area that remains not isolated after ablation of persistent atrial fibrillation predicts long-term outcomes

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Introduction: Arrhythmia recurrence following catheter ablation of persistent atrial fibrillation (AF) is high compared with paroxysmal AF. Patients often have larger atria that require more extensive ablation in addition to pulmonary vein isolation (PVI). However, the quantification and impact of isolated and non-isolated left atrial surface area (LASA) isolated is unevulated.

Aims: To utilize cardiac-computed tomography and electro-anatomical navigation system to evaluate the impact of isolated and non-isolated LASA on long-term arrhythmia recurrence after PVI.

Methods: We recruited 164 patients (female 51, age 62±10 years) presenting for catheter ablation with high symptomatic AF (paroxysmal 95, persistent 69). Pre-procedural cardiac CT’s were acquired and merged with a three dimensional non-fluoroscopic mapping system (CARTO-XP, Biosense Webster). Existing software was used to calculate total LASA. Post procedurally, the surface area enclosed by ablation lesions (marked manually during the procedure) was calculated to determine the LASA not isolated and proportion of LASA isolated.

Results: Parameters were correlated with arrhythmia recurrence in patients with persistent and paroxysmal AF after 62±9 months follow up. Results: One hundred and four (63%) patients had recurrent arrhythmia after AF ablation (paroxysmal 54, persistent 50). Persistent AF patients with arrhythmia recurrence had significantly higher total LASA (202.3±33.4cm² vs 185.7±30.0cm² p<0.05), higher LASA not isolated (150.5±28.2cm² vs 127.9±21.0cm², p=0.002) and lower proportions of LASA isolated (25.6±6.3% vs 30.7±8.3%, p=0.008), compared with patients without recurrence. However, in the paroxysmal AF group there were no differences between patients with and without recurrence. Multivariate survival analysis utilizing a Cox regression model demonstrated LASA not isolated >145cm² independently predicted AF recurrence in persistent AF patients (HR 2.66 95% CI (1.47, 4.80), p<0.001).

Conclusion: LASA not isolated is an important predictor of AF recurrence after ablation of persistent but not paroxysmal AF. Importantly, LASA not isolated is more important for long-term outcomes than total or isolated left atrial surface area. Ablation of persistent AF with less than 145cm² LASA not isolated provides a simple guide to improve long-term outcomes.

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Low amplitude of fibrillatory waves on surface ecg predicts non-responder for ablation in patients with long-standing persistent AF

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Background: Catheter ablation of long-standing persistent atrial fibrillation (AF) was a challenging task.

Purpose: To evaluate the characteristics of non-responder for ablation in patients with long-standing persistent AF.

Methods: Eighty-eight consecutive patients (78% men, age 66±9, LAD 49±6mm, duration of continuous AF 69±67 months) who underwent long-standing persistent AF ablation and were followed at least 12 months were enrolled in this study. Mean amplitude of fibrillatory-waves (f-waves) were measured in V1. Pulmonary vein (PV) isolation, superior vena cava isolation, non-PV foci ablation, and linear ablation including roof line, bottom line, and mitral isthmus line were performed. The recurrent AF was evaluated through auto-triggered external loop recorder for 7 days (3, 6, 12, 24 months after ablation). Non-responder was defined as patients who had recurrence as persistent form even if using antiarrhythmic drugs after the last session. The duration of continuous AF, echocardiographic parameters, the presence of structural heart disease, AF cycle length and mean amplitude of f-waves were analyzed with respect to clinical success and non-responder after ablation. To analyze independent predictive factors of clinical success and non-responder after ablation, univariate factors presenting p<0.1 were analyzed using logistic regression (multivariate analysis).

Results: After the last procedure (mean 1.2±0.4 procedures), the clinical success rate with or without any antiarrhythmic drugs was 71%, while the rate of non-responder was 19%. Follow-up period was 16±9 months. In the univariate analysis, the duration of continuous AF (p=0.018) and mean amplitude of f-waves (p=0.001) were associated with non-responder and the duration of continuous AF (p=0.001), duration of persistent AF (p=0.031) and mean amplitude of f-waves (p=0.004) were associated with clinical success. The mean amplitude of f-waves (p=0.004) was the only independent predictor of non-responder. There was no independent predictor of clinical success. At a cut-off point <0.065mV identified ROC curve, the positive and negative predictive values of the mean amplitude of f-waves to predict non-responder were 75% and 89%, respectively.

Conclusion: Low amplitude of f-waves in V1 predicted non-responder for ablation in patients with long-standing persistent AF.
Abstract P4357 – Table 1. HR and BP variability indices at baseline (preablation), 24 h, 3 months, 1 year and 2 years after CPVA

<table>
<thead>
<tr>
<th>Preablation (n=9)</th>
<th>24 h (n=9)</th>
<th>3 months (n=8)</th>
<th>1 year (n=5)</th>
<th>2 years (n=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>supine</td>
<td>standing</td>
<td>supine</td>
<td>standing</td>
</tr>
<tr>
<td>HR</td>
<td>57.9±9.6</td>
<td>64.6±10.9</td>
<td>70.9±10.7</td>
<td>80.1±16.5</td>
</tr>
<tr>
<td>mMSD</td>
<td>26.3±6.1</td>
<td>16.5±5.7</td>
<td>10.6±14.8</td>
<td>13.6±18.8</td>
</tr>
<tr>
<td>SDNN</td>
<td>36.9±18.2</td>
<td>33±18</td>
<td>10.2±8.7</td>
<td>14.7±3.3</td>
</tr>
<tr>
<td>In HF RR</td>
<td>3.9±1.4</td>
<td>3.1±2.1</td>
<td>1.4±0.8</td>
<td>1.5±2.4</td>
</tr>
<tr>
<td>SD SBP</td>
<td>6.5±1.7</td>
<td>8.5±2.8</td>
<td>9.5±1.8</td>
<td>9.1±4.2</td>
</tr>
<tr>
<td>BRS</td>
<td>8.2±5.9</td>
<td>4.7±3.2</td>
<td>1.7±1</td>
<td>1.2±0.4</td>
</tr>
</tbody>
</table>

Conclusion: The patients with paroxysmal AF had more cranially located EAS and more anteriorly descending FIP at baseline. In persistent AF, after sympathetic stimulation, the EAS and the FIP showed upward shift. The location of the EAS and the FIP was well correlated in most patients, suggesting that the FIP was selected by the EAS rather than the preexisting preferential interatrial pathway.

P4359 | BEDSIDE
LA fibrosis predicts LVEF improvement in HF patients following AF ablation


Background: In pts. with heart failure (HF) and atrial fibrillation (AF) improvement of left ventricular ejection fraction (LVEF) has been described following AF catheter ablation. Not all HF pts. benefit the same way. Furthermore, presence and amount of left atrial (LA) fibrosis is increasingly recognized as a marker of advanced AF disease status and predictor of ablation success. We thought to investigate the relationship between LA fibrosis and the extent of LVEF improvement in HF patients after successful AF ablation.

Methods: Forty-six pts. (36 male, median 64 years, median LVEF 30%, 31 DCM) underwent catheter ablation of symptomatic AF (37 persistent AF). Pulmonary vein (PV) isolation was performed in all pts. LA voltage mapping was used to identify low voltage zones (LVZ, threshold <0.5mV) outside PVs as surrogate of LA fibrosis. Individualized linear ablation lines were added to dissect/isolate/connect LVZs as substrate modification. Follow-up (FU) was performed with device-based long-min recordings in supine and standing positions. We also recorded mean HR, HRV using time domain (RMSSD, SDNN) and spectral (HF power) analysis as well as BP variability (standard deviation -SD- of systolic BP) on selected 5 min periods with stationary HR and systolic BP. BRS was assessed using the sequence method on 10 min periods. We defined 5 time points: the day before CPVA (preablation), 24 h, 3 months, 1 year and 2 years after CPVA. As the study is not finished yet, statistical analysis was not performed. Data are presented in the table as mean±SD.

Results: Mean age was 61±8 years. At 1 year, AF recurrence occurred in 3 patients (24 h after CPVA), in all patients, mean HR increased and HRV and BRS decreased as compared to preablation in both supine and standing positions. At 2 years, 3 of 5 recorded patients had persistent HRV and BRS attenuation while BP variability and mean HR remained high.

Conclusions: AF may be associated with persistent parasympathetic withdrawal. A prospective study is ongoing to exclude confounding factors (e.g. age, medication) and examine clinical consequences of CPVA-induced cardiac autonomic modulation.
An increased sympathetic nervous tone 3 months after ablation is a predictor of AF recurrence.

Results: Overall 35 (76%) pts. were in stable SR after a median of 1 ablation procedure and a median FU of 6 months (IQR 2, 11). LVZs outside PVs were detected and treated in 18/46 (39%) patients. Success rate tended to be higher in pts. with LVZs (82% vs 57%, p=ns). Overall contour LVEF significantly increased from 30% (IQR 25, 35, 43%) to 43% (IQR 35, 50, p < 0.001).

Absolute improvement in LVEF was significantly higher in pts. with successful ablation (median 13% [IQR 10, 20] vs. 5% [IQR -5, 10], p < 0.001) and in pts. with LVZs (median 13% [IQR 10, 20] vs. 5% [IQR -1, 14], p =0.002). In multivariate analysis ablation success and presence of LVZs were significantly associated with LVEF improvement. On a per-patient analysis 22/23 (96%) LVZs negative pts. with successful ablation showed LVEF improvement compared to only 8/12 (67%) LVZs positive pts. with successful ablation (p =0.02).

Conclusions: In addition to the actual ablation success absence of LA fibrosis predicts a significantly larger improvement in LVEF after catheter ablation of AF in HF pts. The data raise the question of AF being the cause or the consequence of HF in patients with and without fibrosis.

P4360 | SPOTLIGHT
An increased sympathetic tone after ablation predicts recurrence of atrial fibrillation: Investigation using cardiac iodine-123-metaiodobenzylguanidine (123I-mIBG) scintigraphy

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Purpose: To investigate the factors associated with the AF recurrence after catheter ablation, including the pre- and post-procedural sympathetic nervous activity assessed by cardiac iodine-123-metiodobenzylguanidine (123I-mIBG) scintigraphy.

Methods: Forty consecutive patients scheduled for AF ablation were enrolled. Extensive encircling pulmonary vein isolation was performed in all patients. At baseline and 3 months after ablation, 123I-mIBG scintigraphy was performed. The heart to mediastinum ratio of the 123I-mIBG uptake, a marker of the sympathetic nervous distribution, was measured at 15 min (H/M15min) and 240 min (H/M240min). Washout rate (WR) was also evaluated as a marker of the sympathetic nervous tone.

Results: During a mean follow-up period of 11±4 months after ablation, excluding the blanking period of the initial 3 months, 8 (20%) patients developed AF recurrences. There were no differences in the age, sex, type of AF between the patients with and without AF recurrences (Table). Univariate analyses demonstrated that presence of LVZs was associated with a significantly higher WR at baseline (p =0.007) and WR at 3 months after ablation 41.3±4.8 30.9±10.1 1.13 0.94–1.34 0.03 (Table). On a per-patient analysis, WR at baseline was also a predictor of AF recurrence (p =0.03). In multivariate analysis, WR at baseline and 3 months after ablation continued to predict AF recurrence (Table).

Conclusions: An increased sympathetic nervous tone 3 months after AF ablation is a reliable predictor of AF recurrence.
A phantom study to assess the accuracy of a new electromagnetic catheter guidance technology (MediGuide).

**Background:**
Minimally invasive surgery for atrial fibrillation (AF) is going through a rapid development lately. The long-term efficacy of most of these procedures is poorly known.

**Methods:**
Patients with drug-resistant, symptomatic, stand-alone AF were enrolled. They underwent fully thoracoscopic, unilateral, off-pump surgical ablation. Microwave or monopolar radiofrequency energy system was used to create a box lesion (isolation of all pulmonary veins and left posterior atrial wall). Patients were prospectively followed at 1, 3, 6, 9, 12 months and every six months further using ECG and Holter monitoring.

**Conclusions:**
Additional catheter ablation was offered to patients with recurrence of arrhythmia.

**Acknowledgement/Funding:** Charles University Cardiovascular Research Programme PRVOUK P35

### Table 3: Comparison of fluoroscopy and procedure times

<table>
<thead>
<tr>
<th>Procedure</th>
<th>CB</th>
<th>RN</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location</td>
<td>HF</td>
<td>CB</td>
<td>RN</td>
</tr>
</tbody>
</table>
| Patient BMI (kg/m²) | 29.3 | 27.7 | 27.1
| Procedure time (min) | 162±43 | 114±22 | 202±33<br>*p=0.003
| Fluoroscopy time (min) | 25±8 | 17±6 | 24±6<br>*p=0.001
| DAP (cGy/cm²) | 3.075±1.923 | 2.037±1.319 | 2.510±1.554<br>*p=0.032
| Patient RAO (mSv) | 6±1 | 17±6 | 11±3<br>*p=0.002
| Patient PA (mSv) | 26±6 | 36±9 | 29±11<br>*p=0.029
| Patient LAD (mSv) | 23±6 | 29±6 | 21±3<br>*p=0.042
| Patient forehead (μSv) | 23±6 | 22±6 | 12±28<br>*p=0.029
| Physician chest H10 (μSv) | 3±1–3 | 2±1–2 | 1±1–2
| Physician hand (μSv) | 6±3–8 | 4±3–6 | 5±3–6
| Physician forehead (μSv) | 1±0–2 | 1±0–2 | 2±0–3

**Figure 1.** Bland-Altman plots comparing distance measurements between MediGuide, EnSite and the CT dataset.

### Conclusions:
The MediGuide system showed a high level of accuracy, which can be ascribed to the magnetic field localization technology; the observed offsets between the geometry visualization and the real phantom were below a clinically relevant threshold.
Ablation of atrial fibrillation III

HF and robotic navigated RN (114 versus 182 versus 202 min; 17 versus 25 versus 24 min). The dose area product (DAP) was significant lower for CB than for HF and RN (2.037 versus 3075 and 2510 CGym²).

Conclusion: Potential advantages in fluoroscopy and procedure time of CB are not reflected in the x-ray dose of the patient. The x-ray dose for patient CB are significant higher than in HF and RN.

P4367 | BEDSIDE
Treatment of atrial fibrillation using second-generation cryo balloon: characteristics of recurrences and periprocedural findings during re-do procedures

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Background: Two years ago a second-generation CB was introduced, aiming more uniform and durable lesions. First mid-term results have been reported, showing significantly higher efficacy as compared to first generation CB. Our aim was to evaluate characteristics of recurrences after PVI with second-generation CB and intraprocedural findings in pts, who underwent repeated ablation for AF.

Methods: Consecutive pts with symptomatic paroxysmal or persistent AF were included. After a single transseptal access PVI was performed utilizing a 28 mm second-generation cryoballoon (Arctic Front Advance™, Medtronic Inc.) and an Achieve™ catheter. In pts with persistent AF, who didn’t convert into SR during additional cryo applications between LSPV and RSPV were performed, creating roof line. Conduction block across the LA roof was assessed using established differential pacing maneuvers. After ablation all pts were prospectively followed with 7 days Holter ECG recordings every three months. The first three months were considered as blanking period. Primary end point was defined as occurrence of any atrial arrhythmia >30 sec without antiarrhythmic drugs. Pts. with symptomatic recurrences of atrial arrhythmias after blanking period underwent repeated ablations or were treated with AADs according to their preference.

Results: We included 348 pts (214 female, 88 persistent AF, age 59±0.6 years, EF 61±0.3%, LA area 20±2.0 cm², CHA2DS2-VASC 1.6±0.1). The mean procedure duration was 210±3.0 h with a fluoroscopy time of 21±0.5 min. Roof line was deformed in 149 pts (43%). After a mean follow up of 14±4.0 months 47 pts (14%) had reached primary endpoint. 35 pts (75%) have developed AF, 5 (11%) both AF±ATS, 6 (13%) AF±ATS only and 1 (2%) typical atrial flutter. The rate of AF didn’t differ between pts treated with and without roof line (4.4% and 3% respectively, p=ns). 22 pts (48%) underwent repeated ablation. During re-do procedure we found recollection of all PVs only in 2 pts (9%), of ≥2 PVs in 1 pt (27%), of ≥1 PV in 7 pts (32%) and persistent isolation of all 4 PVs in 7 pts (32%). Reconnection of LSPV occurred in 6 pts (27%), LIPV in 9 (41%), RSPV in 8 (36%) and RIPV in 8 pts (36%) respectively.

Conclusion: The majority of AF/AT recurrences after initial PVI with second-generation CB seem to be still caused by recovery of PV conduction. Nonetheless almost one third of pts with recurrences have revealed non PV dependent arrhythmias during repeated ablation. Creation of additional linear lesion at LA roof with a second-generation CB didn’t increase rate of LA tachycardias.

P4368 | BEDSIDE
Left atrial size as the strongest predictor of mid-term outcome after ablation of atrial fibrillation using second-generation cryoballoon


Background: Factors predicting outcome after pulmonary vein isolation (PVI) with second-generation CB are significant higher than in HF and RN.

Methods: A total of 133 patients with documented paroxysmal AF were enrolled from 5 centers and randomized to PAR group or PVI group. CARTO was used for left atrial mapping. Event ECG recording and Holter monitoring were conducted during the follow-up for all patients.

Results: The procedure time was 151±23 min in PAR group and 178±43 min in PVI group (P<0.001). The fluoroscopy time was 21±7 min in PAR group and 27±11 min in PVI group (P=0.002). AF triggering foci were eliminated in 59 patients (89.4%) in PAR group compared to 4 patients (6.0%) in PVI group (P<0.001). Vagal reflex occurred during ablation in 48 patients (72.7%) in PAR group compared to 26 patients (38.8%) in PVI group (P<0.001). At median 36 months of follow-up after single ablation procedure, 43 of 66 patients in PAR group (65%) and 28 of 67 patients in PVI group (42%) had no recurrence of AF off antiarrhythmic drug (AAD) (P=0.007); and 47 of 66 patients in PAR group (71%) and 32 of 67 patients in PVI group (46%) had no recurrence of AF with AAD (P=0.006). At the last follow-up, the burden of AF was significantly lower in PAR group than in PVI group (0.9% ± 2.3% vs 4.9% ± 9.9%; P<0.008). No major adverse event was observed except one pericardial tamponade.

Conclusion: The data suggest that PAR ablation is a simple, safe, and effective strategy for the treatment of paroxysmal AF with better long-term outcome than PVI. PAR ablation may work with multiple effective mechanisms against multiple AF mechanisms.

Acknowledgement/Funding: National natural science foundation of China/Registration Number:ChiCTR-TRC-11001191

P4370 | BENCH
Impact of left atrial epicardial adiposity on recurrence of atrial fibrillation after catheter ablation

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Background: Left atrial epicardial adiposity is associated with the mechanism of atrial fibrillation (AF).

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Objective: To investigate the impact of left atrial epicardial adiposity on recurrence of AF after catheter ablation.

Methods: From 2009 to 2010, consecutive patients with AF who underwent circumferential pulmonary vein ablation guided by 3-D mapping system were enrolled in the retrospective study. Left atrial (LA) epicardial fat pad thickness was measured in consecutive cardiac CT angiograms performed for AF patients grouped by AF burden: paroxysmal (n=100), or persistent (n=49) AF. The short-axis view was reconstructed as a plane perpendicular to the long axis of these 2 views at the level of the mid LA. In this short-axis view, the pericardial epicardial fat thickness was measured at the esophagus (LA-ESO), main pulmonary artery (LA-PA), and descending thoracic aorta (LA-TH). A significant percentage of patients undergoing atrial fibrillation (AF) ablation were analyzed.

Results: One-hundred-twenty-two patients undergoing BRF without (n=57) or with (n=65) concomitant right (RA) ablation were assessed for sinus rhythm recovery at a median follow up of 38.8 months (27.0–86.5). A competing risk model was used to appropriately estimate the incidence of AF and surgical techniques were analyzed for their association with AF recurrence employing a competing risk regression model for atrial dimensions using sub-hazard ratios (SHRs) as measure of association.

Conclusions: Our experience suggests that a right-sided ablation should be routinely added to BRF left atrial ablation for atrial fibrillation. Further studies are needed to confirm our results.

ABALATION OF ATRIAL FIBRILLATION IV

P4371 | BEDSIDE
Impact of right atrial lines on eight-line rhythm outcome following bilateral radiofrequency maze
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Background: Eight-year clinical results of surgical bipolar radiofrequency (BRF) atrial fibrillation (AF) ablation were analyzed.

Methods: One-hundred-twenty-two patients undergoing BRF without (n=57) or with (n=65) concomitant right (RA) ablation (RA) were assessed for sinus rhythm recovery at a median follow up of 38.8 months (27.0–86.5). A competing risk model was used to appropriately estimate the incidence of AF and surgical techniques were analyzed for their association with AF recurrence employing a competing risk regression model for atrial dimensions using sub-hazard ratios (SHRs) as measure of association.

Results: The percentage of patients in normal sinus rhythm and off-antiarhythmia drugs were 75.4% (n=43) in the RA ablation and 56.9% (n=37) in the no-RA ablation Groups (p=0.001). Eight-year cumulative incidence of AF recurrence was significantly lower in the Group receiving RA lines (Figure 1). The absence of RA ablation (SHR 3.84 [95% CI 1.27–4.94], p=0.001) was the only surgical factor independently associated with AF recurrence at follow up. Roof (SHR 1.54 [95% CI 1.23–1.93]) and mid LA-ESO (SHR 1.39 [0.92–1.20]) were significant predictors of AF recurrence after adjusting for age, BMI, LA-TH-LA-PA-LAD and LAD were significant predictor of AF burden. After adjusting for age, BMI, LA-TH-LA-PA-LAD and LAD, the association remained significant. Of 149 patients, 98 (65.8%) remained free of recurrence after a single ablation procedure after 12 month follow-up. The recurrence patients had a significantly thicker LA-ESO than the normal patients after ablation. LA-ESO fat depots were individually predictive of the recurrence of AF.

Conclusions: Left atrial epicardial adiposity is associated with the burden of AF, and poorer outcomes after AF ablation. LA-ESO fat depots were individually predictive of the recurrence of AF.

P4373 | BEDSIDE
Improved procedural efficiency using the new technology in cryotherapy for paroxysmal atrial fibrillation: a prospective randomized controlled trial
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Background: Pulmonary vein isolation (PVI) using the arctic front cryoballoon is an established therapy in paroxysmal atrial fibrillation (PFA). The Achieve mapping catheter is designed to work in conjunction with the Arctic Front as an alternative to established circular mapping catheters such as the Lasso. A second-generation cryoballoon, the Arctic Front Advance (AFAdv) has recently superseded the original cryoballoon (OCB).

Methods: We studied 102 patients (age 62±12, 23 - 83 years, 50% men) undergoing their first PVI for AF, randomizing them to 2:1 to an achieve-guided (AGT) or a lasso-guided technique (LGT). During recruitment for this trial the AFAdv was introduced: we staggered its introduction to minimize any order effect.

Results: We analyzed 68 cases in AGT and 34 in the LGT group (age 63±12 v. 59±12 years, p=ns). Procedure and fluoroscopic duration was similar in both groups. Procedure and fluoroscopy duration were shorter in the AGT group in cases performed by operators experienced in the use of the Achieve (Figure). Use of the AFAdv (n=68) gave significantly shorter procedure time than the OCB (n=34) (122±25 v. 140±28 minutes, p<0.002). The use of AFAdv was similar in AGT and LGT group. Transient phrenic nerve weakening was equally prevalent in AGT and LGT group. Transient phrenic nerve weakening was equally prevalent in AGT and LGT group. Transient phrenic nerve weakening was equally prevalent in AGT and LGT group. Transient phrenic nerve weakening was equally prevalent in AGT and LGT group. Transient phrenic nerve weakening was equally prevalent in AGT and LGT group. Transient phrenic nerve weakening was equally prevalent in AGT and LGT group.

Conclusion: The Achieve catheter gives similar results to the Lasso; it shows evidence of improved results with operators of sufficient experience. The 2nd generation cryoballoon has improved procedure efficiency without increasing complications.

Acknowledgement/Funding: Research Funding from the Medtronic

P4374 | BEDSIDE
Body mass index and recurrent atrial fibrillation following catheter ablation: a meta-analysis

Introduction: A significant percentage of patients undergoing atrial fibrillation ablation are overweight or obese. We sought to systematically characterize the
impact of incremental increases in body mass index (BMI) on of recurrent AF post-ablation.

Methods: Comprehensive searches of electronic databases and reference lists were undertaken. Estimates of relative risk (RR) were abstracted or calculated from studies reporting on associations between BMI and post-ablation AF. Where risk estimates were reported as a series of dose-specific risk estimates compared to a reference BMI category, these were transformed into risk estimates per unit of BMI as previously described given linearity between BMI and AF. Authors were contacted for additional data allowing transformation where it was not reported in the publication. Risk estimates per unit of BMI were subsequently pooled using random effects meta-analysis.

Results: A total of sixteen studies involving 5,864 individuals were included (mean age 56, mean percent female 30%, mean follow-up 20 months). The overall summary estimate indicated that there was a 3.1% greater excess risk of recurrent AF post-ablation for every one unit increase in BMI (RR 1.03, 95% CI 1.00–1.07). This translates into a 16% increased risk for every five unit increase in BMI (RR 1.16, 95% CI 1.00–1.34). There was significant heterogeneity due to differences between studies (I2 statistic 68.7%) but no evidence of significant publication bias.

Conclusion: Incremental increases in BMI are associated with significant excess risk of recurrent, post-ablation AF. These data support weight reduction as a strategy to improve AF ablation outcomes.

P4375 | BEDSIDE
Comparison of substrate ablation with or without anatomical ablation for atrial fibrillation: does pulmonary vein isolation prior to substrate ablation improve the outcome?
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Background: The effect of atrial fibrillation (AF) ablation guided by complex fractionated atrial electrogam (CFAE) solely or combined with pulmonary vein isolation (PVI) is still controversy. This study was designed to analyze the additional effect of PVI prior to CFAE ablation on outcome.

Methods: We analyzed 160 consecutive AF patients who underwent catheter ablation with PVI prior to CFAE ablation (PVI+CFAE group, n=80) or without PVI (CFAE group, n=80) in their first session and followed for mean of 30 months. There were 50 paroxysmal and 30 persistent AF in both groups. In PVI+CFAE group, PVI was performed prior to CFAE ablation during either the spontaneous AF or by the induced AF in order to confirm AF termination by PVI. PVI was confirmed with a circular catheter and completed electrically in the end of the session in PVI+CFAE group.

Results: In patient characteristics including age, left atrial (LA) diameter, LA volume, left ventricular ejection fraction, and AF duration in persistent AF, there was no significant difference between two groups. In PVI+CFAE group, AF was terminated during PVI prior to CFAE ablation in 30% of paroxysmal and in 13% of persistent AF patients. AF was not inducible only in four (8%) of paroxysmal AF patients after PVI. There was no significant difference in the total termination rate of paroxysmal and persistent AF between two groups (PVI+CFAE vs CFAE: paroxysmal 94% vs 98%; p=0.62, persistent 73% vs 93%; p=0.08). Radiofrequency (RF) duration (PVI+CFAE vs CFAE: 92.5±5.2 min vs 84.9±24.7 min, P=0.05), fluoroscopic time (22.6±12.9 min vs 12.6±8.9 min, p=0.001), and procedural time (242±45 min vs 196±41 min, p=0.001) were significantly longer in PVI+CFAE group compared to CFAE group. Although acute AF recurrence in three days after the procedure in PVI+CFAE group was less than that in CFAE group (PVI+CFAE vs CFAE: 33% vs 68%, P<0.001), there were no significant difference in AF free rate during follow up period in both groups (PVI+CFAE vs CFAE: 59% vs 50% in paroxysmal; p=0.55, 60% vs 50% in persistent; p=0.60).

Conclusions: Our results suggest that the additional PVI prior to CFAE ablation did not help to improve the outcome, although it required significant longer RF duration, fluoroscopic time and procedural time.

P4376 | BEDSIDE
The impact of time delay after atrial fibrillation diagnosis and ablation on age-based 5-year outcomes after atrial fibrillation catheter ablation
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Background: Catheter ablation of atrial fibrillation (AF) is an established therapeutic rhythm approach in symptomatic patients. Delays from AF diagnosis to catheter ablation have been shown to negatively influence long-term outcomes. We hypothesize that the age at AF diagnosis will enhance the impact of these delays over long-term follow-up.

Methods: 923 patients that underwent their index AF ablation and had 5 years of follow-up were studied. Patients were followed for AF recurrence, heart failure, stroke, death, and cardiac function. Patients were separated and compared in 5 age-based groups (≤50, 51–60, 61–70, 71–80, >80 years) and then from time of initial AF diagnosis to ablation (30–180, 181–545, 546–1825, >1825 days).

Results: The age of the population was 66±11 years and 59% male. The AF was paroxysmal in 55%, persistent in 27%, and longstanding persistent in 18%. Hypertension, heart failure, stroke, and coronary artery disease increased significantly with age. Time from AF diagnosis to ablation increased significantly with age (median: 229, 245, 311, 617, 405, p<0.001). 5-year AF recurrence rates were associated with delays in time to ablation, with the most notable benefit seen in patients ≤60 years of age.

Conclusions: Delays in ablation from AF diagnosis negatively influence 5-year rates of AF/Aflutter recurrence. Older patients experienced greater delays and had more comorbidities. Patients ≤60 years of age received the relative largest benefit in early ablation; a finding that likely highlights the impact of the acquisition of coexistent diseases that drive arrhythmia recurrences.

P4377 | BEDSIDE
Plasma von Willebrand factor activity: a predictor of recurrence after catheter ablation for atrial fibrillation

Background: Plasma von Willebrand factor (vWF) level is associated with ischemic stroke events in patients with atrial fibrillation (AF). High plasma vWF level has been supposed to reflect not only endothelial dysfunction but also atrial structural remodeling. The aim of the present study was to evaluate the impact of plasma vWF activity on recurrence after catheter ablation for AF.

Methods: We enrolled consecutive 76 patients who underwent catheter ablation for AF. Plasma vWF activity measured before the first procedure. We defined recurrence as a standard 12-lead ECG recording or 24-hour Holter recording of atrial tachyarrhythmia lasting more than one minute after a 3-month blanking period. We conducted ROC analysis to examine the predictive value of plasma vWF activity for recurrence and to determine an optimal cut-off point.

Results: The mean age was 65±9 years, male was 78%, persistent or long-standing persistent AF was 26%, and the mean left atrial diameter was 41±5 mm. The mean plasma vWF activity was 167±57%. Circumferential pulmonary vein isolation was completed in all 76 patients. Recurrence of atrial tachyarrhythmia was seen in 18 (24%) patients during a median 181 (range 90–351) days follow-up. ROC analysis revealed the optimal cut-off point of 184% for plasma vWF activity (area under the curve 0.81, sensitivity 72% and specificity 81%). The Cox proportional hazards regression model showed that high plasma vWF activity (184% and above) was a significant predictor of recurrence (HR 8.55, 95% CI 3.02–24.2, p<0.001).

Figure 1

Conclusion: Delays in ablation from AF diagnosis negatively influence 5-year rates of AF/Aflutter recurrence. Older patients experienced greater delays and had more comorbidities. Patients ≤60 years of age received the relative largest benefit in early ablation; a finding that likely highlights the impact of the acquisition of coexistent diseases that drive arrhythmia recurrences.
Methods: We studied 76 patients with AF (61.1±9.1 years, 74% persistent) who underwent catheter ablation. The cardiac autonomic nervous system also plays an important role in sustaining mechanisms for human atrial fibrillation (AF), and can be treated by focal ablation targeting the ganglionated plexi (GP) or autonomic denervation. The potential of improved ablation outcomes through this approach merits further investigation.

Conclusions: Our findings suggest that along with several established pro-inflammatory markers, such as C-reactive protein or interleukins, pre-procedural monocyte TLR-4 expression may serve as a predictor in AF recurrence.

P4378 | BEDSIDE
Ablation of fibrillatory rotors and autonomic denervation in atrial fibrillation

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Introduction: Localized electrical rotors and focal impulse sources are prevalent sustaining mechanisms for human atrial fibrillation (AF), and can be treated by focal ablation. The cardiac autonomic nervous system also plays an important role in AF but the relation of rotors to ganglionated plexi (GP) has not been studied.

Methods: We studied 76 patients with AF (61.1±1.9 years, 74% persistent) subjected to direct or coincidental source ablation according to the CONFIRM trial protocol followed by conventional ablation (FIRM group) or conventional ablation alone (PVI group). Electroanatomic shells were analyzed for lesion overlap with superior/inferior left GP (SLGP, ILGP) or anterior/inferior right GP (ARGP, IRGP) and patients with such overlap were categorized in a GP+FIRM group and patients without such overlap were categorized in a PVI-only group.

Results: Out of 47 patients with AF sources ablated (FIRM group), 40 patients (85%) had lesions overlapping with GPs (GP+FIRM group). At the end of a median follow-up of 875 days (interquartile range: 363–1533), 23 (56.1%) patients in the GP+FIRM group and 9 (32.1%) patients in the PVI group were free from AF after a mean number of 1.3±0.5 procedures. According to Kaplan-Meier analysis, freedom from AF was significantly higher in the GP+FIRM group compared to the PVI group after one (log-rank test, p<0.001) or multiple procedures (log-rank test, p=0.029).

Cumulative freedom from AF

Conclusions: Successful ablation of fibrillatory rotors may inadvertently affect GP and suggests a role of the autonomic nervous system for AF source formation. The potential of improved ablation outcomes through this approach merits further investigation.

P4379 | BEDSIDE
Monocyte toll-like receptor-4 expression is associated with atrial fibrillation recurrence following cryoballoon ablation

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Background: Cryoballoon-based ablation for atrial fibrillation (AF) is considered as a safe and effective treatment alternative for AF, particularly in patients with symptomatic paroxysmal AF refractory to one or more antiarrhythmic drugs. Studies investigating predictors of outcome following cryoballoon-based AF ablation have suggested that pro-inflammatory milieu may have an impact on AF recurrence.

Purpose: In this study, we aim to assess whether monocyte toll-like receptor (TLR)-4 expression, as a surrogate of inflammation, is an independent predictor of recurrence in patients undergoing cryoballoon-based ablation for AF.

Methods: Patients with refractory paroxysmal AF who were scheduled for cryoballoon-based ablation for AF were included. Monocyte TLR-4 expression was evaluated by flow cytometric analysis in peripheral venous blood samples prior to ablation.

Results: 84 patients (52.4% male; 52.3±10.4 years) who underwent cryoballoon-based AF ablation with second-generation cryoballoon were included. At a follow-up of 12 months, 11 patients (13.1%) developed AF recurrence. Pre-procedural monocyte TLR-4 expression was significantly higher in patients with AF recurrence [24 (12:59) vs 19 (9:45), p=0.007]. In multivariate Cox regression analysis, monocyte TLR-4 expression (HR: 1.062, 95% CI: 1.021–1.105, p=0.003) and left atrial diameter (HR: 5.856, 95% CI: 1.641–20.984, p=0.006) were found to be independent predictors of AF recurrence.

Conclusion: AF recurrence.

Conclusions: Plasma vWF activity was associated with recurrence of atrial tachyarrhythmia. It may be a useful marker for recurrence and the risk of ischemic stroke after catheter ablation in AF patients.
Conclusions: Circumferential Pulmonary Vein Isolation (CPVI) with radiofrequency (RF) ablation is now standard care for atrial fibrillation (AF). New improvements and new devices include use of contact force that measure contact-force to improve tissue-contact or irrigated circular catheters that allow simultaneous mapping and ablation from ten electrodes. These novel techniques have not been compared.

Methods: We compared the success rate of CPVI with: 1) “point by point” RF using an irrigated tip ablation catheter with contact force assessment vs. 2) irrigated circular ablation catheter (that is, Navistar Thermocool Smart Touch vs. nMARQ, Biosense Webster) in 86 pts. With AF. The endpoint if the procedure was the elimination of all PV potentials recorded by a second circular catheter inside the PV. Success was defined from AF during follow-up.

Results: The two groups had similar characteristics: Navistar-group with 50 patients, age 59±10 years, 64% male; nMARQ group with 36 patients, 75% male, age 62±9 years. Echocardiographic parameters and comorbidities were also similar. Importantly, both groups had ≥2 PV lesions: paroxysmal and persistent in 68% and 32% in the Navistar group vs. 64% and 36% in the nMARQ group. Finally, follow-up periods were similar (11±7 months).

Conclusions: High and comparable success rate in curing atrial fibrillation by CPVI are now achievable with either point catheters measuring contact force or with irrigated circular catheters.

Methods: Contact mapping using a 64-pole basket catheter and 20-pole circular mapping catheter was performed in 30 patients with persistent AF. Left atrial voltage maps were created during sinus rhythm. LVAs were defined as areas with bipolar peak-to-peak voltage amplitudes of <0.5mV. CFAE maps were created after the PVI. If AF was sustained or induced after the PVI, activation maps to identify AF sources (Rotors) were created using the Velocifero system. A new circular mapping catheter was placed on the left atrial septum, and then a 64-pole basket catheter was advanced into the left atrium through a steerable sheath. The absolute peak of the atrial electrogram was used to automatically detect the local activation. The points of continuous CFAEs were excluded with manual verification. If the AFCL was shorter in the right atrium than left atrium, the basket catheter was advanced into the right atrium. After the basket catheter and circular mapping catheter were set, the activation sequence of AF was defined. A rotator was defined as reproducible reentrant atrial activity, which was repeatedly present for more than 40% of the 3.8 second observation time. Focal sources were identified as sites with a centrifugal activation pattern. The accuracy of the Rotor map was confirmed by the termination of AF.

Results: Thirteen AF sources were identified in 13 patients (42%). The sources were left atrial in 12, right atrial in 1, and 10 were rotors. The percentage of CFAE points was higher in the unsuccessful Rotor maps than in the successful Rotor maps (42% vs. 16%, p<0.01), while the percentage of LVAs was similar (7.4% vs. 5.6%, p=0.6).

Conclusion: Rotor maps were useful for identifying AF sources. AF sources could not be identified in patients with large CFAE areas. The percentage of LVAs was not associated with identifying AF sources.
The peri-procedural complications we encountered were phrenic nerve injury in 3 patients, and early sepsis in 1 patient. The CHADS2 VASC average score was 4.6±1.3; E/E' - marker of left ventricular filling pressure and LA stiffness index - the ratio of E/E' to PALS were assessed with Doppler.

Conclusion: Assessment of LA remodeling by TTE with STE correlates well with the extent of LA fibrosis assessed by EAM. Thus, STE may be useful in non-invasive assessment of LA fibrosis and proper selection of candidates for CA. These preliminary findings warrant further examinations.

P4387 | BEDSIDE
Visually guided laser ablation: a single centre long term experience
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Introduction: Durable isolation of the pulmonary veins (PV) remains the cornerstone of treatment for paroxysmal atrial fibrillation (PAF) and is also used in the treatment of some patients with persistent atrial fibrillation. Visually Guided Laser Ablation (VGLA) has been proven to be safe and effective as a treatment for atrial fibrillation (AF). It has shown high levels of durable PVI, even in the hands of less experienced users. This paper presents the long term clinical outcomes of all patients treated with VGLA over the course of 4 years in the world’s most experienced centre: from early product feasibility working only PAF patients to our work using the commercially available product, when we also treated persistent AF patients.

Methods and results: 194 patients (63 females, mean age 61 years) with either a history of drug refractory PAF (time since initial diagnosis: 60.73 months) or persistent AF (time since initial diagnosis: 62.75 months) were treated in our lab with VGLA between January 2009 and 17th May 2013. Follow-up of all patients was consistent with our standard clinical practice with a 7 day Holter being performed at the first clinic visit between 4 and 6 months and, for most patients, again at 12 months post-procedure. 12 lead ECGs were performed at all clinic visits. Evidence of AF is defined as any documented AF episode - ≥240 seconds. Acute procedural results show that 692 veins were acutely isolated with a mean energy consumption of 9.18J/venous territory.

Conclusion: In a single center with a large experience in EP, initial experience in LAAC was performed with a very low rate of complications. Tailored approach with EP experience team leads to safe procedures and high accurate success rate.

P4389 | BEDSIDE
Comparison of mid-term success rate between single-shot technologies for paroxysmal atrial fibrillation ablation

Conclusion: In the last years, efforts have focused on developing ablation techniques, so-called single-shot ablation, with the possibility of a shortened learning curve, a single transseptal access and the simultaneous application of energy in order to perform easier, faster and safer procedures with less complications and increased success. Aim of this study was to compare the acute and chronic success between three different single-shot technologies available in our Centre for pulmonary vein isolation (PVI): cryoenergy using the Arctic Front Advance™, radiofrequency using the Marathon™ catheter and laser energy using the HeartLight™ catheter.

Methods: We compared 50 patients with paroxysmal atrial fibrillation (AF) who underwent AF ablation with the second-generation cryoballoon (CB) to 50 matched patients with irrigated circular multipolar catheter (ICMC) and 40 patients with the laser balloon (LB). All patients underwent regular follow up with 7-day-Holter- and outpatient clinic evaluation every 3 months for 1 year after AF ablation.

Results: There was no significant difference between the three groups regarding patients’ characteristics and procedure parameters, except for the longer procedure times in the LB group (148±45.5, 150±47.3 min, respectively, p<0.01), which was statistically different compared to the other groups. Complete PVI was achieved in 94% of the CB and LB ablation, and in 92% of ICMC ablation. The 1-year freedom-from-AF in the CB group and in the LB group was 92%, whilst in the ICMC was 84% with no statistically significant difference (p=0.33). The study showed more incidence of periadical effusion in the LB group, one case of cerebral embolization in ICMC group and one case of reversible phrenic nerve palsy in the CB group.

Conclusion: Single-shot technologies for paroxysmal AF ablation are feasible and safe techniques and seem to have a similar mid-term success rate. Fluoroscopy times were similar in all groups, whilst procedural times using the LB were significantly longer than the other groups.
comparing thorascoscopic left atrial (LA) surgical ablation (SA) with conventional percutaneous catheter ablation in patients with de-novo longstanding persistent atrial fibrillation (LSPAF).

Methods: In the SA group, thorascoscopic bipolar radio frequency ablation was performed in 26 consecutive patients with pulmonary vein isolation (PVI) using a bipolar clamp and a posterior wall box lesion was created using linear ablation connecting the two superior and inferior veins. The LA appendage was excluded in 14 patients. In the CA group, 25 consecutive patients underwent a stepwise lesion set: 1) PVI; 2) linear ablation (LA roof and mitral isthmus); and 3) ablation of complex fractionated atrial electrograms in the LA. Bi-directional conduction block was confirmed for all lesions in both arms of the study. 7-day continuous ambulatory rhythm monitoring was used to assess rhythm status at 3, 6 and 9 months. Recurrence was defined as any episode of AF, atrial flutter or atrial tachycardia lasting longer than 30 seconds.

Results: Key baseline characteristics between the SA and CA group were non-significantly different: mean age 64±9 vs. 67±11; p=0.2. LA volume (indexed to body surface area (m²)) 59±14 vs. 60±16; p=0.77, and LV ejection fraction 58±9 vs. 61±10; p=0.21. In the SA group freedom from both AF and anti arrhythmic drugs at 9 months was significantly higher than in the CA group: 21/26 (81%) vs. 10/19 (53%); p=0.01. LA showed large LVZ (≥0.5 mV recorded at ≥30%) in 12 of 21 pt (57%). Median number of sources was 3 (1-7; 17 days). The LA source map of both atria was done during AF (>0.5 mV regarded as LVZ) using EnSite™NavX™ Endocardial source mapping using RhythmViewTM followed. Basket catheter was placed in complementarity positions in case of insufficient LA or RA covering. Endocardial surface area of RA and LA, size and percentage of LVZ areas in RA and LA and the number and localization of sources were determined.

Results: In the study, 24 pt undergoing their first ablation for pers AF (6/24 (25%) long pers, mean age 61±11 years, 17/24 (71%) male) were included. LVZ covered 13±12% of RA endocardial surface and 53±29% of LA endocardial surface. LA showed large LVZ (≥30%) in 12 of 21 pt (57%). Median number of sources per patient in RA was 1 [1–3], and 3 [1–4] in LA. Rate of RA sources correlated with RA size (r=0.513; p=0.018). In the RA only 1 (3%) of sources were located within a LVZ, whereas 5/37 (14%) were adjacent to a LVZ. Of the 37 RA sources 31 (83%) were found remote of LVZ. Of the 59 sources mapped in LA 23 (39%) were localized within LVZ, 12 (20%) adjacent to LVZ, and 24 (41%) remote of LVZ, 10 (17%) were detected within a typical circumferential PVI line. Altogether 16 (27%) of LA sources are not associated to LVZ or pulmonary veins. During ablation of rotors significant AF CL prolongation (at least 10%) was observed in 10/22 (45%) of patients. In two of the patients (9%) AF converted to a regular AF, and in one pt (5%) to sinus rhythm. Of the 11 cases of CL prolongation or AF termination 6 occurred during ablation in RA (55%) and 5 (45%) in LA. In most pt these sites (87%) were observed during ablation of sources remote of LVZ.

Conclusions: LVZ are rare and small in RA, but common in LA of pers AF cases. RA sources have no relation to LVZs. In LA 23 of sources are located in or adjacent to LVZs or within PV. CL prolongation or regularization occurred mostly remote of PVs and LVZ in the RA and LA. This finding suggests, that targeting focal impulses and rotors may focus on LA and RA areas different from PVI and LVZ.

Methods: Intra-operative mapping of the endo- and epicardial right atrial wall was performed in 9 patients with induced (N=4), paroxysmal (N=1), persistent (N=2) or longstanding-persistent AF (N=2). A clamp of two rectangular electrode arrays inserted into the RA and RA at a distance 2mm) was introduced through an incision in the right atrial appendage. Results: Series of 10 seconds of AF were analyzed and the incidence of endo-epicardial dissociation (>15ms) was determined for all 128 endo-epicardial recording sites. In patients with LSAF the averaged degree of endo-epicardial dissociation was highest (24.9% vs. 5.9%). Using strict criteria for breakthrough (presence of an opposite wave within 4mm and <14ms before the origin of the focal wave), the far majority (77%) of all focal fibrillation waves could be attributed to LVZ.

Conclusions: During LSAF considerable differences in activation of the endo- and epicardial wall exist. Endo-epicardial fibrillation waves that are out of phase, may conduct transmurally and create breakthrough waves in the opposite layer. This explains the high persistence of AF and the low success rate of ablative therapies in patients with LSAF.

P4393 | BEDSIDE

Peri-operative atrial fibrillation (POAF) complicating non-cardiac surgery: a case-control pilot study

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Introduction: Retrospective analyses suggest that peri-operative atrial fibrillation (POAF) complicates non-cardiac surgery in 3% of patients. It is not known whether POAF is associated with adverse outcomes.

Purpose: We intended to document the incidence of POAF at our Hospital Civic Campus (OCH) and establish whether POAF had implications for patient outcomes and hospital costs.

Methods: Retrospective case-control study. All ECGs performed at OCH in July 2013 were overread for the presence of atrial fibrillation (AF) and/or atrial flutter (AFL), and then screened for patient surgical status. POAF was defined as ECG documentation of AF/AFL within 30 days of non-cardiac surgery occurring at OCH. POAF patients were matched to controls according to age, gender, and surgical procedure in a 1:3 ratio (p=1). Electronic health records were then reviewed for patient characteristics and outcomes. POAF was documented in 42 of 859 (4.9%) patients undergoing non-cardiac surgery, 12 (29%) had de novo AF. Three matched controls were identified for each of 41 POAF patients, with a similar proportion of emergent procedures. POAF patients had greater median ASA class (POAF [IQ] 4 [1] vs control 3 [1], p=0.004) but similar CHADS2 & CHA2DS2-VASc scores to controls. POAF patients experienced significantly increased rates of ICU admission (POAF 22% vs control 3%, p=0.006) and in-hospital mortality (POAF 17% vs control 3%, p=0.002). While the index admission length of stay was similar, POAF was associated with significantly increased hospital costs (POAF $26724±2306 vs control $15040±2306, p=0.046) and less frequent discharge home (POAF 59% vs control 77%, p=0.04). At median 482 days follow up, readmission rates were almost double in the POAF group; mortality rates remained higher in the POAF group (POAF 22% vs control 5%, p=0.003) but there was no significant difference in rates of ischemic stroke.

Conclusion: POAF occurred in approximately 5% of patients undergoing non-cardiac surgery and was associated with adverse outcomes and increased costs. Prospective research is required to confirm these findings in a larger population and to test the hypothesis that aggressive intervention in POAF improves patient outcomes and/or reduces hospital costs.

P4394 | BEDSIDE

Less than two minutes, second generation cryoballoon applications achieves acute PV in 76% without phrenic nerve palsy: preliminary results of the 1-2-3-2 study

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Purpose: In patients with paroxysmal atrial fibrillation (PAF), the second generation cryoballoon (Arctic Front Advance) significantly improves procedural outcome of pulmonary vein isolation (PVI) compared to the first-generation. However, this goes hand in hand with an increased risk of complications, especially phrenic nerve (PN) palsy (PNP). Considering the increased efficacy and risk of complications, the necessity and safety of the recommended two 4-minutes cryother- apy per pulmonary vein (PV) might be questioned. The aim of the 1-2-3 study is...
to assess PVI after different freeze time cycles with the second generation cryoballon.

**Methods:** This prospective, single blinded study, includes patients with PAF, 4 PVs as assessed by a prior performed CT scan and a left atrial size <40cc/m². Patients are randomised to two times 1.2 or 3 minutes of cryoballoon applications per vein. Time is started after the balloon temperature reaches the plateau phase of the freezing cycle. PVI is checked by 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 excision of the diahragm is monitored manually. If no PVI can be achieved with the assigned cryotherapy duration of 1, 2 and 3 minutes, more and/or longer applications are applied until PVI is successful. This is classified as primary unsuccessful PVI.

**Results:** Until now 26 patients (age 53±8 years) have been included. 8/26 patients were randomized to the 1 minute group, 9 in both the 2- and 3-minutes group. In all patients the 28 mm cryoballon was used. In the 1 minute group 25/32 PVs were primary successful, in the 2 minutes group 27/36 and in the 3 minutes group 27/36. The total mean application time per cryoapplication, from the start of cryotherapy, was respectively 113±13, 151±39 and 213±43 seconds in the different groups. With additional and/or longer applications, PVI could be achieved in all primary unsuccessful applications. In one patient the right inferior PV could not be isolated due to PNP after isolation of the right superior PV. In 9/36 right sided PVs in the 2- and 3 minutes group, applications had to be terminated prematurely due to loss of PN capture whereas no application had to be terminated in one minute group. All PNPs were (eventually) transient.

**Conclusion:** Using the second generation cryoballon two times 113±13 seconds prematurely due to loss of PN capture whereas no application had to be. PV could not be isolated due to PNP after isolation of the right superior PV. In the different groups. With additional and/or longer applications, PVI could be achieved in all primary unsuccessful applications. In one patient the right inferior PV could not be isolated due to PNP capture whereas no application had to be terminated in the one minute group. All PNPs were (eventually) transient. Conclusion: Using the second generation cryoballon two times 113±13 seconds of cryotherapy achieves 78% PVI without PNP. These preliminary results indicate that shorter initial cryoapplications might be considered.

P4395 | BEDSIDE
Having sinus rhythm definitely pays off. PRAGUE-12 randomized study sub-analysis

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**Background:** Concomitant surgical ablation (SA) of atrial fibrillation (AF) is routinely performed in cardiac surgery patients. Recent meta-analyses and reviews have shown its good efficacy in restoring and maintaining sinus rhythm but also an unclear clinical benefit for patients.

**Methods:** PRAGUE-12 is a prospective, randomized study, assessing the effect of adding SA of AF to other cardiac surgery (SA patients vs. Non-SA patients). In present sub-analysis, patients from the study were examined and grouped according to their complete AF-free survival during the first postoperative year (patients who had sinus rhythm in all postoperative check-ups were considered AF-free, patient with AF recurrence were Non AF-Free). Occurrence of death, stroke, heart failure and bleeding was compared between both groups (AF-Free vs. Non AF-Free).

**Results:** One hundred ninety-two patients were analyzed (104 SA patients and 88 Non-SA patients), out of which 61 (32%) were AF-free and 131 (68%) were Non AF-Free. The primary combined endpoint (death, stroke, heart failure) was positive in 6 AF-free patients vs 45 Non AF-free patients (HR 0.25, 95% CI 0.11–0.59, p=0.001; Figure 1). Separately, only heart failure was significantly different between both groups (5 patients AF-Free vs. 39 patients Non AF-Free, HR 0.25, 95% CI 0.09–0.62, p=0.003), other endpoints were nonsignificant. Adjusted Cox-regression analysis has shown that the AF-Free survival (p=0.001), but not the surgical ablation (p=0.844) was the predictor of occurrence of clinical complications after the surgery.

**Abstract P4397 – Table 1. MAIC results**

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<th>Stroke or systemic embolism</th>
<th>Comparison with warfarin arms</th>
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| **Atrial fibrillation V / Atrial fibrillation and anticoagulation**

P4396 | BEDSIDE
High incidence of low esophageal temperatures during second generation cryoballoon therapy for atrial fibrillation

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**Introduction** The second generation cryoballoon (CB) (Arctic Front Advance, Medtronic) achieves significantly lower temperatures after pulmonary vein (PV) isolation times and lower late atrial fibrillation recurrence rates compared to its predecessor. However, the higher efficacy goes hand in hand with an increased risk of complications. Besides an increased incidence of right phrenic nerve (PN) palsy, oesophageal lesions, atro-oesophageal fistulae and vagal nerve injury, which can result in gastroparesis, have been described. The latter complications have been related to low esophageal temperature (ET). Aims of the study are 1) To assess the incidence of low ET, defined as ET <20°C, during regular PV isolation using the second generation CB. 2) To determine if body mass index (BMI) was inversely related to low ET.

**Methods:** Under general anesthesia, 76 consecutive patients underwent regular CB isolation of the PVs. In all but eight the 28 mm balloon was used. In all patients a temperature probe with 3 thermocouples separated by 10mm (SensTherm, St Jude Medical) was inserted into the esophagus under fluoroscopic guidance. The position of the probe was adjusted to the fluoroscopic position of the balloon during each application. When reaching temperatures <16°C the application was stopped prematurely. PN palsy was monitored by continuous pacing of the PN. BMI was calculated as mass/length².

**Results:** Complete PV isolation was achieved in 73/76 patients. Ten patients experienced temporary PN palsy, no other complications occurred. In 17 patients, 2 with the 23 mm balloon, the ET reached <20°C. In 6 patients the ET decreased even <15°C despite the cessation of cryotherapy (latency effect). The lowest ET was measured at the left inferior PV in 9/17, while in 7/17 it was reached in the right inferior PV and in 1/17 it was reached in the left superior PV. The mean BMI was 27±4kg/m². In 9/17 patients with low ET BMI was <25 kg/m². In the 13 patients with a BMI <31 kg/m², ET were all >24°C.

**Conclusions:** 1) In our study population second generation CB PV isolation leads to ET <20°C in 22%, and <15°C in 8% of patients. As low ET can result in serious complications, monitoring of the ET during CB therapy is mandatory. 2) High BMI seems to protect against low ET during CB therapy.

P4397 | SPOTLIGHT
A simulated head to head comparison of stroke and major bleeding with apixaban versus rivaroxaban in high-risk NVAF Patients

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**Background:** No head-to-head trials have been carried out to assess the relative effectiveness and safety of NOACs now approved in EU to treat non-valvular atrial fibrillation (NVAF). Traditional indirect treatment comparisons of NOACs are complicated by differences in the populations studied in trials of these drugs, and administration and outcomes with warfarin in the comparator arms.

**Purpose:** To estimate the relative effectiveness and safety of apixaban and rivaroxaban on stroke or systemic embolism (SSE) and major bleeds (MB), taking into account differences in patient populations using Matching Adjusted Indirect Comparison (MAIC).

**Methods:** The MAIC was based on patient level data from ARISTOTLE and published baseline characteristics and outcomes from ROCKET-AF for rivaroxaban. Balancing weights were derived to match the mean baseline characteristics of the apixaban and rivaroxaban groups. The weights were applied to derive the adjusted rates of SSE and MB, reflecting expected outcomes for apixaban in the ROCKET-AF population. The adjusted apixaban and observed rivaroxaban rates were used to calculate rate ratios (RR) with 95% confidence intervals. Similar analyses were carried out for the warfarin groups to assess comparability of the control arms of the studies. The RRs between matched warfarin arms were used to further adjust the apixaban and rivaroxaban comparisons.
Results: Patients in the ROCKET-AF trial tended to be older and otherwise higher-risk (e.g., CHADS2 score, history of coronary heart disease, and prior stroke or TIA). Reweighting patients in ARISTOTLE to match the ROCKET population yielded an effective sample size of 1,537 for apixaban and 1,574 for warfarin. Comparisons of outcomes based on reweighted results in ARISTOTLE are summarized below.

Conclusions: MAIC suggests that use of apixaban versus rivaroxaban in high-risk patients may be associated with reduction in stroke/systemic embolism and major bleeding.

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P4398 | BEDSIDE

Outcomes of rivaroxaban versus warfarin in women and men with nonvalvular atrial fibrillation: results from the ROCKET AF trial
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Background: Rivaroxaban is non-inferior to warfarin for the prevention of stroke and systemic embolism, with less fatal and intracranial bleeding.

Purpose: The relative efficacy and safety in women versus men are unknown.

Methods: ROCKET AF was a multicenter, randomized, double-blind, double-dummy, event-driven trial that was conducted at 1178 participating sites in 45 countries. The efficacy and safety of rivaroxaban versus warfarin was compared between women and men.

Results: Women, as compared with men, were older 75 vs. 71 (p<0.001), had more hypertension 93% vs. 89% (p<0.001), and had lower creatinine clearance 61 vs. 72 mL/min (p<0.001). Compared with men, women had a lower risk of myocardial infarction (adjusted hazard ratio [HR] 0.70; 95% confidence interval [CI] 0.60, 0.83), death from vascular causes (adjusted HR 0.70; 95% CI 0.53, 0.93), and major or non-major clinically relevant bleeding (adjusted HR 0.91; 95% CI 0.84, 0.98). However, women had a higher risk of stroke or systemic embolism (adjusted HR 1.21; 95% CI 1.01, 1.44) (Figure). There was no interaction between sex and treatment effect of rivaroxaban compared with warfarin for prevention of stroke or systemic embolism.

Conclusion: Women participating in ROCKET AF had a higher risk of stroke but a lower risk of vascular death and overall bleeding events than their male counterparts. There was modest evidence of heterogeneity for sex and treatment effects with rivaroxaban versus warfarin.

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P4399 | BEDSIDE

Predictive value of CHA2DS2-VASc score for thromboembolic events in non selected outpatients without atrial fibrillation
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Background: Nowadays CHA2DS2VASc score is a useful tool to stratify thromboembolic risk and to prescribe antithrombotic therapy in non valvular atrial fibrillation (NVAF) patients (pts). Recently, few papers have suggested a predictive value for thromboembolism also in sinus rhythm (SR) in non-selected general population or in pts with coronary heart disease.

Purpose: To evaluate in a large real world non-selected population, the predictive power of CHA2DS2VASc score for thromboembolic events (TE) in SR and NVAF outpatients.

Methods: Between November 1, 2009 and October 31, 2013 we enrolled 19677 consecutive outpatients with SR without history of atrial fibrillation (n=16298) and with NVAF (n=3379). Clinical data were derived from a E-data chart for outpatients clinic. Thromboembolic risk was evaluated by CHA2DS2VASc score in both SR and NVAF pts. During a median follow-up of 29 months (IGR 14–39), events were obtained from Hospital Discharge Database and ICD-9 reports. We compared the predictive value of CHA2DS2VASc score in the two populations by Receiving Operating Characteristic analysis (ROC), adjusting for antithrombotic therapy.

Results: Comparing pts with SR and NVAF, median age was 68 vs 75 years (p<0.001), male 47 vs 58% (p<0.001), hypertension 63 vs 78% (p<0.001), diabetes mellitus 20 vs 26% (p<0.001), Charlson index >3 in 17 vs 23% (p<0.001), hypertensive heart disease 22 vs 42% (p<0.001), heart failure 6 vs 17% (p<0.001), previous stroke/TIA 4.6 vs 11.8% (p<0.001), GFR < 60 mL/min/m² 17 vs 27% (p<0.001), anticoagulants 3 vs 53% (p<0.001). The median CHA2DS2VASc was 3 (1–4) vs 4 (2–5) (p<0.001) while median HASBLED was 1 (0–2) vs 2 (1–3) (p<0.001). During follow-up we have recorded 31.1 vs 7.5% (p<0.001) TE events in SR vs NVAF pts, respectively, with a progressively increasing incidence with increasing score in both of them. To investigate predictive value of CHA2DS2VASc score in these groups we evaluated Area Under Curve (AUC) of ROC: AUC of ROCKET was 0.812 (95% CI, 0.773–0.851) vs AUC 0.696 (95% CI, 0.664–0.728) (p<0.001) in SR vs NVAF pts.

Conclusions: The incidence of TE events progressively increases with increasing CHA2DS2VASc score in both SR and in NVAF pts. CHA2DS2VASc score is a powerful predictor of TE events in SR vs NVAF pts. This suggests that a simple score, largely available in clinical practice of thromboembolic risk stratification in NVAF pts, could be a useful tool to stratify TE in SR population too. The hypothesis of treating antithrombotic therapy in SR pts with high CHA2DS2VASc score and low hemorrhagic risk should be analysed prospectively.

P4400 | BEDSIDE

Effect of rivaroxaban and warfarin on fibrin clot structure
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Introduction: In atrial fibrillation (AF), oral anticoagulant is vital for stroke prevention. Warfarin, rivaroxaban and aspirin confers different level of protection against thrombosis and bleeding risk, possibly due to different effects on fibrin clot structure.

Methods: Blood samples from 234 subjects were collected: 153 warfarin (Mean INR 2.42, SD 0.69), 44 rivaroxaban and 37 aspirin. Coagulation profile, clot strength and fibrin clot lysis indices are analysed by Thromboelastography (TEG), fibrinolysis and turbidimetric assay.

Results: Using TEG, the ability of warfarin and rivaroxaban to delay fibrin clot formation was confirmed, with delayed clotting times as opposed to aspirin users (7.3 min vs 8.4 min vs 5.0 min, p<0.0001). More gentle u-angle (63.2° vs 63.6° vs 69.1°, p<0.004) was seen in warfarin and rivaroxaban as compared to antiplatelet user.

No significant differences were seen in Maximum Amplitude (MA) of clot achieved between all three groups.

Using fibrinolysis and turbidimetric assay, warfarin and rivaroxaban caused slower rate of clot formation (17.6 optical density per sec [OD/s] vs 12.3 OD/s vs 25.1 OD/s, p<0.0001) and shorter time to lyse 50% of fibrin clot (190 s vs 180 s vs 204 s, p=0.026) when compared to aspirin.

When compared directly with warfarin, rivaroxaban results in more prolonged R-time (p<0.001), slower rate of clot formation (p=0.008) and shorter clot lysis time (p=0.04).

Conclusions: Rivaroxaban and warfarin's efficacy to impede coagulation is demonstrated by the delay in fibrin clot formation (R-time), longer K-time and gentler u-angle, without impact on the tensile strength of clot as shown by similar MA. Both agents also impede the rate of fibrin clot formation and accelerate clot lysis. Rivaroxaban was superior to warfarin, being more efficacious in delaying coagulation, further slowing rate of clot formation and resulting in formation of clots which are more responsive to tPA.
P4401 | BEDSIDE
Determinants of oral anticoagulation control in new warfarin patients: analysis using data from Clinical Practice Research Datalink
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Background: The safety and effectiveness of warfarin therapy depends critically on the quality of anticoagulation control, often assessed using the percentage time in therapeutic International Normalised Ratio (INR) range (TTR). However, few studies have investigated patient-level predictors of anticoagulation control.

Aim: We aim to identify patient characteristics associated with quality of anticoagulation control on warfarin, as measured by TTR.

Methods: We carried out a population-based retrospective study using data from the Clinical Practice Research Datalink. This study included two cohorts of patients starting warfarin treatment after a first diagnosis of atrial fibrillation (AF) or venous thromboembolism (VTE) between 1 January 2000 and 31 December 2013. We used a multivariate mixed regression model and logistic regression models to predict the fully-adjusted effect of each predictor variable upon TTR, and the directional patterns underlying low TTR (sub- and/or supratherapeutic INR range).

Results: The study population comprised 29,717 incident AF patients and 19,113 incident VTE patients who initiated warfarin. For both cohorts, patients treated in primary care were younger and more likely to be female, and had a lower incidence of previous stroke or transient ischaemic attack. The INRs were more likely to be subtherapeutic and supratherapeutic in both AF and VTE patients, with higher proportions of patients with low TTRs. In the high risk, TEE is necessary to detect LA thrombi before cardioversion or radiofrequency pulmonary vein isolation for the prevention of systemic embolization.

P4402 | BEDSIDE
The patients with atrial fibrillation taking non-vitamin K antagonist oral anticoagulants also need the transesophageal echocardiography for the prevention of systemic embolization
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Background: It is well known that the patients with both paroxysmal and persistent atrial fibrillation (AF) are at an increased risk of systemic embolization. Non-vitamin K antagonist oral anticoagulants (NOACs) have been developed as alternatives to warfarin. The current guidelines recommend oral anticoagulation with warfarin (target international normalized ratio [INR] = 2.0–3.0) for 3 weeks before electrical or pharmacological cardioversion without exclusion of LA thrombi by transesophageal echocardiography (TEE). However, there is little information on the safety of cardioversion without TEE on NOAC therapy.

Purpose: The aim of this study was to evaluate the efficacy of screening the presence of the thrombus in left atrium (LA) in AF patients with anticoagulants.

Methods: The 83 AF patients (mean age, 66±19.8 years; 62% men) who underwent transesophageal echocardiography (TEE) to exclude LA thrombus before electrical cardioversion or radiofrequency pulmonary vein isolation for AF were retrospectively evaluated. The patients were divided into 2 groups according to anticoagulation therapy: Warfarin (n=31) and NOAC (n=52): dabigatran: n=25, rivaroxaban: n=22, apixaban: n=5. In all patients, each anticoagulants were continued for more than 4 weeks before TEE.

Results: In the warfarin-group, LA thrombi were detected in 3 patients (9.7%). On the other hand, 7 patients in the NOAC-group had LA thrombi (13.2%). The prevalence of LA thrombi was equivalent between 2 groups. Baseline characteristics and the current guidelines recommend oral anticoagulation with warfarin (target international normalized ratio [INR] = 2.0–3.0) for 3 weeks before electrical or pharmacological cardioversion without exclusion of LA thrombi by transesophageal echocardiography (TEE). However, there is little information on the safety of cardioversion without TEE on NOAC therapy. Purpose: The aim of this study was to evaluate the efficacy of screening the presence of the thrombus in left atrium (LA) in AF patients with anticoagulants.

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Conclusion: The need of dosage adjustment of NOAC along follow-up is frequent in patients with AF after ADHD, especially among the elderly or those with renal impairment. Further studies are needed to clarify the clinical importance of these needs of drug dosing adjustment and the ideal renal function monitoring regime in heart failure and other subgroups of patients with AF.

P4404 | BEDSIDE
Evolving antithrombotic treatment patterns in patients with newly diagnosed atrial fibrillation in GARRFIELD-AF
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Purpose: To study the evolving pattern of antithrombotic therapy in newly diagnosed non-valvular atrial fibrillation (AF) patients with >1 investigator-defined stroke risk factor.

Methods: 27,106 prospective patients were enrolled in three sequential cohorts in 2010–14 in the global GARRFIELD-AF registry: C1 (2010–11), n=5516, mean CHADS2 score 3.2; C2 (2011–13), n=11,652, mean CHADS2 score 3.3; C3 (2013–14), n=9938, mean CHADS2 score 3.2. Baseline characteristics and antithrombotic therapy initiated at diagnosis were analysed by cohort.

Results: Baseline characteristics were similar in all three cohorts. From C1 to C3, proportion of patients on anticoagulant (AC) therapy increased (C1 57.5%; C2 62.3%; C3 67.5%). Use of vitamin K antagonist (VKA) ±antiplatelet (AP) increased (C1 47.3% vs. 46.9% ±AP increased (C2 62.3%; C3 67.5%). Use of vitamin K antagonist (VKA) ±antiplatelet (AP) increased (C1 4.2%; C2 13.8%; C3 26.4%). The increase in use...
Results: During 10±3 months of follow up, 30 (3.3%) developed major bleeding; 9 (1%) were ICH. Although both scores predicted major bleeding and ICH better than chance, their discriminative capacity was rather modest and did not differ significantly between each other regardless if they were considered as continuous (c-statistic =0.71) or categorical (c-statistic = 0.65) variables. While as categorical variable, the HAS-BLED score was strongly associated with ICH (hazard ratio = 6.9; 95% CI: 1.8–28.1; P =0.007), the ATRIA risk score was not significantly associated with ICH (hazard ratio = 3.9; 95% CI: 0.96–15.5; P =0.06). The net reclassification improvement index numerically favored HAS-BLED for predicting major bleeding and ICH (+5.9%; P =0.039). In this cohort, diabetes mellitus (hazard ratio= 2.8, P =0.01) and chronic obstructive pulmonary disease (hazard ratio= 2.9, P =0.005) were also identified as independent predictors of major bleeding.

Conclusions: In this study, HAS-BLED outperformed ATRIA scoring system especially at predicting ICH in a real world cohort of patients with NVAF on VKAs. Diabetes mellitus and chronic obstructive pulmonary disease should be considered at bleeding risk stratification in these patients.

INFARCTION ACUTE PHASE STEMI

P4407 | BEDSIDE
Adherence to performance measures and in-hospital outcomes for myocardial infarction in China: findings from China Acute Myocardial Infarction (CAMI) registry
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Objectives: To describe the hospital-level adherence to performance measures implemented in in-hospital processes at a national level is a priority, especially in rural areas in China.

Methods: From Jan. 2013 to Sep. 2014, 16,113 ST-segment elevation myocardial infarction (STEMI) and 6,463 non-STEMI (NSTEMI) patients from 89 China hospitals were registered in the China Acute Myocardial Infarction (CAMI) Registry. Proportions of eligible participants receiving the following 10 performance measures were calculated: medications within 24 hours of admission (aspirin) and on discharge (aspirin, beta-blockers, angiotensin converting enzyme inhibitors (ACEI), lipid-lowering therapy and P2Y12 antagonists), echocardiography, reperfusion therapy, door to needle time (D2N) or door to balloon time (D2B). A composite adherence score, defined as the total number of successful interventions performed among eligible patients divided by the total number of possible interventions among eligible patients, was calculated.

Results: The provincial level hospitals had higher composite adherence score (0.67±0.20) than the prefecture level hospitals (0.66±0.21) and county level hospitals (0.61±0.25) on all performance measures (P <0.0001). Among all 10 performance measures, the rate of patients undergoing reperfusion therapy (thrombolytic therapy or PCI) in STEMI patients within symptom onset less than 12 hours is significantly different, with 80.4% in provincial level hospitals, 65.3% in prefecture level hospitals and 56.8% in county level hospitals (P <0.0001). The mortality for provincial level, prefecture level and county level hospitals mortality groups for STEMI was 4.3%, 7.6%, and 12.8% (P <0.0001) and that for NSTEMI was 4.9%, 6.1%, and 9.8% (P <0.0001). Composite adherence score was inversely associated with risk-adjusted hospital mortality.

Conclusions: Although process performance was associated with hospital mortality, using STEMI patients as a surrogate for appropriateness of reperfusion therapy at a national level is a priority, especially in rural areas in China.

Acknowledgement/Funding: National Twelfth Five-year Science and Technolog y Support Projects by Ministry of Science and Technology of China (Grant No. 2011BAI1B02)
P4409 | BEDSIDE
Acute phase Glycemic Variability by continuous glucose monitoring system (CGMS) is associated with endothelial dysfunction in patients with ST-Elevation Myocardial Infarction

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Background: Endothelial dysfunction can predict cardiovascular outcomes in coronary artery disease. Previous study demonstrated glycemic variability might affect endothelial function. It remains unclear whether acute glycemic variability is associated with an increased risk of cardiac events in ST-elevation myocardial infarction (STEMI) patients.

Methods: This prospective study enrolled 70 patients with STEMI. CGMS provides glycemic excursion displayed at 5-minutes intervals, 576 points during 48 hours. Endothelial function was assessed before discharge by measuring brachial artery dilatation after 5 minutes of forearm ischemia flow mediated dilation (FMD). Primary endpoint was measurement of endothelial function.

Results: Glycemic variability, as indicated by the mean amplitude of glycose excursion (MAGE), was measured and divided into 3 groups. The FMD values by MAGE tertiles (≤ 5.15 mmol/L, 3.36–5.15 mmol/L, ≥ 3.36 mmol/L) had significant difference among 3 groups (figure). Blood glucose fluctuation was correlated with FMD, (respectively p=0.02 Conclusion: Glycemic variability is significantly associated with impairment of endothelial function after coronary intervention for patients with STEMI. FMD might become the therapeutic target of medical intervention especially for blood glucose.

P4410 | BEDSIDE
Pharmacoinvasive strategy for ST elevation myocardial infarction (STEMI) is able to significantly reduce mortality with a low NNT in a very populated city

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Introduction: Pharmacoinvasive strategy (PIS) can reduce reinfarction and recurrent ischemia, despite having no effect on mortality, according to meta-analyses using developed countries data. In emerging countries, with high mortality rates for STEMI, the results are not yet well defined.

Methods: We analyzed the first 1000 consecutive STEMI patients treated as PIS within a public network coordinated by a tertiary hospital in a very populated city in an emerging country, between the years of 2010 and 2014. PIS was performed in 91% of cases, while primary percutaneous coronary intervention (PPCI) in the remaining 9%. Basically all cases up to 12 hours of symptoms with ST segment elevation or new left bundle branch block on the ECG, judged as STEMI and that could not perform PPCI within 90 minutes, underwent thrombolysis (~90% with tenecteplase). Complementary medications for acute coronary syndrome and systematic transfer to our referral hospital were performed, aiming cardiac catheterization, if possible within 24 hours. Neither case was denied transfer. Hospital mortality in this series was compared to an online government data record from the year of 2013.

Results: The average in-hospital mortality rate for STEMI patients in our public healthcare system is 15%, remaining stable for the last four years. Considering the PIS network in our city, which covers up to 30% of the city area, there were 61 in-hospital deaths from all causes in the first 1000 consecutive STEMI patients (mortality rate of 6.1%). A decline of 89 expected deaths compared to the overall data was observed, meaning that for every 11.2 patients treated, one death was avoided (number needed to treat – NNT – 11.2).

Conclusions: An organized public network performing 91% of PIS for STEMI patients significantly decreased mortality rate in a very populated city in an emerging country. Early results confirm findings from previous developed countries numbers. The NNT of 11.2 found in 1000 consecutive cases of this series suggests that the strategy that has been used is highly cost-effective.

P4411 | BEDSIDE
Cirulating corin concentrations are related to infarct size in patients after ST-segment elevation myocardial infarction

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Background: Corin, a transmembrane serine protease, partially sheds from the cardiomyocyte cell surface and enters the circulation, a process that might be involved in the setting of myocardial injury.

Purpose: We sought to prospectively investigate the potential association between plasma corin concentrations and myocardial infarct size (IS) measured by cardiovascular magnetic resonance (CMR) in the first week after reperfused ST-segment elevation myocardial infarction (STEMI) and 4 months thereafter.

Methods: In this observational, single-centre study, IS was determined at baseline and 4 months after STEMI using late gadolinium contrast-enhanced CMR. Corin concentrations were determined from blood samples drawn at a median of 1.1 (IQR 1.0–1.8) days after STEMI and 1.5 ± 0.8 days after the index event. The IS was determined according to the European Society of Cardiology definition.

Results: This study cohort included 50 patients (median age: 59 years (IQR 51–66 years); males: 35 (70%), females: 15 (30%)). Corin concentrations (median = 751 pg/ml, IQR 321–1778 pg/ml) had not reached an association with 4-month IS (r=0.366, p=0.009) but there was only a trend to correlation with baseline IS (r=0.249, p=0.084). Corin was significantly correlated with maximum high-sensitivity cardiac troponin T (hs-TnT) concentrations (r=0.346, p=0.014). A receiver operator characteristics (ROC) model including hs-TnT provided an area under the curve (AUC) of 0.95 (95% CI 0.89–1) for the prediction of large 4-month IS. Including corin instead of hs-TnT resulted in an AUC of 0.90 (95% CI 0.81–0.98).

Conclusion: Circulating corin at day 2 after acute STEMI is associated with 4-month IS as assessed by CMR.

P4412 | BEDSIDE
Outcome in patients with STEMI undergoing interhospital transfer: similar baseline characteristics and outcome despite a longer treatment delay

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Background: Early reports showed that any delay in reperfusion with primary PCI may be detrimental to clinical outcome. More recent data, however, suggest that PCI may be performed in STEMI patients also in the setting of remote hospital transfer, with results completely different from previous developed countries numbers.

Methods: From January 2006 to December 2014, 1380 STEMI patients under primary PCI at our Centre, arriving directly (75%) or transferred from 3 stroke Hospitals (25%). All STEMI patients were routinely transferred avoiding a selection bias.

No transfer (n=1330) Transfer (n=350) P value

<table>
<thead>
<tr>
<th>Age</th>
<th>67.0±12.6</th>
<th>66.7±13.2</th>
<th>0.642</th>
</tr>
</thead>
<tbody>
<tr>
<td>Females</td>
<td>26.7%</td>
<td>26.6%</td>
<td>0.963</td>
</tr>
<tr>
<td>Diabetes</td>
<td>24.3%</td>
<td>20.6%</td>
<td>0.214</td>
</tr>
<tr>
<td>Anterior MI</td>
<td>41.3%</td>
<td>36.1%</td>
<td>0.088</td>
</tr>
<tr>
<td>TIMI Risk Index</td>
<td>29.9±16.3</td>
<td>31.5±19.1</td>
<td>0.412</td>
</tr>
<tr>
<td>FMCTB time</td>
<td>77 [63–97]</td>
<td>104 [89–132]</td>
<td>0.001</td>
</tr>
<tr>
<td>In-hospital time</td>
<td>180 [123–260]</td>
<td>231 [198–398]</td>
<td>0.001</td>
</tr>
<tr>
<td>Open vessel before PCI</td>
<td>33.2%</td>
<td>37.1%</td>
<td>0.183</td>
</tr>
<tr>
<td>Open vessel after PCI</td>
<td>95.7%</td>
<td>97.9%</td>
<td>0.093</td>
</tr>
<tr>
<td>30-day mortality</td>
<td>7.1%</td>
<td>6.6%</td>
<td>0.743</td>
</tr>
</tbody>
</table>

Downloaded from https://academic.oup.com/cardiovascular-abstracts/article/38/Suppl_1/434/447/6 by guest on 12 March 2019
Results: Transferred patients had a significantly longer FMCTB and total ischemic time, while other baseline characteristics and the outcome of the 2 groups of patients were similar (Table). Multivariate analysis identified age, total ischemic time, TIMI risk index, Killip class, open vessel before and after PCI, but not transfer, as significant predictors of mortality.

Conclusions: In our experience, patients with STEMI requiring interhospital transfer, as compared to non-transferred patients, had comparable baseline characteristics and similar mortality, although they experienced a longer treatment delay.

P4413 | BEDSIDE
Electrocardiographic findings leading to false ST elevation myocardial infarction activations at a percutaneous coronary intervention capable center
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Background: Electrocardiogram (ECG) interpretation is essential for diagnosing a ST Elevation Myocardial Infarction (STEMI). We report the EKG results of patients who presented with False STEMI activation.

Methods: Medical records of all patients presenting to our institution for percutaneous coronary intervention for possible STEMI from January 2012 to November 2014 were reviewed. A false STEMI activation was defined as a lack of clinical and ECG evidence of ongoing myocardial infarction. Patients undergoing cardiac catheterization without obvious culprit lesions were also included. The ECG findings were grouped into a) meeting STEMI criteria per American College of Cardiology/ American Heart Association, b) ST elevation not meeting STEMI criteria, c) new left bundle branch block (LBBB), d) new right bundle branch block (RBBB) without ST elevation, e) ST and/or T wave abnormalities suggesting myocardial ischemia, f) nonspecific ST/ T wave changes and g) paced rhythm.

Results: Of 643 STEMI activations, 29.7% (191/643) were false activations. Only 11% (21/191) met ECG criteria for STEMI. 40.3% (77/191) had ST elevation not meeting STEMI criteria, 12.6% (24/191) had LBBB morphology with no prior ECG available for comparison. 6.8% (13/191) were RBBB. 5.2% (10/191) showed ST and/or T wave changes suggesting ischemia. 23.4% (44/191) showed nonspecific ST/ T wave changes. Among those, 31.8% (14/44) met diagnostic ECG criteria for left ventricular hypertrophy. There were 2 ECGs (1.1%) showing paced rhythm.

Conclusion: The vast majority of ECGs that led to False STEMI activation showed ST elevation that did not meet criteria for STEMI.

P4414 | BEDSIDE
An admission clinical index score for risk stratification of new-onset atrial fibrillation in STEMI patients undergoing primary PCI
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Purpose: New Onset Atrial Fibrillation (NOAF) is common in the setting of ST-Elevation Acute Myocardial Infarction (STEMI) and known to affect outcomes. There are few data on the prognostic value of biomarkers in this setting. We investigated whether a simple clinical risk score, derived from multiple admission biomarkers, improves the prediction of NOAF and outcomes in STEMI patients treated with primary PCI.

Methods: We reviewed admission clinical, echocardiographic, hemodynamic and laboratory data from 1135 consecutive STEMI patients (age range 21–99 years) admitted to our Cardiology Unit for primary PCI from 2006 to 2011. NOAF was defined as atrial fibrillation occurring from the admission until hospital discharge (hospitalization duration, mean 5±5 days). We developed a risk score with available markers in multivariable Cox regression to predict the occurrence of NOAF and outcomes at short (5±6 days) and long term (25.5±18.4 years) follow up.

Results: We documented NOAF in 88 patients with STEMI (7.7%); mean age 73±10 years; 67% men. At multivariate Cox regression analysis, admission independent predictors of NOAF were age (HR=6.97, p<0.001), obesity (HR=2.07, p=0.03), higher BNP (HR=2.37, p=0.02) and total white blood cells (HR=2.65, p<0.001). A risk score, incorporating these biomarkers, identified a high-risk STEMI subgroup with a significantly higher incidence of NOAF (p<0.001), in hospital mortality (HR=3.56, p<0.001) and long term all-cause mortality (HR=2.63, p<0.001) and cardiovascular mortality (HR=2.49, p<0.006) compared with an intermediate and low risk subgroup.

Conclusions: Age, markers of an inflammatory status and adverse cardiovascular remodeling, are strong predictors of NOAF and outcomes in STEMI patients undergoing primary PCI. Such risk score, based on simple markers, detected at admission, improves the prediction of NOAF and mortality and identifies a high risk subgroup.

P4415 | BEDSIDE
Patterns of coronary dominance and long-term prognosis in a Contemporary cohort of patients with ST-elevation myocardial infarction

Introduction and objectives: Long-term prognostic meaning of the coronary artery dominance patterns in patients with ST-elevation myocardial infarction is still poorly characterized. We investigated the prognosis of these patients according to whether the coronary dominance was right, left, or codominance.

Methods: Retrospectively, between 2007 and 2012, we studied 767 patients admitted to our department for ST elevation myocardial infarction undergoing primary percutaneous coronary intervention.

Results: The rate of right and left dominance was 80.9% and 8.6%, respectively. Throughout 40.8 (interquartile range 21.9–58.3) months, 118 (15.4%) patients died; 39 (5.1%) died in hospital. The mortality rate was 7.1%, 36.4%, and 13.8% (p<0.001) for right dominance, left dominance, and codominance, respectively. The cause-specific mortality was cardiovascular in 7.1% in right dominance, 21.2% in left dominance, and 2.4% in codominance. In the multivariate Cox analysis, left dominance was an independent predictor of mortality: hazard ratio=1.99; p=0.035. Coronary dominance improved the discrimination (C=0.837 vs. 0.821) and calibration abilities of the GRACE score. Seventy-one patients (9.3%) suffered reinfarction during follow-up. In the multivariate analysis, left dominance was an independent predictor of reinfarction: subhazard ratio=2.06; p=0.027.

Conclusions: In ST-elevation myocardial infarction undergoing primary percutaneous intervention, left dominance confers increased risk of death and reinfarction, compared with right dominance, and should be taken into account at risk stratification.

P4416 | BEDSIDE
High-sensitivity troponin T for prediction of left ventricular function and infarct size one year following STEMI
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Background: Data relating high-sensitivity cardiac troponin T (hs-cTnT) to long-term myocardial function and infarct size in patients after first ST-segment elevation myocardial infarction (STEMI) treated by primary percutaneous coronary intervention (PCI) are lacking.

Purpose: We aimed to evaluate the use of serial and peak concentrations of hs-cTnT for prediction of myocardial function as well as infarct size assessed by cardiac magnetic resonance imaging (CMR) one year following first STEMI.

Methods: Sixty-six patients (mean age 57±11 years, 12% females), reperfused by PCI for first-time STEMI, were enrolled in this single-centre, observational study. Serial hs-cTnT, creatinine kinase (CK), high-sensitivity C-reactive protein (hs-CRP) and lactate dehydrogenase (LDH) levels were measured on admission as well as 12, 24 and 48 h post PCI. CMR imaging was performed within the first week and 12 months thereafter.

Results: Except for admission hs-cTnT, all single time point and peak hs-cTnT concentrations showed significant correlations with left ventricular ejection frac-
AUC of peak hs-cTnT was 0.82 (95% CI 0.71 to 0.92) for the prediction of de-
large IS (OR=1.128 [95% CI: 1.067–1.193], p=0.005) was the sole independent predictor of LV. SWS at 3 months (OR=1.110 [95% CI: 1.002–1.228], p=0.045) and the non presen-
tion of valvular or conduction abnormalities (OR=0.030 [95% CI: 0.003–0.346], p<0.005) were independent predictors of early LV.

Conclusion: Two clinical patterns of LV were distinguished in our study. Initial adverse events were the dominant determinant of early remodeling whereas SWS and long-term medications were the only independent determinants of late remodeling, in
ting more general and chronic processes.

Infarction acute phase STEMI / Post infraction period I

P4417 | BEDSIDE
Patterns of left ventricular remodeling during the first year after a
repertused myocardial infarction: a prospective MRI study
H. Delagarde, L. Biere, G. Clerfont, M. Audonnet, S. Willoteaux, F. Prunier, A. Forber. University Hospital of Angers, cardiology, Angers, France

Background: Left ventricular remodeling (LVR) is a major concern after a myocardial infarction.

Purpose: To study various patterns of LVR during the first year after a myocardial infarction, without risk redefinition.

Methods: 162 patients with a first ST-elevation MI admitted to our university hospital were prospectively enrolled. CMR was performed at baseline, and repeated at 3-month and 1 year follow-up in order to investigate left ventricular (LV) volumes and function, infarct size (IS), microvascular obstruction (MVO), and systolic wall stress (SWS).

Results: LVR (>10% increase end-systolic volume) occurred in 38 (23%) patients. 19 patients presented with early remodeling (ELVR) (>10% increase end-systolic volume during the first three months) and 19 others with late remodeling (LLVR) (>10% increase end-systolic volume between baseline and one year, except excluding ELVR patients).

In patients without remodeling (NoLVR), LV volumes and mass decreased and ejection fraction increased during follow-up. In ELVR patients, EF decreased during the first three months with no further variation (EF: 45.4%±9.9, 43.9%±9.6, 43.4%±10.4 at baseline, 3 months and 1 year, respectively). In LLVR patients, LV volumes remained stable during the first three months and then increased while EF presented a biphasic parojeptive course (EF: 48.0%±11.4, 50.7%±11.1, 46.3%±11.2 at baseline, 3 months and 1 year, respectively). NoLVR and LLVR patients depicted similar infarct characteristics (Creatinin kinase peak, infarct size, MVO) and similar baseline LV volumes and EF whereas ELVR presented larger infarct size, higher extent of MVO and greater creatin kinase peaks. In multivariate analysis, IS (OR=1.128 [95% CI: 1.067–1.193], p<0.001) was the only independent predictor of ELVR. SWS at 3 months (OR=1.110 [95% CI: 1.002–1.228], p=0.045) and the non prescription of betablockers or angiotensin-converting enzyme inhibitors (OR=0.030 [95% CI: 0.003–0.346], p<0.005) were independent predictors of early LV.

Conclusion: Two clinical patterns of LV were distinguished in our study. Initial infarct severity was the major determinant of early remodeling whereas SWS and long-term medications were the only independent determinants of late remodeling, in

Mediterranean diet. The sample was classified in two categories: low MedDi-
elScore (≤27) vs. moderate/high (≥27). Multiple logistic regression models were applied to evaluate the effect of adopting the Mediterranean dietary pattern in the 10-year ACS prognosis. Furthermore, stratified analysis was carried out including patient’s history of diabetes.

Results: The overall incidence of diabetes mellitus at baseline examination was 30% in males and 38% in females (p=0.001); whereas the 10-year ACS inci-
dence was 40% in males and 32% in females (p=0.001). An inverse associa-
tion was observed between adherence to the Mediterranean diet and recurrent events, after taking into account potential confounders (OR=0.802, 95% CI 0.644–0.999, p=0.049). However, the diabetes mellitus stratified analysis re-
vealed that the adherence to the testing dietary pattern was inversely associated with ACS prognosis only among the non-diabetic patients (OR=0.795, 95% CI 0.613–1.032, p=0.085); whereas a significant association was observed in those with abnormal glucose homeostasis (p=0.360).

Conclusion: Moderate/high adherence to the Mediterranean dietary pattern seems to be protective against recurrent cardiovascular events, but only among diabetic ACS patients. The latter observation highlights a plausible interaction be-
tween history of diabetes and long-term nutritional habits in the ACS prognosis.

Acknowledgement/Funding: None to declare

P4418 | BEDSIDE
The association between adherence to the Mediterranean diet and diabetes mellitus on the 10-year (2004-2014) acute coronary syndrome (ACS) prognosis; the Greeks study
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Background: The Mediterranean dietary pattern has been favorably associated with decreased ischemic stroke, anormal, and cardiovascular disease, both at age and at the time of metabolic syndrome or as a sole pathogenic factor undoubtedly increases

Oroscopoulos1, S. Zombolos4, I. Stergiouli5, Y. Mantas5, C. Pitsavos6 on behalf of The GREECS Study Investigators, Athens, Greece.

Purpose: To evaluate the association between adherence to the Mediterranean Diet (MD) and history of diabetes mellitus, on the 10-year incidence among Acute Coronary Syndrome patients (ACS).

Methods: From October 2003 to September 2004 a sample of 6 Greek hospi-
tals was selected and almost all consecutive 2.172 ACS patients were enrolled.

In 2013–14, the 10-year follow-up (2004–2014) was performed in 1,918 particip-
ants (88% participation rate). Dietary habits were assessed through a validated food frequency questionnaire and adherence to MD was evaluated through the MedDietscore (range 0–55). Higher values indicate greater adherence to the

Infarction acute phase STEMI / Post infraction period I

P4419 | BEDSIDE
Is GRACE Score risk useful for predicting long term prognosis in NSTEMI patients with normal or near-normal coronary angiography?
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Introduction: Current practice guidelines for management of patients with NSTEMI strongly recommend using GRACE risk score for thrombotic risk stratifi-
cation at hospital discharge.

Methods: 1,865 consecutive patients with primary diagnosis of NSTEMI at dis-
charge have been investigated. GRACE score was calculated as a continuous
variable and categorised (High-intermediate-low risk). Patients were classified as NONCA or OCAD depending on their stenosis lesions ≥70% (≥50% in LMCA).

Results: 20.6% had NONCA. GRACE score was 126±27 in the NONCA group (118±18 vs. OCAD, p<0.001). The GRACE score classified more high-risk patients in patients with NONCA 59.9% than in OCAD 50% (p=0.005). There were 454 (24.3%) deaths; 72 in the NONCA group (18.8%). As a continuous variable GRACE score was significantly associated with death (HR=1.034; 95% CI 1.03 to 1.04), this remained in both, NONCA and OCAD, subgroups.

The classification showed a significant association with mortality for high-

risk stratum both in NONCA and OCAD groups. However, in NONCA intermediate risk patients there was no significant association with death (HR=1.017, 95% CI 0.22 to 4.90).

By Youden’s test the optimal cutoff GRACE score was estimated to identify pa-
tients at risk of death within the group of NONCA. A score ≥132 yielded a sensi-
bility (SN) of 84% and specificity (SP) of 65% (vs. SN and SP of 90% and 45%, respectively, exhibited by the original cutoff ≥120 to define high risk death). It also achieve an index of net reclassification improvement of 9.2% (95% CI 2.3%-16.1%; p=0.009).

Conclusions: Data suggests that the GRACE score for predicting risk of post-
discharged death classified erroneously patients with NSTEMI and NONCA, over-

dating the risk of death; since these patients are penalised 14 points by not

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timating the risk of death; since these patients are penalised 14 points by not

timating the risk of death; since these patients are penalised 14 points by not

Conclusion: Moderate/high adherence to the Mediterranean dietary pattern seems to be protective against recurrent cardiovascular events, but only among diabetic ACS patients. The latter observation highlights a plausible interaction be-
tween history of diabetes and long-term nutritional habits in the ACS prognosis.

Acknowledgement/Funding: None to declare
Background: Apolipoprotein J (Apo J) is a cyto-protective and anti-oxidant pro- tein with an important function in lipid metabolism. We previously showed that in the early ischemic phase at the onset of an acute myocardial infarction (AMI) there is a shift in Apo J glycosylation. Moreover, there are evidences of a protective role of Apo J against myocardial injury in the context of AMI. However, it is unknown whether Apo J glycosylation levels are potential markers in the prognosis after AMI.

Purpose: The aim of this study was to investigate if changes in glycosylated Apo J (Apo J-Glyc) levels during AMI are involved in the evolution and progression of the ischemic event.

Methods: Apo J-Glyc levels were measured with a novel and original im- munofluorescence assay in serum samples from AMI-patients at the moment of ad- mission (t=0; N=227) and 3 days after the onset of the event (t=3d; N=68), and compared to an age and gender matched group of control subjects without any previous history of cardiovascular disease (N=144).

Results: AMI-patients at admission had a 20% decrease in Apo J-Glyc levels with respect to control non-ischemic patients (P<0.0001). Multiple linear regres- sion analysis (including drug treatment, gender, presence of diabetes and LDL- c, HDL-c and total cholesterol levels), showed that only the presence of the is- chemic event remained as an independent factor for Apo J-Glyc levels (r=0.428; P<0.0001). Apo J-Glyc levels at admission were able to discriminate the pres- ence of AMI with an area under the ROC curve (AUC) of 0.752 (95% CI: 0.703– 0.801; P<0.0001) and were inversely correlated with the ischemia time (r=0.207; P<0.0007) and with the GRACE risk score (r=0.268; P<0.0002). Follow-up of AMI- patients 3 days after the event revealed a progressive decrease of Apo J-Glyc levels (15% reduction vs. t=0; P<0.0003). Moreover, Apo J-Glyc levels 3 days after the event showed a predictive value for cardiac shock presentation (AUC: 0.766; 95% CI: 0.617–0.914; P=0.006) and mortality (AUC: 0.744; 95% CI: 0.597–0.891; P=0.006) in AMI-patients.

Conclusions: These results indicate that Apo J-Glyc is a novel biomarker of is- chemic events. Moreover, the continuous decrease in Apo J-Glyc levels predicts a warn- ening in the evolution of the cardiac event, likely acting as a prognostic marker.


P4423 | BEDSIDE
Influence of face cooling (diving reflex) on heart rate variability and double product in patients after myocardial infarction

Methods: 51 patients after MI were studied, in the sinus rhythm without AV blocks or branch blocks. Average age of patients was 55.3 years. Patients were randomly divided in the face cooling group (29 patients) and control group (without face cooling: 22 patients). Patients of similar age, sex and site of infarction. All patients were exposed to 25 degrees C ambient air for 30 min., they had their blood pressure taken, as well as, continuously monitored ECG for 5 min, in the lying position. Cooling group patients had cold water bags of 5 degrees C water put on their faces. They had their blood pressure taken and monitored ECG for 5 min again. Control group patients had the same procedure, but without face cooling. Out of 5 min. continuous monitored ECG four parameters were used. "time domain" HRV were assessed: SDNN, RMSSD, NN50 and HRV index. In the cooling group the SDNN was increased (P<0.05), RMSSD was increased (P<0.05) as well as the NN50 (P<0.05).

Conclusions: The aim of this study was to assess the influence of face diving reflex on heart rate variability and double product in patients after myocardial infarction.
both heart rate and double product, that is myocardial oxygen uptake, at rest. Face cooling also significantly increased HRV parameters, which represent vagal activity. Face cooling could be possibly used in the treatment of ischemic chest pain.

P4424 | BEDSIDE
The influence of pre-hypertension on long-term major adverse cardiac events in patients with acute myocardial infarction and preserved left ventricular systolic function
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Background: We evaluated the independent prognostic value of pre-HT on long-term MACE after acute MI with preserved LV systolic function.
Methods: Using data from Korea Working Group on Myocardial Infarction, a total of 2538 patients who were diagnosed with acute myocardial infarction, had no history of previous hypertension and whose LV ejection fraction (EF) was equal or higher than 45%. The eligible patients were classified into two groups according to initial systolic blood pressure (sBP): optimal group (sBP < 120 mmHg and diastolic BP (dBP) < 80 mmHg; n=1314, 51.8%) vs pre-HT group (120 ≤ sBP < 140 mmHg or 80 ≤ dBP < 90 mmHg; n=1224, 48.2%). Predefined MACE was all cause mortality, repeated MI, revascularization and new onset heart failure. In addition, we investigated the predictive value of pre-HT for MACE with multivariable Cox regression analysis.
Results: Patients in pre-HT group were younger, less male, and prescribed with beta-blockers more. The initial sBP was 104.4 vs 124.2 mmHg in each group (p<0.001). Their angiographic findings were not different. Total incidence of MACE was similar between the two groups, which was 15.8% and 14.5% in optimal and pre-HT group, respectively (p=0.413). Among individual component of MACE, only target vessel revascularization rate was marginally higher in pre-HT group (0.3% vs 1.0%, p=0.06). After adjusting confounding factors, pre-HT was not predictor of 12-month MACE (HR 0.914, p=0.459). Only initial LVEF was a significant predictor (HR 0.982, 95% CI 0.967–0.998).

KM curve for 12 month MACE

Conclusions: This study showed that the existence of pre-HT at admission was not associated with long-term MACE in HT-naive patients with AMI and preserved LV systolic function.

P4425 | BEDSIDE
Prognostic impact of left ventricular spontaneous echo contrast in patients with acute anterior wall myocardial infarction
Background: This study is designed to investigate the clinical impact of LV spontaneous echo contrast (SEC) and association with LV thrombus (LVT) formation in patients with acute anterior wall myocardial infarction (anti-AMI) and underwent percutaneous coronary intervention (PCI).
Methods: 38 anti-AMI patients with LV SEC were enrolled and divided into 2 groups depending on future development of LVT. We compared the demographic and procedural characteristics and clinical outcome of the two groups.
Results: Median clinical follow-up period was 80 (2–267) months. In 9 (23.7%) patients, LV developed 40 (3–690) days after anti-AMI. Although 15.8% of LV SEC patients were NSTEMI, LV developed only in STEMI. No embolic events occurred in all LV SEC patients even in patients with future LVT formation, whereas LV SEC with future LV formation was associated with CHF hospitalization during post-MI follow-up. In STEMI patients with LV SEC, LV formation was related to poorer LV systolic function and more decline of hemoglobin than in patients without future LVT (Table). Male gender and smoking were inversely related to LVT formation. STEMI patients with SEC and future LV formation who had undergone primary PCI were associated with longer door-to-balloon time, lower initial TIMI flow and more frequent thrombus aspiration procedure than those of no LVT.

Conclusions: Pre-AMI patients with LV SEC presented with higher CHF hospitalization rate and more frequent thrombus aspiration procedure than those of no LVT. LVT (+), N=5 LVT (−), N=17 P value

P4426 | BEDSIDE
Clinical impact of left ventricular spontaneous echo contrast in patients with acute anterior wall myocardial infarction
Background: Patients with AMI after prior CABS had smaller infarct, but more reinfarction, reoperation, heart failure and angina. Previous angina, diabetes and age undependable as well as use of digitalis, diuretic and angina together and reinfarction, older pts and diabetes together, influenced worse survival in post bypass group of pts.
Methods: Among ant-AMI patients with LV SEC, LVT developed in 23.7%, male gender, older pts and diabetes together (p=0.0401). Use of digitalis and diuretics, together with previous angina influenced on survival too (p=0.0174) as well as male gender, older pts and diabetes together (p=0.0001).

Conclusions: Patients with AMI after prior CABS had smaller infarct, but more reinfarction, reoperation, heart failure and angina. Previous angina, diabetes and age undependable as well as use of digitalis, diuretic and angina together and reinfarction, older pts and diabetes together, influenced worse survival in post bypass group of pts.

P4427 | BEDSIDE
Predictive value of plasma galectin-3 levels for in-hospital and long-term complications of patients with right ventricular myocardial infarction
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Background: There is uncertainty regarding the risk of major complications in patients with the right ventricle (RV) myocardial infarction (MI) on the background of the posterior Q-MI of the left ventricle (LV). Galectin-3 takes part in many mechanisms of atherothrombosis, such as inflammation, proliferation and fibrosis, and
has prognostic value in patients with heart failure and acute coronary syndrome. However relationship between galectin-3 and complications after RV MI is still unknown.

**Purpose:** To evaluate the significance of galectin-3 as a predictor of complications at 2.6-year follow-up in patients with RV MI on the background of the posterior Q-MI.

**Methods:** The study involved 155 patients (60% males and 40% females) with acute RV MI on the background of the posterior Q-MI aged 64.11±7.87 years. Galectin-3 levels were determined with enzyme immunoassay on day 2 of MI. Follow-up was 2.6±2.7 years. Study endpoints were: unstable angina (UA), recurrent myocardial infarction (Re-MI), stroke and death.

**Results:** Study endpoints reached 62 (40%) patients: UA - 51 (32.9%), Re-MI - 16 (10.3%), stroke - 9 (5.8%) patients, 14 people (9.0%) died. Patients with complicated follow-up period had significantly higher concentration of galectin-3 than those of patients without complications (34.3±2.58 mg/L vs 27.1±6.52 mg/L, p<0.0001). Multivariable analysis demonstrated that galectin-3 level is an independent risk factor for paroxysmal atrial fibrillation (AF) and cardiogenic shock in acute period of RV MI. It was proved that galectin-3 level is a predictor of Re-MI during 2.6 years follow-up.

**Conclusion:** Evaluation of galectin-3 level in patients with RV MI on the background of the posterior Q-MI may be useful as an additional marker of life-threatening complications in acute period of MI and as a predictor of Re-MI during long-term follow-up.

**P4428 | BEDSIDE**
Clinical impacts of high-sensitivity C-reactive protein reduction for secondary prevention in Asian patients with one-year survivor after acute myocardial infarction

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**Background:** Reduction of inflammation using statins after acute coronary syndrome has prognostic value in patients with heart failure and acute coronary syndrome. However, there are few convincing data about secondary prevention in Asian acute myocardial infarction (AMI) patients.

**Objectives:** The aim of this study was to investigate the clinical impacts of high-sensitivity C-reactive protein (hs-CRP) reduction for secondary prevention in stabilized Asian AMI patients after statin therapy.

**Methods:** Between February 2008 and November 2011, 1,031 AMI patients who had baseline low-density lipoprotein cholesterol (LDL-C) levels >70 mg/dL, hs-CRP level >1 mg/L, and underwent successful percutaneous coronary intervention (PCI) with stent at three large national university hospitals were enrolled in the present study. They were divided into 2 groups at the approximate median of hs-CRP reduction during one-year (>20% reduction from baseline n=510, <80% reduction n=521). The entire study population completed the 2-year follow-up period.

**Results:** During the 2-year follow-up period, cardiac death or myocardial infarction (MI) was occurred in 22 patients (2.1%). More hs-CRP reduction group included higher risk patients such as history of hypertension, systolic heart failure, and pre-procedural total occluded lesion. After multivariate analysis, less hs-CRP reduction group exhibited worse outcomes after multivariate analysis [Hazard ratio (HR) 3.05, 95% confidence interval (CI) 1.07–8.64, p=0.036]. In patients with LDL-C reduction <50%, cardiac death or MI rates were significantly different in the 2 groups (HR 4.18 95% CI 1.13–15.4, p=0.032). However, no significant differences were existed in whose LDL-C level reduced over 50% in one-year after statin therapy (OR=0.760, 95% CI 0.429–1.346, p=0.347).

**Conclusions:** For secondary prevention, hs-CRP reduction decreased the risk of cardiac origin death or recurrent MI among stabilized Asian AMI patients. The clinical impact was prominent especially in patients who did not achieve LDL-C reduction goal.

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**P4429 | BEDSIDE**
Long term prognostic value of worsening renal function and uric acid in-hospital changes in patients with acute myocardial infarction

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**Purpose:** We investigated the incidence and prognostic value of worsening renal function (WRF) and uric acid (UA) in-hospital changes regarding 1 year mortality in acute myocardial infarction (AMI) patients.

**Methods:** We studied 375 consecutive AMI patients (either ST or non-ST segment elevation) within 12 hours of symptoms’ onset. UA and creatinine levels were daily measured throughout hospitalization and their peak values were recorded in each patient. WRF was defined as >0.3mg/dl increase in creatinine during hospital stay. Primary end-point was 1 year mortality.

**Results:** Mortality rate at 1 year was 10.9%. Optimal value for predicting 1 year mortality was 1.1 mg/dl for UA elevation. Based on the presence of WRF and UA elevation (1.1 mg/dl) AMI patients were classified in those with both WRF and UA elevation (9.1%), WRF only (8.3%), UA elevation only (27.5%) and those with neither WRF nor UA elevation (controls, 55.2%). AMI patients with both UA elevation and WRF experienced increased 1 year mortality compared to those with UA elevation only significantly (38.2 vs 11.7%, log-rank p<0.0001) and controls (38.2 vs 2.9%, log-rank p<0.001). Patients with WRF only had increased 1 year mortality compared to those with UA elevation only and controls (32.3 vs 11.7 vs 2.9%, log-rank p=0.003 and <0.001, respectively). Finally, patients with UA elevation only had increased 1 year mortality compared to controls (11.7 vs 2.9%, log-rank p=0.002) (Figure 1). In multivariate Cox regression analysis, EF (HR 0.929, p<0.001) and co-existence of WRF and UA elevation (HR 8.605, p<0.001) were independent predictors of 1-year mortality.

**Conclusions:** In-hospital WRF and UA elevation >1.1 mg/dl have a synergistic adverse effect on 1-year outcome in AMI patients. Among them WRF appear as a stronger predictor of adverse outcome.

**P4430 | BEDSIDE**
The role of unprocessed meat consumption on the 10-year (2004-2014) acute coronary syndrome (ACS) prognosis

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**Background:** Results of recent studies are equivocal regarding the effect of unprocessed red meat consumption on the increased risk of Cardiovascular Disease (CVD), in the general population; while processed meat has been linked to a significantly higher risk for developing heart disease. However, similar studies on the secondary coronary heart disease prevention are scarce.

**Purpose:** The present study aimed to investigate the association between long-term meat consumption and the 10-year ACS prognosis.

**Methods:** From October 2003 to September 2004 a sample of 6 hospitals was selected and almost all consecutive 2,172 ACS patients were enrolled. In 2013–14, the 10-year follow-up (2004–2014) was performed in 1,918 participants (88% participation rate). Multiple logistic regression models were applied to estimate the impact of unprocessed red meat consumption (as assessed by using a validated semi-quantitative food frequency questionnaire) in the ACS prognosis.

**Results:** No significant association was observed between red meat intake and CVD incidence after taking into account various potential confounders; red meat intake 1–2 times/week (OR=0.870, 95% CI 0.536–1.412, p=0.572), 3–5 times/week (OR=0.851, 95% CI 0.518–1.399, p=0.524) and >5 times/week (OR=0.760, 95% CI 0.429–1.346, p=0.347).

**Conclusion:** The guidelines or recommendations, about the total red meat intake, either in primary or secondary heart disease prevention should probably be re-evaluated. Further research on the consumption of processed vs. unprocessed meat on the long-term ACS prognosis is needed to evaluate the different effects on heart health.

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P4431 | BEDSIDE
The long-term prognosis of patients diagnosed as type 2 myocardial infarction does not differ from that of patients with myocardial injury
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Introduction: The differentiation between patients (pts) with type 2 myocardial infarction (T2MI) and pts with troponin (cTnI) values above the decision limit, indicating myocardial injury but otherwise not fulfilling the diagnostic MI criteria remains a clinical challenge.

Purpose: To describe the clinical features and the long-term survival of pts with T2MI and those with myocardial injury.

Methods: During 2010–2011 we prospectively studied unselected pts admitted to a 1000-bed university hospital, having cTnI measured on clinical indication. The diagnosis of a T2MI was according to the universal MI definition including established criteria for myocardial oxygen supply/demand imbalance. A cTnI value > 30 ng/L (CV -10%) was considered the decision limit. Pts were followed for up to 4 years with all-cause mortality as the clinical endpoint.

Results: Within the one-year period of inclusion a total of 1577 consecutive hospitalized pts with cTnI values > 30 ng/l were considered. Of these 119 were classified as T2MI, and 1089 were found to have myocardial injury. No difference in the median age between the two groups was observed: 78 (IQR 67–85) yrs vs. 77 (IQR 67–85) yrs (P=0.9). Moreover, neither gender, risk factors nor medical history differed significantly between the two groups. Peak cTnI values, however, were higher in T2MI pts, 850 (390–3270) ng/L, than in pts with myocardial injury, 90 (50–270) ng/l (P<0.0001). During a median follow-up of 3.2 yrs 720 pts (60%) died with no difference in mortality between the two groups (P=0.5; Figure).

Conclusions: It appears that the long-term prognosis of pts diagnosed as T2MI does not differ from that of pts with myocardial injury. Due to the high mortality demonstrated more attention to both patient groups is warranted.

P4432 | BEDSIDE
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Incidence of statin non-prescription at discharge and long-term mortality in patients with ST-elevation myocardial infarction undergoing primary percutaneous coronary interventions

Background: Guidelines uniformly recommend statin therapy at discharge to all patients following ST-elevation myocardial infarction to reduce the risk of subsequent cardiovascular events.

Objective: We sought to investigate the impact of statin non-prescription at discharge on long-term mortality in patients who underwent urgent coronary angiography for planned primary PCI.

Methods: From January 2009 to December 2010, in a single high-volume center, 1949 consecutive patients underwent urgent coronary angiography for myocardial infarction and survived hospitalization period. Long-term mortality was compared between 149 (7.6%) pts without statin prescription at discharge and 1800 (92.4%) pts with statins.

Results: Statin non-prescribers were older (61.7±13 vs. 59±11; P<0.02), had less hyperlipidemia (42% vs 64%; P<0.01), had less ad-hoc PCI (70% vs. 91%; P<0.01), higher rate of baseline TIMI 3 flow (20% vs. 13%; P<0.01), but lower rate of TIMI 3 flow in infarct related artery post PCI (87% vs. 94%; P<0.01) and were more likely a CADILLAC high risk patients (37.8% vs. 21.6%; P<0.01). At a mean follow-up of 48±20 months, non-prescribers had significantly higher mortality than patients on statins (37.6% vs. 13.5%; P<0.001). After multivariable adjustment using Cox regression model, statin non-prescription remained independent predictor of long-term mortality not only in CADILLAC high risk patients (OR 2.5; 95% CI 1.4–4.6; P<0.01) but also in CADILLAC low/medium risk patients (OR 2.45; 95% CI 2.01–4.13; P<0.001) (figure 1 and 2).

Conclusion: Statin non-prescription at discharge is low and long-term survival benefit of statin therapy was seen in all CADILLAC risk strata.

P4433 | BEDSIDE
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Strong predictive value of left ventricular global longitudinal strain on mortality and heart failure admissions following ST segment myocardial infarction
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Purpose: Left ventricular (LV) function is a key determinant of outcome after ST-segment elevation myocardial infarction (STEMI). LV global longitudinal strain (LV-GLS) has shown to be a sensitive measure of myocardium deformation and may act as a major prognostic marker. Our aim is to assess the predictive value of LV-GLS on all-cause mortality and heart failure (HF) hospitalization and compare it to other echocardiographic parameters, to GRACE and TIMI risk scores and to BNP on admission.

Methods: We retrospectively analysed consecutive patients (P) with STEMI and no prior cardiovascular event who were admitted to our centre during 18 months. Clinical profile and laboratory data were collected on admission and transthoracic echocardiogram was performed 72 to 96h after STEMI. Semi-automated LV-GLS was calculated offline as the mean value of longitudinal strain from apical (long axis, 4 chamber and 2 chamber) views. P who did not present adequate image loops for analysis were excluded. Clinical follow-up (FU) time of at least 12-months was performed to assess the occurrence of composite end-point of death and hospital admission for HF. For statistical analysis we used chi-square and T-student test, Cox regression analysis, Roc and Kaplan-Meier curves.
Results: 155 P (mean age 58±14.9 years, 80% male) were included with a median FU of 509 days and 16 P reached the composite end-point (5 deaths and 11 HF hospitalizations). Significant prognostic value was found for LV-GLS (AUC 0.836; HR: 1.46; 95% CI: 1.20–1.78; p<0.001). There was a trend associated with E/e' ratio (95% CI 0.99–1.24; p=0.054) and left ventricular ejection fraction (LVEF) (95% CI 0.89–1.00; p=0.07). Other possible predictors held non-significant results towards the end-point, mainly: E/e' ratio (95% CI 0.51–4.54; p=0.39), BNP on admission (95% CI 0.99–1.03; p=0.88), GRACE score (95% CI 0.99–1.04; p=0.21) and TIMI score (95% CI 0.82–1.36; p=0.69). Multivariate analysis showed that LVEF remained independently associated with the composite end-point (HR: 1.85; 95% CI: 1.28–2.09; p<0.001). From the ROC curve analysis, the best cut-off value to predict the combined end-point was LV-GLS worse than –11% with AUC 0.842.

Conclusions: Semiautomatic LV-GLS is a rapidly accessible tool to assess LV function and provides strong prognostic value for death and heart failure hospitalizations following STEMI. In our population, LV-GLS had greater accuracy to predict outcomes than LVEF, E/e' and E/A ratios, BNP on admission, GRACE and TIMI scores. LV-GLS worse than –11% is an excellent cut-off value to predict poorer outcome after STEMI.

P4434 | BEDSIDE

Improvement after out-of-hospital cardiac arrest most substantial in younger patients - results from a statewide quality improvement initiative in North Carolina during 2010-2012

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Background: Bystander cardiopulmonary resuscitation (CPR), first responder defibrillation, and survival to discharge in out-of-hospital cardiac arrest patients increased significantly following a quality improvement initiative in North Carolina (NC), USA; during 2010–2013. We assessed how these changes varied according to patient age.

Methods: From the CARES registry, we identified out-of-hospital cardiac arrests of presumed cardiac cause and not witnessed by emergency medical services from counties with complete case capture in NC (n=17, population≈3.0 million) during 2010–2013 and excluded cases with missing age (n=11) and age <18 (n=142).

Results: Of 6,234 patients, 965 (15.5%), 1938 (31.1%), 1983 (31.8%) and 1348 (21.6%) were 18–49, 50–64, 65–79 and ≥80 years of age. Lower proportions of witnessed arrest (p<0.003) and shockable rhythm (p<0.001) were seen with increasing age. Bystander CPR rates increased in all age groups during 2010–2013 (33.1 to 49.2% for age 18–49; p<0.001; 41.1 to 45.1% for age 50–64, p=0.11; 37.4 to 53.4% for age 65–79, p<0.001; and 40.4 to 50.8% for age ≥80, p=0.003); similar was seen for first responder defibrillation rates (33.3 to 47.8% for age 18–49, p=0.034; 40.1 to 46% for age 50–64, p=0.55; 45.2 to 49.8% for age 65–79, p=0.53; and 37.5 to 50% for age ≥80, p=0.23). Survival only increased in younger patients (see Figure) and only among those who received bystander CPR (7.2 to 21.9% for age 18–49, p=0.028; and 10.9 to 19.9% for age 50–64, p=0.003); minimal changes were seen in cases who did not receive bystander CPR (12.3 to 11.3% for age 18–49, p=0.86; and 7.9 to 8.5% for age 50–64, p=0.76).

Conclusions: Bystander and first responder intervention rates increased in all age groups, but survival only improved in younger patients.

P4435 | BEDSIDE

CPR quality in out-of-hospital cardiac arrest patients treated with basic–versus advanced life support with and without mechanical chest compressions

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Background: Hyperglycaemia is known to be associated with adverse outcomes for patients after acute myocardial infarction. However, little is currently known regarding in patients after cardiac arrest.

Purpose: We assessed the hypothesis that higher glucose levels are associated with worse outcomes in patients after cardiac arrest in the current therapeutic hypothermia era.

Methods: Patients who were resuscitated and treated with targeted temperature management were enrolled in this study. Blood glucose was measured at the time of admission, and the time intervals from collapse to the return of spontaneous circulation (median, Q1 and Q3) were reviewed. Quality of CPR was assessed in terms of no-flow time (NFT), no-flow fraction (NFF) and chest compression rate.

Results: Attempt of resuscitation was reported on 85% of patients of which 111 comprised the Pre-intervention group (BLS=31 and ALS=80) and 482 comprised the Post-intervention group (BLS=66, ALS=259 and ALS + LUCAS=157). A total of 263 patients were excluded due to missing data. The post-intervention group receiving LUCAS CPR was more likely to have a witnessed, bystander cardiac arrest with VF/VT, lower comorbidity and received better CPR quality with a NFF of 25% vs. 36% (p<0.001) and shorter pre- and post-shock pauses, NFT of 18 seconds vs. 24 seconds (p<0.001), compared with the Post-intervention group receiving manual CPR only. The majority of patients (84%) were resuscitated with the involvement of physicians (ALS group), and these patients had significantly lower NFF compared with the BLS group, 31% vs. 38% (p<0.001). The quality of BLS and ALS provided CPR seen in this study was remarkable improved compared to the previous evaluation of CPR quality in 2005.

Conclusions: Implementation of mechanical chest compressions during CPR was associated with lower no-flow fraction. The physician provided ALS was superior to the paramedic provided BLS, however, both BLS and ALS have improved remarkable during the past 10 years.

Acknowledgement/Funding: The Danish Heart Foundation, The Riisfort Foundation, The Arvid Nielson Foundation and The Savvaerkejfeu Foundation

P4437 | BEDSIDE

Does hyperglycaemia predict the prognosis in patients after cardiac arrest? The higher the glucose level, the worse the outcome?

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Background: Hyperglycaemia is known to be associated with adverse outcomes for patients after acute myocardial infarction. However, little is currently known regarding in patients after cardiac arrest.

Purpose: We assessed the hypothesis that higher glucose levels are associated with worse outcomes in patients after cardiac arrest in the current therapeutic hypothermia era.

Methods: Patients who were resuscitated and treated with targeted temperature management were enrolled in this study. Blood glucose was measured at the time of admission, and the time intervals from collapse to the return of spontaneous circulation (median, Q1 and Q3) were reviewed. Quality of CPR was assessed in terms of no-flow time (NFT), no-flow fraction (NFF) and chest compression rate.

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Acknowledgement/Funding: The Danish Heart Foundation, The Risfot Foundation, The Simon Fouger Hartmann Foundation, The Arvid Nielson Foundation and The Havaerkejfeu Foundation

P4436 | BEDSIDE

CPR resuscitation
P4438 | BEDSIDE
Out-of-hospital cardiac arrest with no obvious extra cardiac cause: impact of coronary angiography on early survival
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Background: Out-of-hospital cardiac arrest (OHCA) is mainly driven by coronary artery disease. However, the functional prognosis remains poor with a very high in-hospital mortality, and less than 10% of patients will survive without neurological damage. Accordingly, early coronary angiogram (CA) has been proposed in OHCA patients in order to improve survival.

Aim: To identify the impact of coronary angiogram on survival without neurological sequelae in OHCA patients with no obvious extra-cardiac cause.

Methods: In a prospective study between January 2011 and December 2013, we analyzed clinical and biological data in OHCA patients referred in two centers with CA facilities. Uni- and multivariate analysis were used to identify factors associated with in-hospital survival.

Results: 125 patients were included, with 60% survival rate. CA was performed in 108 (86%) patients and coronary angiography realized in 85 (68%) patients. Univariate analysis identified factors associated with hospital survival: age (<0.002), duration of no-flow (2.7±4 vs 5.6±4.6 min, p=0.0003), initial shockable rhythm (p<0.001), dosage of adrenaline bolus (p=0.0003), APACHE II score (p<0.0001), lactate level (p<0.0001), and left ventricular ejection fraction at admission (p=0.0005). The added value of coronary angiography on survival was significantly better (p<0.001) than the one of CA (p=0.02).

In a multivariate analysis, APACHE II score (p=0.002), level of lactates at admission (p=0.006), initial shockable rhythm (p=0.011) and coronary angioplasty (p=0.014) are both independent predictors of survival. However, only APACHE II score (p=0.001) and not coronary angiography (p=0.18) was associated with a good neurological survival (CPC score 1).

Conclusions: Parameters reflecting pre-hospital care (APACHE II score and resuscitation delays) were the most important factors predicting survival and neurological prognosis. Survival could be influenced by coronary angiography but triage for CA is not mandatory to select those who require immediate coronary angiography. Further studies with larger groups of patients are necessary to confirm the role of CA in OHCA.

P4439 | BEDSIDE
Using of LUCAS II device for CPR by regional non-urban Medical Emergency Service
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Background: LUCAS II was developed for automatic chest compressions during cardiopulmonary resuscitation (CPR). Current evidence on the use of this device in out-of-hospital cardiac arrest (OHCA) is still insufficient.

Purpose: The main purpose of this study was to compare the effect of CPR for OHCA with and without LUCAS by Regional non-urban Medical Emergency Service (EMS) in physician-present pre-hospital medical system (randes-vous system).

Methods: We analyzed a prospective registry of all consecutive OHCA patients in four EMS stations, two of them used LUCAS device in all CPR, the EMS crews in other two stations used manual CPR. Individuals with contraindications to LUCAS or with EMS-witnessed arrest were excluded.

Results: From May 2010 to June 2014 337 patients were included in the OHCA registry. Fifty-nine patients were excluded from the analysis because of contraindications to LUCAS or EMS-witnessed arrest. Data from 278 patients were included in the analysis, 144 with LUCAS and 134 with manual CPR. Baseline characteristics are shown in Table 1.

We observed more witnessed arrests in LUCAS group (64.18% vs. 79.17%, p=0.0074) and more asystoly as initial rhythm in LUCAS group (48.51% vs. 69.44%, p=0.0004). We did not find significant differences in return of spontaneous circulation (ROSC) between the groups (30.6% in non-LUCAS vs. 25% in LUCAS). We also did not observe an increase in incidence of cardiac etiology (31.25% vs. 25% in non-LUCAS vs. 24.18% in LUCAS, p=0.31) and in ROSC II initial rhythm was ventricular fibrillation (51.43% in non-LUCAS vs. 46.43% in LUCAS, p=0.80). In LUCAS group we observed significant more conversions from non-shockable to shockable rhythm (10.10% vs. 20.7%, p=0.0396). 180 days follow up was provided by in-patients (85% in all patients with ROSC in both groups). We observed significant more survivors in non-LUCAS group (p=0.0198), Figure 1. We did not find any survival difference in arrests of presumed cardiac etiology (p=0.3175), Figure 2.

Conclusions: The use of automated chest compressions with LUCAS device in our study did not improve survival rate in OHCA. We observed significantly higher 180 days mortality in LUCAS treated patients by regional non-urban EMS.

P4440 | BEDSIDE
Vitamin D deficiency is associated with severe shock in patients with sudden cardiac arrest
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Background: Vitamin D deficiency is associated with various cardiovascular diseases, including sudden cardiac arrest (SCA). Severe shock is related to morbidity and mortality in patients resuscitated from SCA. This study investigated the association of vitamin D deficiency with severe shock in patients with SCA.

Methods: We enrolled patients who were successfully resuscitated from out-of-hospital cardiac arrest of presumed cardiac cause. Severe shock was defined as hypotension requiring mechanical circulatory support such as extracorporeal membrane oxygenation (ECMO) in spite of high-dose vasopressor therapy. The vitamin D level was measured as plasma 25(OH)D concentrations and severe vitamin D deficiency was defined as 25(OH)D < 10 ng/mL.

Results: A total of 96 patients [men (70%), mean age 55.4±15.8 years] were included in this study. First monitored rhythm was shockable rhythm in 59 patients (62%) and non-shockable rhythm in 37 patients. Vitamin D level was significantly lower (7.2±4.1 vs. 11.2±5.2 ng/mL, p=0.001) and vitamin D deficiency was observed more frequently (82 vs. 49%, p=0.004) among patients with severe shock. Patients with severe shock were likely to have more left ventricular systolic dysfunction (LVEF < 40%, 78 vs. 44%, p=0.002) and to be obese [body mass index (BMI) > 24 kg/m², 74 vs. 51%, p=0.038]. In multivariate logistic analysis, vitamin D deficiency was the significant independent predictor of severe shock after SCA (OR 4.83, 95% CI 1.56–14.91, p=0.006) with left ventricular systolic dysfunction (OR 4.83, 95% CI 1.66–14.91, p=0.006) after adjusting for confounding variables such as first monitored rhythm, bystander CPR, baseline renal function, and BMI.

Conclusion: Vitamin D deficiency was strongly associated with severe shock in patients resuscitated from SCA.

P4441 | BEDSIDE
Deoxyribonucleic acid damage in humans successfully resuscitated from cardiac arrest
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Background: Cardiac arrest is a highly stressful event with a transient whole body ischaemia and common ischaemic-reperfusion injury in successfully resuscitated victims. The prognostic outcome of resuscitation remains limited.

Purpose: To investigate whether cardiac arrest may induce severe deoxyribonucleic acid (DNA) damage in successfully resuscitated humans and evaluate its prognostic value.

Methods: The prospective study (1/2013–1/2014). In successfully resuscitated patients from non-traumatic out-of-hospital cardiac arrest (n=41;64±14 years; men 73%, arrest of cardiac aetiology 76%; witnessed arrest 88%) the most severe DNA damage (double strand breaks) in lymphocytes sampled at admission were analysed using phosphorylation of histone H2AX (γH2AX). Data records: according to the Utstein protocol. The prognostic outcome: in-hospital mortality/discharged alive.

Results: 68% (28/41) of patients were discharged alive, 32% (13/41) died in a hospital (Fig). Regarding DNA: 83% (34/41) of patients had DNA damage, 17% (7/41) had intact DNA. Of patients discharged alive (n=28): DNA damage was in 86% (24/28). Of patients who died in hospital (n=13): DNA damage was in 100% (13/13). Of patients with DNA damage (n=34): 71% (24/34) were discharged. From patients with intact DNA (n=7): 57% (4/7) were discharged. Lenght of hospitalization was 13 (11;10) days. Among Utstein parameters the differences in DNA results was only for asystole (damage vs intact; 18% vs 57%; p=0.048).

DNA damage is not suitable for prediction of poor outcome (AUC 0.398/95% CI 0.195–0.569).

Figure 1
Conclusions: This study for the first time demonstrates the severe DNA damage in successfully resuscitated patients. Data showing better prognosis of patients with DNA damage contrast with the authors’ hypothesis.

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POST INFACTION PERIOD III

P4442 | BEDSIDE
Results of stem cell therapy in anterior STEMI patients with severe systolic dysfunction. Pilot study. Romanian experience

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Background: Stem cell therapy seems to be a promising adjuvant treatment for patients with ST-segment elevation myocardial infarction (STEMI) and low left ventricular ejection fraction (LVEF). It addresses a major health care problem, and cardiac progenitor cell therapy holds potential for treating myocardial ischemia. After STEMI, myocardial regeneration could be promoted through interactions between the injected stem cells and resident cells which stimulate endogenous repair mechanisms.

Methods: A group of 18 patients with anterior myocardial infarction with elevated ST segment (STEMI) and LVEF <40% were divided into 2 groups: the autologous bone marrow stem cell group (ABMSC) and the control group. After obtaining the informed consent the first group was treated at 7 to 10 days after myocardial infarction, when mononuclear cells with requisite coronary artery injection: all the patients were treated in accordance with up to date guidelines. Mononuclear cells were obtained by iliac crest puncture, separated by density gradient and administrated within 5 hours. Patients were followed for 12 months by the same pathomethods and imagic by echocardiography 2D, 3D and speckle tracking analysis.

Results: During 12 months no adverse effects were observed following administration of stem cell therapy. LVEF recovery at 1 year follow-up is concerned and with statistica significance in treated group: for 2D measurements, LVEF increasing 9%, p<0.00, vs. 6.72%, p<0.77 in control group; for 3D measurements, LVEF increasing 8.41%, p<0.02 in ABMSC group vs. 5.7%, p<0.28 in control group; the improvement in global longitudinal strain (GLS) was greater in stem cell treated patients than in the control group with absolute value 2.75 vs 1.2 (from 8.2 to 11.25 vs. 6.97 to 10.92). Tests applied failed in proving a significant difference between the two groups. After 12 months patients treated with stem cells had a increased ventricular end-diastolic volume and ejection fraction estimated both by biplane Simpson method 2D and 3D ultrasound. These data were supported by speckle tracking analysis at 12 month after STEMI. Coronary angiography showed permeability of the artery responsible for myocardial infarction in both cases.

Conclusions: At 12 months we observed improved ejection fraction in patients treated with stem cells, evaluation performed both by echocardiographic methods (2D, 3D) and speckle tracking analysis. Our results are similar with those from literature, but larger studies are required for more accurate data.

P4443 | BEDSIDE
Could pulmonary hemodynamic impact diffusion lung capacity in patients with STE TMEI elevation myocardial infarction?

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Some data suggest that lung dysfunction presents in early stages of myocardial damage but little data exist that explain pathological mechanisms behind this phenomenon.

Aim of the study: To estimate the pulmonary circulation effects on alveolar-capillary membrane conductance in patients with myocardial infarction.

Methods: Patients with ST-segment elevation myocardial infarction hospitalized within 24 hours from symptoms onset were included in the study. The study protocol was approved by the local IRB. Every patient voluntarily signed an informed consent before being included in the study. Transthoracic cardiac echo was done on 10th hospital stay day and diffusion capacity of lung for carbon monoxide (DLCO) was measured on 10th to 14th days. The statistical analysis was done with statistical software package SPSS for Windows, version 13.0. Quantity data are presented as mean and standard deviation for median and lower and upper quartiles. Relationships between 2 numerical variables were calculated with a linear regression analysis. All the p values described are 2-sided and a p<0.05 was considered statistically significant.

Results: 107 patients (mean age 56±9±3 yrs) were included in the study, of which 88 (82%) males. Univariate analysis showed that there were significant relationships between pulmonary resistance and DLCO. Patients with low DLCO (i.e., < -80%) had markedly higher mean pulmonary pressure (mean PP): 16.7 (14.0; 20.3) mm Hg versus 14.0 (10.7; 16.7) mm Hg in patients with DLCO above the normal range (i.e., >80%), p<0.002. Moreover, in the patients with DLCO <80%, pulmonary hypertension was seen more than 2 times frequent as compared to the patients with “normal” DLCO (27% and 12%, respectively, p=0.04).

We conducted a regression analysis which yielded the linear regression equation: DLCOcor, % = 109.5 - 1.8 x mean PP, mm Hg (F=21.0, R2=0.17, p<0.001). It can be suggested that DLCO might be inversely associated with pulmonary pressure and for each 1 mm Hg increase in mean pulmonary pressure alveolar-capillary membrane conductance decreased by 1.8%. The further analysis, in which myocardial structure and remodeling variables were included in the model, confirmed that pulmonary pressure has an impact on diffusion lung capacity with mean pulmonary pressure and left atrium (LA) volume being in the final model: DLCOcor, % = 121.9 - 0.5 x LA volume, ml - 1.2 x mean PP, mm Hg (F=18.6, R2=0.27, p<0.001).

Conclusions: It can be assumed that even a slight pulmonary pressure increase might be associated with a DLCO drop.

P4444 | BEDSIDE
Renal dysfunction strongly predicts adverse short and long term survival in patients undergoing reperfusion for STEMI


Background: Reperfusion therapy (RT) in ST elevation myocardial infarction (STEMI) reduces mortality and long-term complications. The benefit of RT in those renal insufficiency remains less well validated.

Methods: We tested the hypothesis that renal insufficiency (GFR <60 cc/min) would significantly impact survival following RT for STEMI in a large community registry study. Patients presenting within 2 hours of symptom onset at non PCI-capable hospitals received IV fibrinolytic therapy unless contraindicated, while those presenting beyond 2 hours had delayed primary PCI after transfer to the referral center. We report survival as a function of RT and renal function.

Results: 1871 patients with STEMI were evaluated; 1439 had normal renal function (GFR >60) while 432 had renal impairment. Patients with renal impairment were older, more likely to be female and slightly higher rates of diabetes those with normal renal function (p<0.01). There were no differences in location of the STEMI on the presenting ECG or in the timing of and mode of reperfusion (lysis vs PCI) between the groups. Patients with renal dysfunction had significantly higher in –hospital mortality (16% vs 4%, p<0.001) and rates of stroke (3% vs 1%, p<0.001) but no difference in rates of re-infarction (2%). Mortality at 1 month (18.6% vs 4.2%), 6 months (23.9% vs 6.2%), 12 months (28.2% vs 7.3%), 24 months (33.1% vs 9.1%), 60 months (55.1% vs 17.3%) and 84 months (60.9% vs 23.1%) was substantially higher in the renal dysfunction group (p<0.001).

Conclusions: Patients with STEMI who have underlying renal insufficiency have significantly worse short and long term survival despite prompt RT compared with those with normal renal function. Renal failure remains a challenging risk to mitigate in treatment of STEMI.

Acknowledgement/Funding: Mayo Clinic
patients (24%) received prehospital fibrinolysis and 7,756 patients (76%) were directly admitted to the cath-lab for pPCI. Main results are shown in table 1.

**Conclusion:** Increase of in-hospital mortality for unselected STEMI patients transported from scene to cath-lab is strongly correlated to time to pPCI beyond 120 min., out of recommended delay. A system delay <120 min remains a major goal to achieve for prehospital teams.

P4446 | **BEDSIDE**
Infarct size assessment after spontaneous, guide wire or angioplasty induced reperfusion in acute myocardial infarction
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**Background:** Reopening of the infarct related artery (IRA) occurring prior to percutaneous coronary intervention (PCI) is a major prognostic factor in acute ST segment elevation myocardial infarction (STEMI).

**Purpose:** To evaluate impact of reperfusion obtained spontaneously, after guide wire crossing or after PCI on the infarct size (IS) and clinical outcomes in patients admitted for STEMI.

**Methods:** Between October 2012 and August 2013, all patients admitted for STEMI were included and obtained successful reperfusion (TIMI 3 flow). Three groups were defined: spontaneous reopening of the IRA (group 1), reopening due to guide wire (group 2) and obtained only after PCI (group 3). Infarct size (IS) was evaluated by cardiac magnetic resonance (CMR) imaging using total scar score at 7 days and secondary endpoints evaluated 30 days ischemic clinical outcomes.

**Results:** We included 74 consecutive patients. Procedural characteristics and pain duration were not different in the 3 groups. Group 1 (n=24) exhibits a significantly smaller IS (p=0.001) in comparison with both groups 2 (n=28) and 3 (n=22). Groups 2 and 3 showed not different IS (p=0.34) (figure). Group 1 presented less microvascular obstruction (n=1, 4.17%; p=0.01) when compared to groups 2 and 3 (respectively 35.71%, n=1 vs 38.10%, n=8; p=0.20). Results after stratification on IRA remained unchanged. Group 1 had significantly less major cardiovascular adverse events, (n=0, 0%) compared to groups 2 (n=5, 27.8%) and 3 (n=4, 26.7%) (p=0.05) with no difference between these latter two groups (p=1).

**Conclusion:** While spontaneous reperfusion was associated with a better prognosis and a reduced IS, reopening of the occluded IRA by obtaining across the guide wire was not associated with IS reduction compared with PCI induced reperfusion.

P4447 | **SPOTLIGHT**
The Zwolle risk score as a guide to early discharge
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**Background:** Patients with ST elevation myocardial infarction (STEMI) are a heterogeneous group with varying length of hospital stay. The Zwolle percutaneous coronary intervention (PCI) score is an externally validated score and may help with early discharge of low risk PCI patients.

**Purpose:** The aim of this study was to use the Zwolle score to identify patients who potentially could be suitable for early discharge.

**Methods:** We retrospectively analysed all STEMI patients presenting to our University Hospitals over a 1 year period (January 2013 to December 2013). All patients were scored according to the Zwolle and length of stay calculated.

**Results:** 309 patients (age 63±8 years, 39% female, left ventricular ejection fraction (LVEF) 36±5%) with chronic ischemic cardiomyopathy underwent strain echocardiography and CMR within 3±1 days. LVEF and global circumferential strain (CS) were powerful predictors of mortality. However, application is limited by general availability of strain echo. The concentration of MPO in the improvement of left ventricular function after ST-segment elevation myocardial infarction
K. Kupcynska1, A.M. Fawzy, S. George, P. Calvert, P.F. Ludman, S.N. Doshi, J.N. Townend, Arnaud de Villeneuve, Department of epidemiology and medical statistics, Montpellier, France

**Background:** Myeloperoxidase and monocyte chemoattractant protein-1 (MPO-MCP-1) are the predictors of LV function improvement in patients with chronic ischemic left ventricular dysfunction.

**Methods:** We retrospectively analysed all STEMI patients presenting to our University Hospitals over a 1 year period (January 2013 to December 2013). All patients were scored according to the Zwolle and length of stay calculated.

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**Conclusion:** The Zwolle risk score enables identification and facilitation of early discharge. In those with a score of <3, there were no mortalities. If used routinely the use of the Zwolle score is safe and could have significant cost savings in terms of beds saved days.

P4448 | **BEDSIDE**
The role of myeloperoxidase and monocyte chemoattractant protein-1 in the improvement of left ventricular function after ST-segment elevation myocardial infarction
K. Kupcynska1, A.M. Fawzy, S. George, P. Calvert, P.F. Ludman, S.N. Doshi, J.N. Townend, Arnaud de Villeneuve, Department of epidemiology and medical statistics, Montpellier, France

**Background:** Myeloperoxidase and monocyte chemoattractant protein-1 (MPO-MCP-1) are the predictors of LV function improvement in patients with chronic ischemic left ventricular dysfunction.

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**Purpose:** To evaluate the impact of reperfusion obtained spontaneously, after guide wire crossing or after PCI on the infarct size (IS) and clinical outcomes in patients admitted for STEMI.

**Methods:** Between October 2012 and August 2013, all patients admitted for STEMI were included and obtained successful reperfusion (TIMI 3 flow). Three groups were defined: spontaneous reopening of the IRA (group 1), reopening due to guide wire (group 2) and obtained only after PCI (group 3). Infarct size (IS) was evaluated by cardiac magnetic resonance (CMR) imaging using total scar score at 7 days and secondary endpoints evaluated 30 days ischemic clinical outcomes.

**Results:** We included 74 consecutive patients. Procedural characteristics and pain duration were not different in the 3 groups. Group 1 (n=24) exhibits a significantly smaller IS (p=0.001) in comparison with both groups 2 (n=28) and 3 (n=22). Groups 2 and 3 showed not different IS (p=0.34) (figure). Group 1 presented less microvascular obstruction (n=1, 4.17%; p=0.01) when compared to groups 2 and 3 (respectively 35.71%, n=1 vs 38.10%, n=8; p=0.20). Results after stratification on IRA remained unchanged. Group 1 had significantly less major cardiovascular adverse events, (n=0, 0%) compared to groups 2 (n=5, 27.8%) and 3 (n=4, 26.7%) (p=0.05) with no difference between these latter two groups (p=1).

**Conclusion:** While spontaneous reperfusion was associated with a better prognosis and a reduced IS, reopening of the occluded IRA by obtaining across the guide wire was not associated with IS reduction compared with PCI induced reperfusion.

P4449 | **BEDSIDE**
Prediction of mortality by strain echocardiography compared to CMR
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**Background:** Cardiac magnetic resonance (CMR) has been established as a powerful predictor of mortality. However, application is limited by general availability and various contraindications. This study evaluated the predictive value of layer specific myocardial deformation analysis for mortality in patients with chronic ischemic left ventricular dysfunction.

**Methods:** We retrospectively analysed all STEMI patients presenting to our University Hospitals over a 1 year period (January 2013 to December 2013). All patients were scored according to the Zwolle and length of stay calculated.

**Results:** 309 patients (age 63±8 years, 39% female, left ventricular ejection fraction (LVEF) 36±5%) with chronic ischemic cardiomyopathy underwent strain echocardiography and CMR within 3±1 days. LVEF and global circumferential strain (CS) were powerful predictors of mortality. However, application is limited by general availability of strain echo. The concentration of MPO in the improvement of left ventricular function after ST-segment elevation myocardial infarction
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**Conclusion:** The Zwolle risk score enables identification and facilitation of early discharge. In those with a score of <3, there were no mortalities. If used routinely the use of the Zwolle score is safe and could have significant cost savings in terms of beds saved days.
Impact of proportion of rapid eye movement sleep on all-cause mortality: A 10-year follow-up study of acute coronary syndrome

Background: The risk of all-cause mortality and stroke decreased as the proportion of REM sleep increased.

Methods: From October 2003 to September 2004 a sample of 6 hospitals was selected and almost all consecutive 2,172 ACS patients were enrolled. In 2013–14, the 10-year follow-up (2004–2014) was performed in 1,918 participants (88% participation rate). Age, sex, Body Mass Index (BMI), current smoking, MedDietScore categories (>27 vs. ≤27), physical activity, history of CVD, hypertension, hypercholesterolemia and diabetes mellitus were evaluated in relation to the development of 10-year CVD incidence, in each sex subgroup, based on hierarchical classification analysis using Fisher linear discriminant function.

Results: The 10-year incidence was 40% in males and 32% in females (p = 0.001). The classification of CVD risk factors was not the same in the two gender groups while only some of them led to a significant association concerning the ACS prognosis. Thus, in males the predominant risk predictors were diabetes (Wiks L < 0.997, p < 0.079) and current smoking (Wiks L < 0.997, p < 0.083); while history of CVD, hypercholesterolemia, BMI, MedDietScore and physical activity were in the second highest rank. Respectively, in females, physical inactivity (Wiks L < 0.952, p < 0.071), low adherence to the Mediterranean diet (<27) (Wiks L < 0.993, p < 0.086) and current smoking (Wiks L < 0.993, p < 0.108) were the most commonly observed characteristics. Age specific analysis confirmed that the aforementioned ranking was irrespective of participants’ age.

Conclusion: This present analysis revealed the gender differences in the prevalence of the major CVD risk factors and the 10-year ACS prognosis. Women’s lifestyle habit modifications, like unhealthy diet, physical inactivity and increased smoking prevalence, contribute to the development of cardiovascular disease and impose a substantial clinical and public health burden which should not be underestimated or ignored.

Acknowledgement/Funding: None to declare

Impact of rapid eye movement sleep on all-cause mortality and stroke in patients with acute myocardial infarction

Aims: We hypothesized that proportion of rapid eye movement (REM) sleep may have significant clinical outcomes.

Methods: This study included 392 patients undergoing primary percutaneous coronary intervention. All patients underwent polysomnography on first admission and were divided into two groups based on the third tertile of the proportion of REM sleep (19.0% – 35.6%). Main outcomes measured were all-cause mortality, recurrent acute coronary syndrome (ACS), and stroke.

Results: The median follow-up duration was 4.0 years. Patients with a higher proportion of REM sleep (n=132) showed lower all-cause mortality (6.8% vs 10.4%) and a significantly lower incidence of stroke (1.2% vs 6.2%, p=0.028) as compared with patients with a median and lower proportion of REM sleep (n=260). ACS equally occurred between the two groups (10.6% vs 10.4%). Kaplan-Meier curve demonstrated that stroke-free survival estimates in patients with a higher proportion of REM sleep was significantly better than those of a median and lower proportion of REM sleep. A stepwise forward Cox regression analysis adjusted for relevant variables, apnea-hypopnea index > 15 events/h, higher age > 75 years, hyper- tension, diabetes, dyslipidemia, current smoking, anterior infarct, and peak creatine kinase levels indicated that the proportion of REM sleep was negatively correlated with all-cause mortality and stroke (hazard ratios: 0.945, 95% confidence interval (CI) 0.894–0.999, p=0.045, hazard ratio: 0.920, 95% CI 0.853–0.992, p=0.042, respectively).

Conclusion: The risk of all-cause mortality and stroke decreased as the proportion of REM sleep increased.
rapid rule-out of acute myocardial infarction (AMI), several novel strategies have been developed. Due to the lack of direct comparisons in the same dataset, selection of the best strategy for clinical practice is challenging. We therefore aimed to directly compare the safety and efficacy of two previously defined strategies: LOD (Undetectable levels of high-sensitivity cardiac troponin (hs-cTnT) T at presentation) in combination with hs-cTnT 1h-algorithm versus hs-cTnT 2h-algorithm.

Methods: In a prospective international multicentre diagnostic study enrolling 1697 patients presenting with suspected AMI to the emergency department, the final diagnosis of AMI was adjudicated by two independent cardiologists using all available clinical information including serial hs-cTnT concentrations. Safety was quantified as the negative predictive value (NPV) for AMI in the rule-out zone of the respective rule-out strategies. Efficacy was quantified as the percentage of the overall cohort assigned to the rule-out zone by the respective strategy. The 2h-algorithm was defined as 0h- and 2h values <12ng/l and A0–2h<4ng/l. The combination LOD and 1h algorithm was defined as LOD <3ng/L or 0h<12ng/l and A0–1h<3ng/l. As both strategies should only be applied once ST-elevation MI (STEMI) has been excluded by the initial ECG, STEMI patients were excluded from the analysis.

Results: Acute myocardial infarction was the final diagnosis in 16% of patients. The safety was very high and comparable with both algorithms (2h algorithm: NPV 100%, 95% CI 99.7–100% versus LOD+1h Algorithm: NPV 99.9%, 95% CI 99.5–100%, p=ns). The efficacy 2h-algorithm allowed rule-out in 64% of patients versus 60% with 1h-algorithm +LOD (p=0.018).

Conclusion: Both investigated rule-out strategies allow a safe rule-out of AMI. The 2h-algorithm has a slightly higher efficacy; however the combination of LOD+1h-algorithm has the obvious advantage of allowing rule-out already after 1h.

P4456 | BEDSIDE
Can we utilize pharmaco invasive strategy in patients with chest pain needle time over 3 hours?

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Background: The STREAM study utilized 3 hours as the maximum time to implement Pharmaco Invasive Strategy (PIS). It is not clear if this period of time there is scarce real world information about PIS in the literature.

Methods: We analyzed 1147 consecutive STEMI patients who were treated by PIS between January 2010 and December 2014, network of 12 ER, 22 advanced ambulance and one PCI hospital organized as a Registry (NCT 02090712). We have included patients until 12 hours of symptoms as per guidelines. Sixty one patients were excluded because there was no complete record of pain onset or time to tenecteplase (TNK) dosage. Rescue coronary angiography was performed if fibrinolysis failed. Patients were divided as follows: Group 1 (427) had chest pain-needle time (CPNT) until 3 hours from the initial symptoms; Group 2 (442) had CPNT between 3 and 6 hours; Group 3 (278) had CPNT greater than 6 hours. All events from first medical contact until hospital discharge were analysed. The primary end point was intra hospital death and co-primary a composite of intra hospital death, shock, congestive heart failure and reintantion. Group 1 was considered gold standard to time of treatment and all groups were compared to it.

Results: Ages varied between 18 and 93 years. Age was significantly lower in group 2 than group 1 (p=0.003) and 3 (p=0.003). Men were more frequent in group 1 than the other groups (77% in group 1 vs 65,4 in group 2, p<0.001; 66,4% in group 3, p=0,003). Diabetes mellitus was more prevalent in group 3 than in group 1 (38,2% vs 26,9%, p<0,002). Other demographics and risk factors were non significantly different among the 3 groups. In relation to hospital follow up, group 1 and 2 have the same event rate. Cardiogenic shock was more frequent in group 3 than group 1 (14,2% vs 8,7%, p=0,02). We observed major bleeding (BARC) in 2,3% in group 1, 3,8% in group 2 and 4,6% in group 3 without significance. We observed combined events in 27,9% in group 1, 29% in group 2 (p=0,7) and 30,6% in group 3 (p=0,48). And death for all causes was 4,2% in group 1, 4,5% in group 2 (p=0,87) and 11,5% (p=0,001).

Conclusions: PIS mortality increased significantly for those treated with CPNT between 3 and 6 hours; however the results of those treated from >6 hours were not different from those treated with CPNT less than 3 hours, for mortality and the combined co-primary events, suggesting that PIS could be safely employed until 6 hours.

P4456 | BEDSIDE
Troponin T elevation in acute aortic syndromes: frequency and impact on diagnostic delay and misdiagnosis

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Background: Despite troponin assay being a part of the diagnostic work up in many conditions with acute chest pain, little is known about its clinical implications in Acute Aortic Syndromes (AAS).

Purpose: To evaluate frequency, impact on diagnostic delay, inappropriate treatments, and prognosis of troponin elevation in AAS.

Methods: Data were collected from a prospective metropolitan AAS registry (398 patients diagnosed between 2000 and 2013). Cardiac troponin test, using either standard or high sensitivity (HS) assay, was performed according to standard protocol used in chest pain units. The following time intervals were recorded: 1) symptoms onset to presentation; 2) hospital presentation to final AAS diagnosis; 3) symptoms onset to final AAS diagnosis.

Results: Troponin T values were available in 248 patients (80%) of the registry population; the overall frequency of troponin positivity was 28% (range from 16% to 54%, using standard or HS assay respectively, p=0.001). Troponin positivity was frequently associated with Acute Coronary Syndromes (ACS)-like ECG findings, and with a twofold increased risk of long in-hospital diagnostic time (OR 1.92, 95% CI 1.05–3.59, p=0.03). The combination of positive troponin and ACS-like ECG abnormalities resulted in a significantly increased risk of in-hospital de-lay/coronary angiography/antithrombotic therapy due to a misdiagnosis of ACS (figure). However, troponin positivity was not associated with in-hospital mortality (OR 1.63, 95% CI 0.86–3.10, p=0.131).

Conclusions: Troponin positivity was a frequent finding in AAS patients, particularly when a HS assay was employed. Abnormal troponin values were strongly associated with ACS-like ECG findings and with in-hospital diagnostic delay but they did not influence in-hospital mortality.

P4457 | BEDSIDE
Combined cardiac and lung ultrasound protocol for differential diagnosis of acute dyspnea in the emergency department

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Objectives: To combine Echo and LUS into a “thoracic FAST exam”, a rapid ultrasound protocol to be used to examine acutely dyspneic patients immediately after arrival in the emergency department (ED). To use the protocol for diagnosing left sided AHF, and to examine it’s yield in differential diagnosis of acutely dyspneic patients.

Methods: We included 99 cognitively intact adult patients presenting with dyspnea at rest in our ED. Patients with mitral stenosis and pulmonary fibrosis were excluded. LUS of 2–3 pulmonary fields and pleuras bilaterally, medial E’e and visual estimation of the right side of the heart was performed. Other alarming findings were reported if seen. The patients were classified as having AHF if having E’/e’ < 15 and either bilateral B-lines (BBL) or rightsided/bilateral pleural fluid (PF) on LUS.

Results: According to the protocol, 53 (53,5%) of the 99 patients had AHF, and 46 (46,5%) had an alternative diagnosis. The mean E’/e’ was 21,14 (sd 4,30) for AHF patients, and 9,75 (sd 2,96) for the control group (p<0,001). In the AHF group 51
patients (96.2%) had BBL, and 37 (69.8%) PF, compared with 7 (15.2%) and 2 (4.3%) in the non-AHF group (p = 0.001 for both). In the non-AHF group, the thoracic FAST protocol was indicative of an alternative diagnosis in 21/46 (45.7%) and normal in 18 (38.1%) of the patients. The clinicians used Thorax X-ray, BNP, and other standard methods to establish their clinical diagnosis as usual, and they would also have access to the Echo and LUS exams if they wished to.

Conclusion: A focused ultrasound protocol combining LUS and Echo might be a fast and helpful tool in diagnosing AHF; also providing aid with differential diagnosis of life threatening cardiopulmonary conditions among dyspneic patients in the ED.

P4458 | BEDSIDE
Risk stratification in patients with acute chest pain with normal high-sensitivity cardiac troponin levels and need for downstream testing

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Background: High sensitivity cardiac Troponin (hs-cTn) profoundly increases the ability to rule out myocardial infarction (MI). However, major adverse cardiac events (MACE) follow-up and the usefulness of risk stratification in patients with hs-cTn levels below the 99th percentile is unknown.

Purpose: To evaluate MACE during follow-up and whether clinical characteristics can contribute to risk stratification.

Methods: All patients with acute chest pain and normal hs-cTnT levels (<14 ng/L) were prospectively included during one year. Number of MACE (cardiac death, MI, revascularization and heart failure) was assessed during 1-year follow-up. A risk stratification algorithm was developed based on clinical characteristics predicting MACE. Additionally, downstream tests were evaluated.

Results: 924 patients were included. No patient suffered from MI during index presentation and <1% experienced cardiac death or MI during follow-up. MACE mainly comprised of revascularizations (86%) and occurred in 6% of patients. Presentation with typical angina, more risk factors and higher hs-cTnT levels on admission were independent predictors of MACE with odds ratios of 30.61 (95% CI: 11.4–82.1), 1.30 (1.0–1.7) and 1.08 (1.0–1.2), respectively. A diagnostic algorithm (Figure) based on the initial hs-cTnT level and patient history classified 88% of patients as very low risk for cardiac death and MI or MACE (0.5% and 2.3%). However a high rate of additional testing (84% of all tests) was observed in this very low risk group.

Conclusions: Patients with acute chest pain and normal hs-cTnT levels have a very low risk of MI and mortality. The majority (88%) of these patients can be identified as very low risk based on clinical characteristics. Downstream testing in very low risk patients does not seem meaningful.

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P4459 | BEDSIDE
Direct comparison of the safety and efficacy of two rule-out strategies for acute myocardial infarction: combination of copeptin and hs-cTn versus undetectable limits of hs-cTn and 1h-algorithm


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

Methods: In a prospective international multicentre diagnostic study enrolling 15030 patients presenting with suspected AMI to the emergency department, the final diagnosis of AMI was adjudicated by two independent cardiologists using all available clinical information including serial hs-cTn concentrations. Safety was quantified as the negative predictive value for AMI in the rule-out zone of the respective rule-out strategies. Efficacy was quantified as the percentage of the overall cohort assigned to the rule-out zone by the respective strategy. Both strategies were applied using the two best-validated hs-cTn assays (hs-cTn Roche: LOD <5ng/L; 1h-algorithm 0h–1h<2ng/l and 0–1h–<3ng/l; and hs-cTn Abbott: LOD <2ng/L; 1h-algorithm 0h–5ng/L and 0–1h–<2ng/l) to ensure that findings are independent from the hs-cTn assay used. As both strategies should only be applied once ST-elevation MI (STEMI) has been excluded by the initial ECG, STEMI patients were excluded from the analysis.

Results: Acute myocardial infarction was the final diagnosis in 18.7% of patients. Universal hs-cTn, the safety and high-sensitivity and recurrent myocardial infarctions (dual marker strategy: NPV 98.7%, 95% CI 97.6–99.4% versus below LOD and 1h-algorithm: NPV 99.8%, 95% CI 99.2–100%, p = 0.02). Regarding efficacy, dual marker strategy allowed rule-out in 47.2% of patients versus 57.4% with the LOD and 1h-algorithm (p = 0.002). Using hs-cTnT, the safety was very high and comparable with both algorithms (dual marker strategy: NPV 96.0%, 95% CI 94.3–97.2% versus LOD and 1h-algorithm: NPV 99.2% (95% CI 98.2–99.7, p = 0.001). Regarding efficacy, combination of copeptin and hs-cTnT allowed the rule-out in 54.3% of patients versus 51.2% with LOD and the 1h-algorithm (p = 0.4).

Conclusion: The combination of LOD and the 1h-algorithm allows a better rule-out of AMI than the dual marker strategy, irrespective of the underlying hs-cTn assay. Both strategies show a comparable effectiveness with ruling-out around half of the population.

P4460 | BEDSIDE
Differential diagnosis at admission between Takotsubo cardiomyopathy and acute apical-anterior myocardial infarction in postmenopausal women

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Background: Takotsubo cardiomyopathy (TTC) typically affects postmenopausal women and clinically presents with chest pain, ST-segment elevation, elevated cardiac enzymes and apical left ventricular (LV) wall motion abnormalities that mimic “apical-anterior” acute myocardial infarction (AMI). This study assessed whether at-admission clinical evaluation helps in differential diagnosis between the two conditions.

Methods: The study compared at-admission clinical, ECG and echocardiographic findings of 31 women (median age 67 years, IQR 62–76) with typical TTC and 30 women (median age 73 years, IQR 61–81) with apical-anterior AMI due to acute occlusion of the midventricular anterior descending coronary artery.

Results: Women with TTC significantly more often showed PR-segment depression (62% versus 3%, p = 0.001). J-waves (26% versus 3%, p = 0.03), maximum ST-segment elevation ≥2mm (84% versus 37%, p < 0.001) and ST-segment elevation in lead II (42% versus 10%, p < 0.01) than those with AMI. At multivariate analysis, PR-segment depression (OR=37.2, 95% CI: 3.4–424, p=0.002) and maximum ST-segment elevation ≥2mm (OR=11.1, 95% CI: 1.7–98.4, p=0.01) remained the only independent predictors of TTC and the coexistence of both parameters excluded AMI with 100% specificity. The two cohorts did not differ with regard to age, first troponin-I value, echocardiographic LV ejection fraction and distribution of hypo/akinetid LV segments.

Conclusions: At-admission ECG (but no clinical, laboratory and echocardiographic features) allows differential diagnosis between TTC and apical-anterior AMI in postmenopausal women. The combination of PR-segment depression and maximum ST-segment elevation predicted TTC with greater accuracy than traditional ECG parameters such as localization of ST-segment elevation and reciprocal ST-segment depression.
and was similar for men and women. Use of this threshold identified 2,296 patients (47%) at low risk of acute coronary events.

Conclusions: Cardiac troponin concentrations less than 5 ng/L on presentation correctly ruled out fatal and non-fatal cardiac events at 30 days in more than 99% of patients with suspected acute coronary syndrome. Implementation of this approach could allow almost half of all patients with suspected acute coronary syndrome to be safely discharged and would have major benefits in reducing unnecessary hospital admissions.

Purpose: To identify if chest pain patients presenting in a chest pain unit can be safely discharged after establishing a low-risk profile with two high-sensitivity troponin assays, to identify chest pain patients at risk. This approach may be applied to improve decision guidance at the emergency department (ED), in combination with established risk scores.

P4463 | BEDSIDE
Myocardial deformation by strain echocardiography identify patients with acute coronary syndrome and non-diagnostic ecg presenting in a chest pain unit
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Objective: Clinical assessment often cannot risk stratify patients hospitalized with chest pain and non-diagnostic ECG or myocardial enzymes. An appropriate admission of patients with non-cardiac chest pain is an enormous cost factor.

Methods: 2315 patients who presented in the chest pain unit (CPU) with symptoms suggestive of acute coronary syndrome (ACS) were screened. All patients with relevant changes in electrocardiography (ECG) or myocardial enzymes were excluded. 264 consecutive patients (mean 58±7 years, 88 men) were prospectively included and underwent myocardial deformation imaging by echocardiography and a coronary angiography (CA) within 2±1 days after admission.

Results: Anatomically obstructive coronary artery disease (CAD) (<70% diameter stenosis) was present in 110 patients (42%). Longitudinal, circumferential and radial strain and strain rate data were evaluated and differed between patients with and without CAD. Global systolic circumferential (GCS) and longitudinal strain (GLS) showed greatest area under the curves (AUC) with 0.835 (95% CI 0.735 to 0.918) and 0.823 (95% CI 0.739 to 0.906). Optimal cut-off values were calculated as -22.7% for GCS (sensitivity 87%, specificity 76%, accuracy 76%) and as -18.8% for GLS (sensitivity 86%, specificity 73%, accuracy 79%) to differentiate between these patients.

Conclusions: In patients with suspected ACS but without ECG changes or myocardial enzymes abnormalities myocardial deformation imaging can identify patients at risk. This approach may be applied to improve decision guidance at the CPU for fast discharge of patients with non-cardiac chest pain or prompt cardiac allocation of patients with CAD.

P4464 | BEDSIDE
Hybrid coronary revascularization in 100 patients with multivessel disease: what can we expect?
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Introduction: Hybrid coronary revascularization (HCR) arises as a combined approach of surgical and percutaneous coronary intervention (PCI). This strategy joins the best of two traditionally isolated treatment options in multivessel coronary artery disease (CAD).

Purpose: We aim to assess the safety and clinical outcomes of patients submitted to HCR.

Methods: From May 2008 to December 2014 one-hundred consecutive patients underwent two-staged coronary revascularization (PCI after coronary artery bypass grafting), in our hospital, after Heart Team evaluation. Death, myocardial infarction and repeated target vessel revascularization (MACE) were analyzed in index hospitalization and at follow-up.

Results: Mean age was 67±10 years and 66% of patients were male. HCR was performed after an acute coronary syndrome in 47% of the population and two-thirds of the patients had preserved left ventricular ejection fraction. In all cases an arterial graft to the left main was performed. Forty-nine percent of patients also underwent other arterial or veins grafts. CABG was carried out off-pump in 76% of patients. PCI occurred 5±3 days after surgery, with 100% of angiographic success and using drug-eluting stents (67%), bare-metal stents (32%) or both (1%). No intra-operative or in-hospital deaths were reported. At a mean follow-up of 22±14 months, eighty-three patients were evaluated and overall population freedom from MACE was 97%: one case died from pneumonia and two had non-STEMI, treated with conservative approach. No cardiac death occurred.

Conclusion: Hybrid coronary revascularization may be considered a viable option in patients with multivessel CAD. In our experience HCR has a good outcome at short and mid-term follow-up. In spite of the lack of large randomized controlled trials with long term follow-up, it seems reasonable to consider that this strategy can have an important role in CAD treatment.

P4465 | BEDSIDE
The impact of risk factors on predicting significant stenosis in the presence and absence of coronary calcification: results from the Euro-CCAD study
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Background: There are numerous chest pain risk scores available, however a suitable approach may be applied to improve decision guidance at the ED. There is important variation in the performance of risk scores and hs-cTn assays which has implications in the clinical use of rapid rule-out protocols.

Purpose: To develop a chest pain risk score that combines established risk factors with high-sensitivity cardiac troponin (hs-cTnT) analysis.

Methods: Prospective observational study conducted in our District General Hospital. Consecutive adults with suspected ACS and non-ischemic ECG whom at attending physicians determined inpatient evaluation was required were recruited. Index tests were pre-determined definitions of low risk applied to modified Gold- man (m-Goldman), Thrombolysis In Myocardial Infarction (TIMI), Global Registry of Acute Cardiac Events (GRACE) and History, ECG, Age, Risk Factors and Troponin (HEART) scores and the Vancouver Chest Pain Rule incorporating a single presentation hs-cTnT result. To be clinically useful a rule-out protocol had to achieve a negative predictive value (NPV) >99.5% and identify >30% of patients as low risk. The endpoint was index fatal or non-fatal acute myocardial infarction (AMI) adjudicated using hs-cTnT.

Results: 959 patients underwent hs-cTnT and 867 hs-cTn analysis. In the hs-cTnT group, 79/959 (8.2%) had an AMI and 66/867 (7.5%) in the hs-cTn group (P=0.622). Hs-cTnT in combination with four risk scores achieved an NPV of >99.5% for the diagnosis of AMI: m-Goldman; 1; 99.7% (95% CI 98.4–100), TIMI 0; 100% (98.9–100), TIMI 1; 100% (93.5–100) and Vancouver; 100% (97.1–100). Only m-Goldman ≤1 and TIMI 0 achieved this whilst identifying <30% of patients as low-risk, with m-Goldman identifying a significantly higher proportion (39.8% vs. 32.1%; p=0.0004). Hs-cTnT in combination with only one risk score achieved an NPV of >99.5%; Vancouver; 100% (96.7–100), this strategy identified only 15.4% as low-risk.

Conclusion: It may be possible to identify over 30% of low-risk patients with an NPV of >99.5% for the diagnosis of AMI using an hs-cTnT result taken at presentation to the ED, in combination with established risk scores. There is important variation in the performance of risk scores and hs-cTnT assays which has implications in the clinical use of rapid rule-out protocols.

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P4466 | BEDSIDE
Myocardial deformation by strain echocardiography identify patients with acute coronary syndrome and non-diagnostic ecg presenting in a chest pain unit
E. Carlton1, K. Greaves2, 1North Bristol NHS Trust, Emergency, Bristol, United Kingdom; 2University of the Sunshine Coast, University of Queensland, Cardiology, Sunshine Coast, Australia.

Background: The aim of this study was to assess the individual impact of the con- tinual strain (GLS) showed greatest area under the curves (AUC) with 0.835 (95% CI 0.735 to 0.918) and 0.823 (95% CI 0.739 to 0.906). Optimal cut-off values were calculated as -22.7% for GCS (sensitivity 87%, specificity 76%, accuracy 76%) and as -18.8% for GLS (sensitivity 86%, specificity 73%, accuracy 79%) to differentiate between these patients.

Conclusions: In patients with suspected ACS but without ECG changes or myocardial enzymes abnormalities myocardial deformation imaging can identify patients at risk. This approach may be applied to improve decision guidance at the CPU for fast discharge of patients with non-cardiac chest pain or prompt cardiac allocation of patients with CAD.

P4467 | BEDSIDE
The impact of risk factors on predicting significant stenosis in the presence and absence of coronary calcification: results from the Euro-CCAD study
E. Carlton1, K. Greaves2, 1North Bristol NHS Trust, Emergency, Bristol, United Kingdom; 2University of the Sunshine Coast, University of Queensland, Cardiology, Sunshine Coast, Australia.

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The c statistic of the MACE prediction model changed from 0.583 to 0.481%, \( p < 0.001 \) after the addition of CHA2DS2-VASc as a continuous variable (35%, CI: 21.9–48.1%, \( p < 0.001 \)).

**Conclusion:** In symptomatic patients with CAD, most risk factors were predictive of significant stenosis, the most important being obesity, although hypertension and dyslipidemia were not predictive. In patients with zero CAD, obesity was the sole independent predictor of stenosis. These results highlight the need for stringent management of metabolic syndrome.

### P4467 | BEDSIDE

**Prognostic impact of contrast volume on the basis of renal function and CHA2DS2-VASc score in patients with coronary artery disease**

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**Purpose:** To investigate the association among clinical outcomes, CHA2DS2-VASc score, and contrast volume on the basis of renal function in patients undergoing percutaneous coronary intervention (PCI) with coronary artery disease (CAD).

**Methods:** A cohort of 2489 patients (69.8±10.8 years old, 77% male) who underwent PCI for CAD was analyzed from CAS (Cardiovascular Assessment Study) multi-center registry. We divided patients into 3 groups according to tertile of contrast volume/e-GFR ratio (CV/GFR): Low (≤2.21: n=829), Mid (2.22–3.30: n=830), and High (3.31–≤: n=830). And we also divide into 3 subgroups on the basis of CHA2DS2-VASc score (Low: 0–1, Mid: 2–3, High: 4–8 point). Clinical outcomes were defined as major adverse cardiovascular event (MACE) which included all cause death, myocardial infarction, stroke, or hospitalization for worsening heart failure.

**Results:** Mean follow up period was 455 days. There was a stepwise increase in MACE with increasing CHA2DS2-VASc score and CV/GFR (figure). CHA2DS2-VASc score and CV/GFR were the independent predictor of MACE after adjustment of multiple confounders (CHA2DS2-VASc: per increase, OR: 1.39, 95% CI: 1.28–1.51, \( p < 0.001 \); CV/GFR: per increase, OR: 1.02, 95% CI: 1.007–1.04, \( p = 0.036 \)). The c statistic of the MACE prediction model changed from 0.583 to 0.654 (\( p = 0.001 \)), and the net reclassification improvement increased significantly after the addition of CHA2DS2-VASc as a continuous variable (35%, CI: 21.9–48.1%, \( p = 0.001 \)).

**Conclusions:** The combination of CHA2DS2-VASc score and CV/GFR predicts clinical outcomes in patients with CAD in this registry.

### P4468 | BEDSIDE

**Predictors of longterm outcomes in spontaneous coronary artery dissection**

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**Introduction:** Spontaneous coronary artery dissection (SCAD) is an unusual cause of acute coronary syndrome. Although the prognosis is good the management is not well established.

**Purpose:** Describe the clinical presentation, management and long term outcomes of a retrospective cohort with SCAD.

**Methods:** A total of 37 patients registered in our institution from 2000 to 2014 were retrospectively studied. The definition of SCAD was based on the presence of medial dissection or intramural hematoma that was recognized by angiography and according with the classification proposed by Saw.

**Results:** 21 patients were diagnosed by SCAD in a 15 year period. SCAD developed after physical or emotional stress in 4 patients (10%) and 7 patients (20%) had hypothyroidism. The left anterior descending artery was involved in 22 patients (60%) and left main was involved in 1 patient. 5 patients had multi-vessel SCAD (13.5%). Recurrences of SCAD were shown in 2 patients (5%). According to the classification proposed by Saw 21 patients (57%) had type 1 dissection (evident arterial wall stain), 11 patients (30%) had type 2 (diffuse stenosis of varying severity) and 5 of them (13%) had type 3 (mimic atherosclerosis) dissection. Coronary artery tortuosity was present in 17 patients (46%) and it is significantly related with MACE (p<0.001) and complications during PCI (p<0.001). The management of SCAD was revascularization of the culprit lesion in 67.5% of patients (23 - PCI, 1- ACTP, 1- CABG) with in-hospital death of 8% (3 patients: 2 cases which the dissection progressed retrogradely during PCI and involved the left main and complicated by cardiogenic shock and 1 case involving also the aortic root), 21.6% of cases were initially treated with fibrinolysis which was also significantly related with MACE (p<0.001). PCI was successful in 95.5% of cases. 2 or more stents were needed in 50% of cases and the medium stent length was 46.7±32.4 mm [SD]. During a median follow-up of 1023 days angiography and 85% of them didn’t have any images of dissection.

**Conclusions:** The registry showed that after spontaneous dissection the prognosis in the longterm follow up is acceptable and most of the MACE occur during the acute phase. PCI of these types of lesions are generally successful but usually involve a long stent length. Tortuosity in coronary arteries, previous thrombolysis and the retrograde progression of dissection during PCI involving the left main are related to bad prognosis.
Background: HIV has been associated with accelerated vascular disease including a higher incidence of coronary artery disease and myocardial infarction, partly due to a higher burden of traditional risk factors and metabolic complications of anti-retroviral treatment. It is not well established whether HIV vasculopathy, in a contemporary group of treated patients is a diffuse multi-vessel process or secondary to vulnerable high-risk plaque.

Purpose: We sought to quantify the burden of coronary artery disease in a group of well treated patients with HIV using quantitative data from coronary angiograms in patients presenting for investigation of suspected coronary ischemia.

Methods: Demographic and angiogram data from 160 males who presented acutely with STEMI/NSTEMI or unstable angina (73 patients with HIV and 87 age and clinical presentation matched, HIV negative controls) were obtained from our hospital (a major public teaching hospital). The sample was pooled and coronary vessel pathology was calculated using the Gensini Angiographic Scoring System by an experienced cardiologist blinded to HIV status. The statistical software package SPSS v22 was used to analyze the data to assess the relationship between HIV status, traditional risk factors and coronary vessel pathology.

Results: The two groups were matched for age and there was no difference in cholesterol profiles, rates of smoking or hypertension. Statin use was higher in patients with HIV (59% vs 33% p < 0.001). There was a significant difference (p < 0.05) in the mean Gensini score, between the HIV positive group (22.72) compared to HIV negative group (36.55) of 10.83 (95% CI 0.83, 20.82). The mean number of vessels affected was lower in the HIV positive group (1.97) compared to the control (2.26), with a mean difference of 0.29 however, this was not significant (p = 0.19).

Conclusions: Previous studies have shown a higher burden of coronary artery disease in people living with HIV. Our single centre study has perhaps surprisingly demonstrated a lower burden of coronary disease in a group of well treated, virally suppressed, HIV positive patients with HIV and similar traditional risk factors. These findings may represent more aggressive risk factor management in our cohort, including statin use, lowering the burden of coronary vascular disease.

P4470 | BEDSIDE Novel association factor in spontaneous coronary artery dissection and recurrences

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Introduction and purpose: Spontaneous coronary artery dissection (SCAD) is a rare but challenging clinical entity of unknown etiology. Patients with hypothyroidism have more risk of re-infarction, dissection and comorbidities. The purpose of our study was to determine the association of hypothyroidism and SCAD.

Methods and results: A total of 38 patients registered in our Hospital from 2000 to 2014 were retrospectively enrolled. The definition of spontaneous coronary artery dissection was based on the presence of medial dissection or intramural hematoma that was recognized by angiography and according with the classification proposed by Saw. Finally, 38 patients diagnosed as SCAD (male/female 16/22, age 54±12 years) were included in the analysis. The clinical presentation was myocardial infarction in 87% of patients, 10% SCAD developed after physical or emotional stress and 20% had hypothyroidism. The left anterior descending artery was involved in 22 patients (50%) and left main was involved in 2 patients. 13% had multi-vessel SCAD and 8% recurrences, mostly women (66%). There was significant relationship between having hypothyroidism and present a SCAD (p=0.03), experience a recurrence (p=0.025) or having multiple dissection (p=0.002). The average time between relapses was 1023 days.

According to the classification proposed by Saw the majority of them was type 1 (50%). Coronary artery tortuosity was present in 17 patients (45%) and it is significantly related with MACE (p=0.001) and complications during PCI (p=0.001). The management of SCAD was revascularization of the culprit lesion in 68.6% of patients (24 PCI, 1 ACTP, 1 CABG) with in-hospital death of 8%. fibrinolysis was initially performed in 21.6% of cases which was also significantly related with MACE (p<0.001). Coronary artery tortuosity was present in 17 patients (45%) and it is significantly related with MACE (p<0.001) and complications during PCI (p<0.001). PCI was successful in 96% of cases, 2 or more stents were needed in 50% of cases and the median stent length was 45.5±32.3 mm. During a median follow-up duration of 3.8 (interquartile range: 1.9–5.9) years, cardiac death occurred in 40 (5.9%) of the β-blocker group versus 29 (5.2%) of the no-β-blocker group (p=0.88). After propensity-score matching analysis, there were no significant differences in the rates of cardiac death (hazard ratio [HR]: 1.16, 95% confidence interval [CI]: 0.72–1.85; p=0.55) and major adverse cardiac events, defined as the composite of cardiac death, myocardial infarction, or repeat revascularization (HR: 1.15, 95% CI: 0.87–1.51, p=0.32).

Clinical outcomes of propensity-matched population

<table>
<thead>
<tr>
<th>p-blocker group (n=475)</th>
<th>No-p-blocker group (n=475)</th>
<th>HR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac death</td>
<td>28 (5.9)</td>
<td>26 (5.5)</td>
<td>1.16 (0.72–1.85)</td>
</tr>
<tr>
<td>All-cause death</td>
<td>61 (12.8)</td>
<td>62 (13.1)</td>
<td>1.06 (0.79–1.43)</td>
</tr>
<tr>
<td>Non-fatal MI</td>
<td>2 (0.4)</td>
<td>6 (1.3)</td>
<td>0.99 (0.28–3.44)</td>
</tr>
<tr>
<td>Any coronary revascularization</td>
<td>73 (15.4)</td>
<td>59 (12.4)</td>
<td>1.19 (0.86–1.66)</td>
</tr>
<tr>
<td>Major adverse cardiac events*</td>
<td>98 (20.6)</td>
<td>85 (17.9)</td>
<td>1.15 (0.87–1.51)</td>
</tr>
</tbody>
</table>

Conclusions: β-blockers therapy at discharge was not associated with favorable long-term clinical outcomes in stable CTO patients treated with either PCI or medical therapy alone.
P4473 | BEDSIDE
High triglycerides, low HDL cholesterol and a low LDL cholesterol per apolipoprotein B ratio predict incident diabetes in patients with established coronary artery disease
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Background and introduction: Patients with type 2 diabetes mellitus (T2DM) exhibit a typical pattern of dyslipidemia with low HDL cholesterol, high triglycerides and a low LDL cholesterol per apolipoprotein B (LDL-C/apoB) ratio reflecting small LDL particles. We investigated whether these risk factors are also associated with incident diabetes in non-diabetic patients with established coronary artery disease (CAD).

Methods: We enrolled 655 non-diabetic patients with angiographically proven stable CAD. Prospectively, the incidence of T2DM was recorded over a mean follow-up period of 6.1±3.7 years. Diabetes was diagnosed according to ADA criteria.

Results: From our non-diabetic coronary patients, 358 (54.7%) at baseline had fasting glucose (NFG) ≥100 mg/dl and 297 (45.3%) had impaired fasting glucose (IFG) ≥100 mg/dl. During follow-up, T2DM was newly diagnosed in 17.4% of our patients. Baseline IFG compared to NFG was associated with a 2.5-fold increased risk of developing T2DM (26.6% vs. 9.8%; adjusted OR 3.38 [2.17–5.16]; p<0.001). Low HDL cholesterol, high triglycerides, and a low LDL-C/apoB ratio after multivariable adjustment including fasting glucose significantly predicted incident diabetes in the total study cohort (OR 0.65 [0.49–0.91]; p=0.02, 0.52 [0.41–0.71]; p<0.001, respectively) and also when we separately analyzed patients with IFG (OR 0.60 [0.39–0.90]; p=0.02, 0.45 [0.33–0.63]; p<0.001, respectively) and NFG (OR 0.62 [0.40–0.96]; p=0.03, 0.52 [0.40–0.70]; p<0.001, respectively). Serum triglycerides, HDL cholesterol and apoB were highly correlated with each other (r=0.85–0.98).

Conclusion: We conclude that among patients with angiographically proven stable CAD the incidence of diabetes is high, particularly among those with IFG. Importantly, high triglycerides, low HDL cholesterol and a low LDL-C/apoB ratio significantly predict incident diabetes independently from baseline glycemia.

P4474 | BENCH
Impact of diabetes on 2-year clinical outcomes in patients with acute myocardial infarction: Korean registry of DIAMOND (diabetic Acute Myocardial Infarction Disease)
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Background: We established diabetic acute myocardial infarction (AMI) cohort in order to extend knowledge of AMI with diabetes mellitus (DM) and to provide a better understanding of clinical consequences following AMI in DM patients.

Methods: Korean registry of DIAMOND (Diabetic Acute Myocardial Infarction Disease) study is a prospective, observational study where consecutive AMI patients with DM were enrolled from 22 hospitals in South Korea between April 2010 and June 2012. In order to compare clinical outcomes between diabetic and non-diabetic AMI, we retrieved non-diabetic AMI from KAMIR cohort (3,178 patients from Korea Acute Myocardial Infarction Registry) on the basis of a 1:1 propensity score matching (PSM) by age and gender. The primary end point was the incidence of major adverse cardiac events (MACE, a composite of all-cause death, recurrent MI, and target vessel revascularization) at 2-year follow-up.

Results: In diabetic cohort, patients were older (64.9±9.8 vs. 62.2±13.1, p<0.001), left ventricular ejection fraction was lower (50.8±11.8 vs. 54.0±10.9, p<0.001), estimated glomerular filtration rate was lower (73.5±31.9, 84.6±28.8, p<0.001) and there were more female patients (34.2% vs. 23.4%, p<0.001). Patients with DM were more likely to have other comorbidities such as hypertension (66% vs. 43.7%, p<0.001) and hyperlipidemia 27.1% vs. 12.5%, p<0.001) with more history of prior MI (5.5% vs. 2.3%, p<0.001). After PSM analysis, the 2-year incidence of MACE was significantly higher in DM (9.2% vs. 3.6%, p<0.001).

Conclusions: AMI patients with DM in Korea had worse clinical characteristics and more accompanied with comorbidities. In this PSM comparison with non-diabetic AMI, DM increases the risk of MACE in AMI patients at 2-year follow-up.
visit than at hospital discharge: FU-GFR <60 ml/min (20% vs. 7.8%; p=0.05), FU-GFR <30 ml/min (4.4% vs. 0.3%; p=0.05), discharge-GFR <60 ml/min (6.7% vs. 9.5%; p=ns), discharge-GFR <30 ml/min (0% vs. 0.7%; p=ns). There were no statistically significant differences between newDM and controls with respect to the incidence of in-hospital contrast induced acute kidney injury (2.2% vs. 7.2%; p=ns), as well as the number of patients in whom PCI (22.2% vs. 19.9%; p=ns) or CABG (4.4% vs. 7.1%; p=ns) procedures had been performed during FU. Patients within newDM group were more often treated with diuretics (44.4% vs. 24%; p=0.05). Univariate logistic regression analysis revealed that newDM was associated with FU-GFR <60 ml/min occurrence at 7-month FU (OR: 2.95 CI: 1.28-6.88).

Conclusions: New onset diabetes mellitus is associated with increased prevalence of decreased renal function at 7-month follow-up after AMI.

P4477 | BEDSIDE
Temporal trends in clinical features and outcomes in the elderly following percutaneous coronary intervention
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Background: Accompanied by aging society, percutaneous coronary intervention (PCI) has been widely performed in the elderly patients for the past few decades. However, a paucity of published data examining clinical features and outcomes is available.

Methods: We analyzed data of patients with the age of 70 to 85 following PCI in Juntendo University (Tokyo, Japan) from 1985 to 2010. The patients were divided into three groups according to the timing of PCI (March, 1985–December, 1997; plain old balloon angioplasty (POBA)-era, January, 1998–July, 2004; bare metal stent (BMS)-era, August, 2004–December, 2010; drug-eluting stents (DES)-era). Primary endpoint was a composite of all-cause mortality and acute coronary syndrome assessed at three-year after the initial procedure.

Results: A total of 1070 patients were examined (POBA-era: 184, BMS-era: 363, and DES-era: 519). Mean age and BMI, a prevalence of diabetes, hypertension and dyslipidemia were higher in DES-era. Lipid profiles were better and prescription rates of evidenced-based medicine including aspirin, statin and beta-blocker were higher in DES-era. Kaplan-Meier estimation for 3-year all-cause mortality and acute coronary syndrome was not different between the groups (Figure 1). In univariable Cox regression analysis, hazard ratio for the primary endpoint was not significantly different between DES-and POBA-era. A similar result was found between BMS-era and POBA-era. Multivariable Cox regression analysis revealed that lower BMI, statin use, higher LVEF and eGFR were associated with reduction of the long-term clinical outcomes.

Kaplan-Meier curves for 3-year All-cause mortality and ACS

Conclusions: Despite the higher risk profiles of the elderly patients in the current DES-era, long-term clinical outcomes following PCI were similar among POBA-, BMS- and DES-eras.

P4478 | BEDSIDE
Circulating monocytes are strongly associated with coronary artery calcification (CAC) density in a population of asymptomatic subjects
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Background: Coronary artery calcification (CAC) is an active and regulated inflammatory process in the natural history of atherosclerosis, strongly associated with clinical conditions conferring a high risk of cardiovascular disease (CVD). However, a clearly established association between the spreading of CAC and the circulating level of inflammatory/metabolic markers is still lacking. We aimed to investigate the relationships between CAC density score and peripheral inflammatory/metabolic parameters in a wide population of asymptomatic subjects.

Methods: We evaluated 1606 subjects from the population of the Montignoso Heart and Lung Project (MHLP), a community-based study of asymptomatic general populations ≥45 years. The enrolled subjects underwent a complete routine peripheral blood laboratory examination, including high-sensitivity C-Reactive Protein (hsCRP) measurement. Individual body mass index (BMI) was calculated according to standard formulas. Computed Tomography (CT) Calcium Score was obtained and CAC density was determined according to previously described Agatston score-derived formulas.

Results: Multiple regression statistical analysis showed independent positive correlations of CAC density score with blood levels of gamma-glutamyltransferase (GGT) (P=0.0011), creatinine (P=0.0047) and triglycerides (P=0.0088), as well as with age of subjects (P<0.0001) and circulating monocyte number (cells/ml) (P<0.0001). On the other hand, CAC density score exhibited independent inverse correlations with blood high-density lipoproteins (HDL) (P=0.0426) and platelet number (P=0.0179).

Conclusions: Our results demonstrate for the first time that the blood monocyte number represents a powerful inflammation marker independently associated with the CAC density score in a wide population of asymptomatic subjects, so suggesting a key functional role of this leukocyte subset in the histopathological process of arterial calcification.

P4479 | BEDSIDE
Coronary CT angiography in patients with a zero agatston score: results from the German cardiac CT registry
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Background: The absence of coronary calcification has been shown to be associated with a favorable prognosis in asymptomatic individuals, but it is unclear whether the lack of coronary calcium permits to rule out coronary stenoses and avoid further diagnostic workup in symptomatic patients. We report the clinical characteristics, symptom status, risk profile and in the vast majority of patients CAD, is excluded with no need for further diagnostic workup in symptomatic patients. We report the clinical characteristics, symptom status, risk profile and clinical consequences of coronary CTA in patients with an Agatston Score of zero.

Methods: Nine centers participated in the German cardiac CT registry (at least a 64-slice system, adequate expertise in the reporting of coronary CT angiography). In the time period between 2004 to 2009, 7061 patients were enrolled in the registry. Data concerning patients baseline characteristics, procedural parameters, indication, coronary findings as well as clinical consequences were documented.

Results: A total of 2016 individuals with absence of coronary calcification (Agatston Score zero) were identified (47% female, mean age 54±11 years, mean BMI 26.4±4.5). CT was performed in 88% of the patients in an elective setting and 12% in an acute setting. In the vast majority of patients, CT was performed either for risk stratification for CAD or for detection/exclusion of obstructive CAD (97.1%). 43% of patients with a zero Agatston score were asymptomatic. In 70.8% of patients a previous stress test was performed, out of which 90.8% was normal. 5% were falsely positive and 4% were false negative. Further diagnostic workup was performed in only 0.8% of patients. CT was performed either for risk stratification for CAD or for detection/exclusion of obstructive CAD (97.1%).

Conclusions: Patients with an Agatston score of zero show a low cardiovascular risk profile and in the vast majority of patients CAD, is excluded with no need for further downstream testing. Albeit seldom, significant coronary stenoses are detectable in a small percentage of patients without coronary calcifications.

P4480 | BEDSIDE
Machine learning applied to clinical and coronary CT angiography variables for prediction of MACE
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Purpose: We investigated a machine learning (ML) approach for prediction of MACE from clinical and coronary CT angiography (CTCA) data available from the CONFIRM registry.

Methods: Data from 10030 patients (58±13yrs; 5628 males) without known CAD, and with 5 yr outcomes from the CONFIRM registry were considered. All patients underwent CTTA for clinical purposes and were followed for MACE
Long-term prognostic performance of low-dose 64-slice coronary CT angiography with prospective eCG triggering

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Background: Little is known about prognosis ≥2 years after coronary CT angiography (CCTA), only about older CCTA methods. Purpose: We assessed the long-term prognostic performance of low-dose 64-slice CCTA with prospective ECG triggering in patients with known or suspected coronary artery disease. Methods: We included 434 patients undergoing low-dose CCTA, stratified according to maximal coronary lesions in CCTA: normal, non-obstructive (narrowing <50%), obstructive (narrowing ≥50%) and previously revascularised. Coronary artery calcium score (CACS) was assessed. Follow-up was performed using hospital records and telephone interviews regarding major adverse cardiac events (MACE): cardiac death, non-fatal myocardial infarction or elective revascularisation. Revascularizations within 6 weeks after CCTA were excluded to avoid a bias between diagnosis and prognosis of CCTA. Results: Mean effective radiation dose was 1.7±0.5 mSv. At baseline, 153 (35%) patients had normal arteries, 87 (20%) non-obstructive lesions, 131 (30%) obstructive stenosis and 34 (8%) were revascularised. Twenty-nine (7%) patients were lost to follow-up. After a median follow-up of 6.1 years, MACE occurred in 0% of normal, 6% of non-obstructive, 30% of obstructive and 39% of revascularised patients (all comparisons p<0.003, except obstructive versus revascularised non-significant). Multivariate Cox analysis identified obstructive stenosis and CACS as independent MACE predictors (p<0.001). Area under receiver operating characteristic curve was higher for CCTA than CACS: 0.804 (0.742–0.866) vs. 0.738 (0.644–0.832).

Conclusion: Low-dose 64-slice CCTA with prospective ECG triggering has an excellent prognostic performance with a warranty period of at least 6 years for patients with normal coronary arteries.

Acknowledgement/Funding: This study was funded by an NIH grant (2R01HL089765) and also in part by a grant from the Dowager Countess Eleanor Peel Trust, UK
vascular territories among 67 vascular territories. With invasive FFR, 20 (30%) coronaries had significant coronary stenosis, as FFR < 0.80. The area under the receiver-operating curve for first pass CT-MPI was 0.758 (95% confidence interval [CI]: 0.627 to 0.889) for invasive FFR (p = 0.001). First pass CT-MPI without stress showed sensitivity 0.75, specificity 0.77, positive predictive value 0.58 and negative predictive value 0.88 for detecting vascular territories with significant coronary stenosis as determined with invasive FFR < 0.80.

Conclusion: First pass CT-MPI without stress shows excellent diagnostic accuracy compared with invasive FFR as the reference standard. This technique could complement CCTA for diagnosing CAD.

P4484 | BEDSIDE
Carotid plaque predicts severity of coronary atherosclerosis in asymptomatic diabetics: a prospective study

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Aims: We sought to prospectively evaluate the prevalence and significance of carotid plaque and carotid IMT measurements in asymptomatic diabetics with or without coronary atherosclerosis.

Methods: As part of a ongoing trial (PROCEDURE-Progression of coronary atherosclerosis in diabetics: Evaluation of CT coronary angiography and novel biomarkers to evaluate the effects of intensive or standard statin therapy with/without eicosapentaenoic acid on the progression of coronary calcium score (CACS)). This trial demonstrated that annual progression rate of Agatston score was similar among groups and 40% (95% CI: 19–61%) in all patients irrespective of a significant reduction of LDL cholesterol). Previous study showed that the greater progression of CACS was associated with future cardiovascular events. Therefore, it is of interest to find markers involving CACS progression. Among several cardiovascular risk factors, the number of circulating CD34 positive cells was reported to be associated with vascular function and cardiovascular risks.

Purpose: To examine the association the number of CD4+3 positive cell and annual progression of CACS in the PEACH trial.

Results: The PEACH trial analyzed 156 patients with CACS of 1 to 999, hypercholesterolemia, and no history of cardiovascular disease from 27 sites in Japan from May 2010 to August 2011. Patients were assigned into three groups of pta- vastatin 20mg/day alone, or 40mg/day alone, and 20mg/day + eicosapentaenoic acid 1800mg/day/day, MDCT and a blood test were performed again at one year follow-up. The number of circulating CD34 positive cell was counted with flow cytometry.

Results: Correlation analyses among circulating biomarkers revealed that the annual change in CACS was significantly associated with the baseline number of CD34 (r = 0.19, p = 0.037), but not with age, gender, body mass index, baseline levels of HDL-cholesterol, triglyceride, hsCRP, uric acid, serum creatinine, and adiponectin. On the other hand, the number of CD34+ positive cells was significantly correlated with age, gender, body mass index, baseline value of LDL-cholesterol and HDL-cholesterol. Multiple logistic analysis demonstrated that lower CD34 positive cell number (< 0.84μl/μl) (Odds ratio: 2.70, 95% confidential interval: 1.26–5.81, p = 0.01) and CD4+3 positive cell number (Odds ratio: 2.74, 95% confidential interval: 1.23–6.12, p = 0.01) were independent predictors of the CACS progression, even after adjustment of age > 60 years, hypertension, diabetes, and current smoking.

Conclusion: The study demonstrated the lower number of circulating CD34+ positive cell is a novel predictor of CACS progression in patients with hypercholesterolemia under statin therapy.

P4485 | BEDSIDE
Duration of diabetes is a major determinant of optimal time to initiate vascular screening in asymptomatic type-2 diabetic subjects: results from the proceed study

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Introduction: Evidence from cardiac imaging with CT coronary angiography (CTCA) and coronary artery calcium (CAC) imaging suggest there is significant coronary artery disease (CAD) in asymptomatic type-2 diabetic patients. However, there is currently no consensus about the optimal time to screen for cardiac vascular disease (CVD) in this higher risk population.

Aim: The aim of this study was (1) to determine what factors are predictive of significant CAD and (2) when is the optimal time to screen asymptomatic diabetic subjects.

Methods: 263 asymptomatic diabetic patients were investigated with CAC scoring and CTCA as part of the Progression of Coronary Atherosclerosis in Asymptomatic Diabetic Subjects: Evaluation of the Role of CT Coronary Angiography and Magnetic Resonance Endothelial Function and Vascular Inflammation (PROCEED) study. Regression analysis was used to determine which of the demographic and clinical parameters best predicted significant CAD. Significant plaque was defined as one causing more than 50% luminal stenosis.

Results: Median duration of diabetes in the study population was 13 years. Mean age was 62.05±8.5 years with 58.6% males and mean BMI was 29.54±6.7 kg/m². Median CAC score for the entire study population was 105.91 (316.97) Agatston Units. 47.5% of patients were known to have documented microvascular disease. In a regression multi-variable analysis, duration of diabetes (p = 0.018), CAC score (p = 0.001), BMI (p = 0.018) and HLD (p = 0.002) were significant predictors of a >50% plaque. When CAC was excluded, systolic blood pressure (p = 0.032) also became significant. Using a ROC curve analysis, we determined that duration of diabetes, from diagnosis, of 12.5 years predicted the significant CAD with a sensitivity of 71.3% and a specificity of 57%. Combining all the multi-variate predictors, the area under the curve increased to 0.84 from 0.65 for duration of diabetes alone.

Conclusion: Patients with a diagnosis of diabetes for at least 12.5 years should be considered for screening for CAD.

Acknowledgement/Funding: British Cardiac Research Trust
Results: Mean diameter of the BVS implanted was 2.9±1.3mm, and mean length was 20.7±1.3mm. BVS were located in LAD (n=14), RCA (n=8), RCX (n=4), diagonal branches (n=2) and marginal branches (n=2), respectively. Out of 32 coronary scaffolds, 30 (94%) were determined assessable. Assessability is impaired by motion artefacts in two scaffolds (one BVS in RCA and one in a diagonal branch), but no BVS was classified unassessable due to beam-hardening artefacts, partial volume effects or other artefacts caused by scaffold components. Regarding unassessable scaffolds as being potentially stenotic, 28 BVS were correctly determined to be patent, 2 scaffold occlusions were detected accurately, and 2 false positive findings occurred. Consequently, the overall diagnostic accuracy was 94%, revealing a sensitivity of 100% and a specificity of 93%. Positive and negative predictive values were 50% and 100%, respectively.

Conclusion: In contrast to conventional coronary artery stents, MDCCT allows for the non-invasive implantation of BVS without revascularization. In those patients with coronary artery stenosis with good angiographic accuracy independent of scaffold diameter or length. Only a small number of BVS is unassessable in MDCCT, which is due to motion artefacts.

TECHNICAL DEVELOPMENTS IN COMPUTED TOMOGRAPHY ANGIOGRAPHY

P4488 | BEDSIDE
Bail out intravenous esmolol for heart rate control in cardiac computed tomography angiography
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Background: Adequate heart rate (HR) control is paramount for optimal cardiac CT, but no BVS was classified unassessable due to beam-hardening artefacts, partial volume effects or other artefacts caused by scaffold components. Regarding unassessable scaffolds as being potentially stenotic, 28 BVS were correctly determined to be patent, 2 scaffold occlusions were detected accurately, and 2 false positive findings occurred. Consequently, the overall diagnostic accuracy was 94%, revealing a sensitivity of 100% and a specificity of 93%. Positive and negative predictive values were 50% and 100%, respectively.

Conclusion: In contrast to conventional coronary artery stents, MDCCT allows for the non-invasive implantation of BVS without revascularization. In those patients with coronary artery stenosis with good angiographic accuracy independent of scaffold diameter or length. Only a small number of BVS is unassessable in MDCCT, which is due to motion artefacts.

P4489 | BEDSIDE
Coronary artery calcium quantification in the optimization of a comprehensive cardiac CT protocol for the diagnosis of hemodynamically significant coronary artery disease

Background: High coronary artery calcium (CACS) undermines the role of coronary CT angiography (CTA) in the investigation of obstructive coronary artery disease (CAD). Myocardial CT perfusion (CTP) may represent an opportunity to overcome this limitation to CAC. An issue is to understand this relationship.

Purpose: To explore the role of CAC in the optimization of a protocol including coronary CTA and CTP for the detection of hemodynamically significant CAD (hsCAD).

Methods: Symptomatic patients with intermediate pretest probability of CAD were prospectively recruited and underwent both cardiac CT and invasive coronary angiography (including fractional flow reserve assessment–FFR). We defined hsCAD by the presence of occlusive/subocclusive stenoses or FFR<0.80. Uninterpretable segments in CAC were considered positive in the CTA group; in the CTA-intention-to-diagnose (CTA-ID) group they were considered as false positives or false negatives (“worst case scenario”). An integrated protocol including CTA and CTP for uninterpretable segments was tested (CT-I).

Results: 95 patients were involved in the analysis (62±2 years, 68% males). Inclusion of CAC was associated with a significant increase in the AUC of the models including CTA-ID and CTP for prediction of hsCAD. The model including CTP and CAC showed the highest AUC (0.92, 95% CI 0.86–0.98). The protocol including CTA-ID, CAC and FFR was best (AUC 0.90). The protocol including CTA-ID, CAC and CTP, but not FFR at CAC > 100 showed the highest AUC (0.81, 95% CI 0.73–0.89).

Conclusion: In our population, quantification of CAC allowed the optimization of the subsequent CT protocol; proceeding to a stress-rest perfusion protocol if CAC was greater than 100 maximized both sensitivity and specificity in the detection of hsCAD.

P4490 | BEDSIDE
Ethnicity and coronary artery calcification: normal reference range for hemodynamically relevant coronary stenoses by computed tomography angiography
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Background: Several studies have demonstrated differences in the prevalence of symptomatic coronary artery disease (CAD). Myocardial CT perfusion (CTP) may represent an opportunity to overcome this limitation to CAC. An issue is to understand this relationship.

Purpose: Several studies have demonstrated differences in the prevalence of hemodynamically relevant coronary stenoses by computed tomography angiography (CCTA). These differences are pre-determined by ethnicity and therefore could be used in the clinical decision making process.

Methods: From August 2009, ethnicity was recorded as Caucasian, Afro-Caribbean, Chinese, Other or Asian (non-Chinese). The odds ratio of having coronary calcification (CACS > 0) are 0.98 (95% CI: 0.86–1.13, p=0.82) for white patients, 0.52 (95% CI: 0.39–0.69, p<0.001) for Afro-Caribbean, and 0.75 (95% CI: 0.41–1.35, p=0.33) for Chinese patients.

Conclusion: In the large cohort of asymptomatic individuals with no previous history of coronary revascularisation, a substantial proportion of patients had CAC score >0. In contrast to previously held assumption, Asians are not at higher risk of having coronary calcification, compared with white subjects, although Afro-Caribbean subjects appear to have lower risk than Asians.

Table 1

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>No. of Patients</th>
<th>CACS ≤ 25%</th>
<th>CACS &gt; 25%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asian (non-Chinese)</td>
<td>0</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>White</td>
<td>0</td>
<td>0</td>
<td>98.6%</td>
</tr>
<tr>
<td>Afro-Caribbean</td>
<td>0</td>
<td>0</td>
<td>95.5%</td>
</tr>
<tr>
<td>Chinese</td>
<td>0</td>
<td>0</td>
<td>96.6%</td>
</tr>
</tbody>
</table>

Normal reference ranges of the 4 different ethnic groups.

Conclusion: In this large cohort of asymptomatic individuals with no previous history of coronary revascularisation, a substantial proportion of patients had CAC score >0. In contrast to previously held assumption, Asians are not at higher risk of having coronary calcification, compared with white subjects, although Afro-Caribbean subjects appear to have lower risk than Asians.

P4491 | BEDSIDE
Predictive value of coronary artery lumen area quantification for hemodynamically relevant coronary stenoses by computed tomography angiography
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Purpose: Coronary CTA is validated to rule out coronary artery disease (CAD). Invasive angiography often represents the false positive high-grade lesions result in lower sensitivity. Additional quantitative lesion measurements may increase accuracy and identify hemodynamic relevance of a stenosis. Therefore the purpose was to evaluate the added value of minimal lumen area (MLA) quantification by CTA to predict hemodynamic significance of coronary stenoses by invasive angiography (ICA) requiring coronary revascularization.

Materials and methods: One-hundred fifty-six patients (mean age 65.8, 28% female) who underwent multislice CTA presented with at least one high-grade stenosis (>50%) in a proximal coronary vessel (lumen diameter >5 mm2) and subsequently underwent invasive angiography (ICA). The stenoses were quantified in CT, including minimal lumen area (MLA) and diameter (MLD) and maximal area and diameters stenoses. Reference was ICA including percutaneous intervention (PCI) or coronary bypass grafting (CABG). ROC–Analysis with incremental testing was performed.

Results: Overall, 220 high-grade stenoses (26 RCA, 10 LM, 137 LAD, 47 CX) in proximal segments were evaluated. Eighty-eight (42%) were positive. Minimal lumen area ≤1.8 mm2 was identified as the most accurate cut-off
value to predict hemodynamic relevant stenoses > 70% in ICA (Sensitivity 90.9%, specificity 89.3%) with an AUC of 0.97 (p < 0.0001; 95% CI 0.95–0.99).

Minimal lumen diameter cut-off was 1.2 mm (sensitivity 90.9% and specificity 85.25) with an AUC of 0.92 (p < 0.0001; 95% CI 0.88–0.95).

Maximal area and diameter stenoses (%) showed lower AUC values with 0.89 and 0.87 respectively.

Conclusion: Minimal lumen area of < 1.8 mm² is the most accurate cut-off for high-grade CT stenoses in proximal coronary vessels and may add information to identify hemodynamic relevant stenoses that require revascularization in invasive angiography.

Lesions with positive FFR had larger mean LMM (Table 1). At the same MLD, functionally significant ischemia was produced at lesions with larger LMM (Figure 1). Based on this slope of regression lines, lesions can be divided into 2 groups according to FFR value. Diagnostic performance of a new index with LMM divided by MLD to predict functionally significant ischemia was assessed. With the best cut-off value of 38.4, the AUC of the ROC were 0.82 with 62% of sensitivity and 92% of specificity, which is higher than that of %DS (AUC = 0.74). LMM showed weak correlation with RD and MLD, and weak negative correlation with DS. A new index, LMM/MLD was predictive for ischemia as well as DS (FFR < 0.5). Our study suggests that 1mm of MLD CT can supply 34.8(g) of myocardium.

Table 1. Lesion characteristics

<table>
<thead>
<tr>
<th>Total (n=208)</th>
<th>FFR &lt; 0.8 (n=102)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FFR</td>
<td>0.75±0.11</td>
</tr>
<tr>
<td>% DS_CCA</td>
<td>63.55±1.15</td>
</tr>
<tr>
<td>MLD_CCA</td>
<td>1.05±0.03</td>
</tr>
<tr>
<td>LMM</td>
<td>36.51±11.49</td>
</tr>
</tbody>
</table>

P4494 | BEDSIDE
Feasibility of coronary computed tomography angiography using multi slice attenuation-corrected low radiation dose turbo flash mode in third generation 192-slice dual-source
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Objective: New generation dual-source multi slice computed tomography (CT) scanners allow low radiation dose in coronary computed tomography angiography (CTA). Purpose of this study was to evaluate the image quality and radiation dose of low dose cardiac CTA using automated attenuation-based selections of tube parameters in daily clinical practice.

Methods: Patients were referred to the heart center due to suspected coronary artery disease (CAD). CTA was performed using a 192-slice dual-source CT scanner. Images were recorded by prospectively electrocardiogram (ECG)-triggered high-pitch acquisition (" turbo flash") mode (collimation 2x192x0.6mm; 50ms contrast agent; Ultrasound 370; flow 5ml/s). Automated attenuation-based selections of tube parameters were used. Image quality (4-point rating score from 0 = nondiagnostic to 3 = excellent) and radiation dose were evaluated.

Results: 65 patients and 198 coronary arteries (mean age 59;14 years, 24 females) were analyzed by CTA. Mean heart rate was 61±6bpm after application of intravenous betablocker up to 20mg metoprolol prior CT scan. Mean radiation dose was 0.98±0.65mSv. Tube parameters were 49.8±73mAS and 84±110 kV. Subjective image quality was 2±0.5. 3 studies (9 coronary arteries, 4.5%) could not be interpreted due to poor image quality. Relevant coronary artery disease (stenosis >50%) was estimated by CTA in 8 patients (14 coronary arteries) who were referred to invasive coronary angiography. In 7 patients (13 coronary arteries) CTA findings were proofed. In one patient LAD stenosis was overestimated in CTA.

Conclusion: The combination of prospectively ECG-triggered high-pitch acquisition mode and automated attenuation-based selections of individualized tube parameters is a powerful and reliable tool to assess coronary arteries in third generation 192-slice dual-source computed tomography with low radiation dose.
nents (r=−0.27, p=0.01), but not age, body mass index. The EAT density in pa-
tients with metabolic syndrome was significantly lower than that in pa-
ients without metabolic syndrome (−78 to −83 vs. −71 to −65 mmH2O, p=0.01). EAT density was significantly associated with serum levels of triglyceride (r=0.31, p<0.01), adipopectin (r=0.53, p<0.01), and MCP-1 (r=0.21, p=0.03). The EAT density was also involved in the number of stenosis (r=0.22, p=0.03) and Genissini score (r=0.20, p=0.04). On the other hand, The EAT volume was signifi-
cantly associated with body mass index, HDL-cholesterol, adiponectin, and oxi-
dized LDL-cholesterol. Finally, multiple logistic analysis revealed that lower EAT density was associated with the presence of CAD (odds ratio of lower EAT=2.717, 95% CI 1.03 to 7.12, p=0.04) after adjustment of age, gender, hypertension, dia-
betes mellitus, dyslipidemia, and current smoking.

Conclusions: Lower EAT density is associated with cardio-metabolic risk factors. Our findings support that the quality of epicardial fat may affect the development of coronary artery disease.

P4490 | BEDSIDE

Improved visualization of the coronary arteries using model-based iterative reconstruction for cardiac CT

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Purpose: To evaluate the image quality characteristics of coronary CT angiog-
raphy (CTA) images reconstructed with standard filtered back projection recon-
struction (FBR), hybrid iterative reconstruction (HIR) and model-based iterative recon-
struction (IMR).

Methods: 252 patients (39 male, age 64.7±9.3 years, BMI 28.2±5.6 kg/m2) who underwent 256-slice coronary CTA were reconstructed with FBR, HIR and IMR. Two readers evaluated the datasets qualitatively and quantita-
tively. A four-point scale was used to rate overall image quality from 1=excellent to 4=poor, non-diagnostic. Image quality was graded from 1=non image noise to 4=se-
vere noise, while image sharpness was evaluated on a five-point scale. Mean im-
age noise (SD) and contrast-to-noise ratio (CNR) were measured in proximal and
distal coronary segments.

Results: Qualitative analysis showed that IMR improves image quality and im-
age sharpness as compared to FBR and HIR (p<0.0001 all). Image noise was significantly lower with HIR as compared to FBR and was further reduced with IMR as compared to HIR (p<0.0001 all). The mean image noise as measured in the ascending aorta was lowest with IMR (42.1±10.7 vs 28.7±17 vs 12.9±2.7; FBR vs. HIR vs. IMR, respectively; p<0.001 all), while mean attenuation did not differ among the three reconstruction methods (517.1±93.6 vs. 517.9±93.1 vs 517.7±93.1 HU, p=1.0 all). Proximal CNR in FBR, HIR and IMR was 17.4±5.8 vs. 25.3±8.4 vs 54.2±12.0 (p=0.001 all), while distal CNR was 18.6±5.0 vs. 23.3±7.4 vs. 55.2±12.4, respectively (p<0.001 all).

Conclusion: IMR significantly improves image quality accompanied by a sub-
stantial increase in CNR and decrease in image noise in coronary CTA.

COMPUTED TOMOGRAPHY USE IN STRUCTURAL HEART DISEASE

P4491 | BEDSIDE

Left atrial antral wall thickness around pulmonary veins is associated with stroke and the reconnection of pulmonary venous potential after catheter ablation on atrial fibrillation

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Background: Circumferential pulmonary vein isolation (CPVI) is most important strategy of catheter ablation on atrial fibrillation (AF). However, the reconnection of PV is a main mechanism of AF recurrence. Although it is important to un-
derstanding an atrial antral wall thickness (LAAWT) around PVS prior to catheter ablation, its clinical implications were not well known.

Methods: In 28 (22males, 53.6±12.4 years old) patients who underwent redo-
ablation, its clinical implications were not well known.

Results: Thirty patients (15 female, mean age 75±3y) with at least moderate
stenosis (0.67±0.24mm vs. 0.60±0.26mm, p=0.004) had signifi-
cantly thinner LAAWT than those with low CHA2DS2-VASc score (−3).

In redo ablation, PVPs were detected at 62 (4.6%) points of total 1344 points, and
60 PVS (53.6% of) of 112 PVS during mean 16.6 months (3–38 months) after CPVI.

LAAWT with reconnected PVPs (n=62) was significantly thicker than those with intact PVS (n=128) (0.82±0.30 vs. 0.63±0.29 mm, p=0.001) and area under curve (AUC) of LAAWT on PV reconnection was 0.7.

Conclusion: LAAWT was associated with diabetes, heart failure and had also significant inverse correlation with stroke. And thicker LAAWT is associated with the recurred PVPs after CPVI, which is related with AF recurrence.

P4492 | BEDSIDE

Paced GRS morphology is closely correlated with the right ventricular pacing lead position: a study by cardiac computed tomography

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Background: The rightward lead position on the left anterior oblique projection by floroscopy is often used as a maker of lead positioned in the right ventricular (RV) septum. Nonetheless, whether the lead is truly located in the septum remains unclear.

Purpose: The purpose of this study was to investigate the association between paced GRS morphology and the RV lead position revealed by computed tomog-
ography.

Methods: Consecutive 36 patients who underwent cardiac CT after pacemaker implantation were enrolled. The lead position was confirmed by using both tomo-
graphic images and 3-dimensional reconstruction. A paced GRS morphology was obtained by 12-lead ECG.

Results: Thirty leads were aimed to be positioned in the RV septum using flu-
orscopy. However, only 10 leads (33%) were confirmed to be placed in the septum by CT. LR duration was significantly shorter in the septal group (137±13 msec) than those in the apex group (162±18 msec, p=0.006) and in the free wall group (188±31 msec, p=0.001). GRS duration <154 msec predicted leads located in the septum with sensitivity of 90%, specificity of 81% and predictive accuracy of 83%. GRS morphology of R pattern in aVL was more frequently observed in the apex group than in the septal (95% vs 40%, p=0.002) and free wall group (95% vs 59%, p=0.043). R pattern in aVL estimated the lead positioned at the apex with sensitivity of 95%, specificity of 56% and predictive accuracy of 78%.

Conclusion: Implantation of RV lead using fluoroscopy alone was often misleading. Paced GRS morphology and duration should be taken into account for the RV lead insertion.

P4493 | BEDSIDE

Assessment of the coronary sinus vein with multi-detector computed tomography angiography - implications for mitral valve reshaping in patients with functional mitral valve regurgitation

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Background: There are few treatment options for functional mitral valve regurgitation (FMR), which is caused by mitral annulus dilatation. Recently introduced annuloplasty devices are percutaneously implanted into the coronary sinus vein (CS), reshaping the mitral valve annulus. However, data on CS length, diameters and its location in relation to the left circumflex artery (RCX) are crucial for device implantation. Multi-detector-computed tomography (MDCT) is well applicable for that purpose by providing an assessment of the CS in any arbitrary plane with high spatial resolution.

Methods: Thirty patients (15 female, mean age 75±3y) with at least moderate FMR underwent contrast-enhanced, retrospectively ECG-gated dual-source CT (Siemens Somatom Definiton, injection of 70 – 90ml of contrast) as part of a plan-
ing procedure prior to percutaneous mitral valve annuloplasty. Curved multipla-
erent reconstructions (CMR) were closely related with RCX. Curved multipla-
erent reconstructions (CMR) were closely related with RCX.
We sought to evaluate the agreement between TEE and CTA for mitral annuloplasty is feasible and yields information on the course of the CS as well as specific values for CS dimensions. These values are normally distributed, and they correlate with the LV-EDD in patients with relevant FMR.

Results: Mean LVEF of all patients was 41±4%, mean LV-EDD was 61±2mm. The CS length ranged between 66 and 131mm (mean 98±4mm, median 94mm), enclosing 38% of the mitral valve circumference on average (range 25–50%). Mean ostial CS diameter was 15±10.6mm (range 9–22mm, median 15mm), and mean distal CS diameter was 4.9±0.2mm (range 3–7mm, median 5mm). In 70% of all patients (n=21) the CS took a course superior to the RCX. There was no difference in mean CS length between men and women (99±6mm vs. 97±4mm, p=0.65), and there was no correlation between LV-EDD or LVEF and CS length (r=−0.11, p=0.6 and r=0.03, p=0.16). However, mean ostial CS diameters varied significantly between men and women (13.7±7mm vs. 13.5±10.9mm, p=0.04), whereas distal CS diameters did not (5.3±3.0mm vs. 4.5±0.3mm, p=0.12). LV-EDD correlated with distal CS diameters (r=0.45, p=0.05) and showed a trend for correlation with ostial CS diameters (r=0.4, p=0.07). There was no correlation of LV-EDD with CS diameters (ostial: r=−0.17, p=0.47; distal: r=0.3, p=0.16). However, all CS parameters were normally distributed.

Conclusion: Assessment of the CS with MDCT prior to percutaneous mitral valve annuloplasty is feasible and yields information on the course of the CS as well as specific values for CS dimensions. These values are normally distributed, and they correlate with the LV-EDD in patients with relevant FMR.
Multidetector-computed tomography (MDCT) corresponding to the same cross-sectional image from echocardiography (Smart Fusion, Toshiba). The aim of this study is to assess the usefulness of this fusion imaging in ACHD patients.

Methods: This study consisted of consecutive 46 patients (38 women, 58±16 years with ACHD who underwent TTE and MDCT. All patients underwent echocardiography within a week of MDCT. Both MDCT and echocardiographic images were displayed simultaneously in the same screen side by side and then, MDCT images act in synchronization with echocardiography.

Results: Fusion imaging was safe and feasible in all patients with ACHD. Cardiac chamber size and maximum size of the defect was accurately measured. This integrated fusion imaging also revealed unexpected and incremental findings and exclusively provided correct anatomical classification or clarified suspected abnormal findings on echocardiography.

Example cases (figure):
2. To clarify the etiology of unorinary severe tricuspid regurgitation.
3. To identify anomalous pulmonary venous connection undiagnosed by echocardiography.
4. Assessment of RVOT stenosis; precise location and grade.

Conclusions: This novel cardiac fusion imaging is clinically useful. Especially, integrated anatomical and functional multi-modality imaging provides incremental role over echocardiography in complex anatomy, and allows functional information in ACHD patients.

P4504 | BEDSIDE
Left atrial appendage sizing for percutaneous occlusion with amplatzer cardiac plug: a multimodality imaging approach
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Background: the morphology of the LAA and the LAA ostium are extremely complex and heterogeneous. Acute sizing of the landing zone is crucial for the optimal choice of the device diameter. Cardiac CT has been shown to provide accurate measurement of the LAA. Transesophageal echocardiography (TOE) and selective LAA angiography can provide discordant results during the procedure, and there is no consensus about the most reliable imaging modality.

Aim of the study: Compare the sizing of the LAA using a multimodality imaging approach.

Methods and results: We retrospectively included 45 patients (aged 67.6±16 years) who underwent LAA occlusion using the Amplatzer® cardiac plug (ACP). Mean diameter of the landing zone (average of the smallest and largest diameters) was determined using the different imaging modalities: MPR for cardiac CT and 3D TOE, multiple angle view at 0, 45, 90 and 120° using 2D TOE, and monoplanar projection (RAO30° cranial 20°) for angiography. We also compared the mean diameter derived from the area of the landing zone, with the diameter derived from the average of min and max diameters measured by CT.

High intra and inter observer reproducibility were found for both (r=0.93 and 0.87, p<0.01 respectively with mean difference of −0.1 mm [−1.8; +1.8] and −0.1 mm [−2.9; +2.5] respectively) and area measurement (r=0.94 and 0.88, p<0.01 respectively with a mean difference of 0 cm² [−0.15; +0.16] and 0 cm² [−0.9; +0.9] respectively) of the landing zone by CT.

2D TEE mean diameter was underestimated compared to CT (−2 mm [−2.7; +4.6]). Angiographic diameter was weakly correlated with CT (r=0.35, −1.4 mm [−5.7; +8.5]).

Conclusions: We found significant variability in the sizing of the LAA landing zone, using different imaging modalities. 3D data set provided by Cardiac-CT and 3D TOE looks interesting to get a complete overview of LAA anatomy. Multiple angle view from 0 to 120° are mandatory when using 2D TOE. Monoplanar LAA selective angiography seems not accurate for LAA sizing and may be avoided when non invasive imaging modalities are available.

P4506 | BEDSIDE
Usefulness of myocardial imaging by 64 multidetector-row computed tomography using stress test to assess myocardial ischemia and stenotic coronary artery
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Both anatomical and physiological assessment of coronary artery disease is important.

We hypothesized that contrast-enhanced 64 multidetector-row computed tomography (MDCT with adenosine 5'-triphosphate (ATP) stress test can describe a hypo-perfusion area in a myocardial ischemia part which was concordant with a coronary artery territory. This study sought to evaluate myocardial ischemia and stenotic coronary artery using contrast-enhanced 64-MDCT with ATP stress.

Methods and results: We performed contrast-enhanced 64-MDCT with ATP stress test and conventional coronary angiogram (CCA) in 85 patients with coronary artery disease. By the CCA analysis, a coronary stenosis was defined as significant based on when the degree of percent diameter stenosis as measured was > 50, CT values [Hounsfield Unit] of subendocardium was measured as the mean. The hypo-perfusion area on contrast-enhanced MDCT was defined as <30% attenuation of the surrounding subendocardium. By the CT myocardium image analysis, a coronary significant stenosis was defined as the presence of hypo-perfusion area concordant with the coronary territory. Five patients who had poor image quality of myocardium because of motion artifact and banding artifact were excluded. In addition, 7 myocardial infarction areas and the diagnosed arteries in patients with previous myocardial infarction were not analyzed. Consequently, we analyzed 233 arteries and those territories in 80 patients by CCA and MDCT. On the basis of the CCA analysis, 38 arteries in 28 patients were detected to have stenotic arteries that were noted in 19 left anterior descending arteries, 8 left circumflex arteries and 12 right coronary arteries, respectively. Sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy of the CT myocardium image analysis to identify significant coronary stenosis with use of CCA as the standard reference were 86%, 98%, 91%, and 97%, respectively. Twenty-four moderate stenotic (50 to 75% narrowing) coronary ar-
A.K. Kaltoft 1, J.F. Lassen1, B.L. Norgaard 1.

FFRct/FFR ≤ tation between rest and adenosine-stress was performed in a subset of the study cohort. Perfusion 40–70% at coronary CTA. Routine 82Rb PET (positive if any regional intermediate pretest risk of coronary artery disease and intermediate coronary stenosis. FFRct analysis was performed in patients with atypical angina and FFRct ≤ 0.80 was considered diagnostic of ischemia. FFR was performed if FFRct was < 0.80 or 82Rb PET was positive. Results: Between April and November 2014, 123 consecutive patients were included. Mean age 60±12 years; 61% male; mean BMI 29 (range 46–79), mean Agatston score 91 (range 0–1133; 23% with score 0). FFRct analysis could be performed in 106 (6%) patients the 82Rb PET result was positive, of whom FFRct < 0.80 was performed in 22 patients (27 vessels) with FFRct ≤ 0.80 (Table). In 20 of these, 82Rb PET was performed (Table). Mean (range) FFRct in false positive vessels was 0.78 (0.74–0.80).

Conclusions: FFRct is an efficient gatekeeper to the cath lab in stable patients with intermediate coronary stenosis. FFRct and PET results show significant discordance. The relative diagnostic value of FFRct and conventional ischemia testing needs further delineation.

Methods: The clinical data from 1868 consecutive patients (1046 men, age 60±12 years) undergoing cardiac CT between May 2012 and May 2014 were collected in a prospective registry. The indication and appropriateness of each test were categorized according to the 2010 Appropriateness Criteria issued by the Society for Cardiovascular Computed Tomography (SCCT).

Results: The most frequent indications for cardiac CT were: suspected coronary artery disease (CAD) in patients with a previous positive, inconclusive or doubtful exercise ECG (37%, n=694), suspected CAD with no previous testing (16%, n=269), and pre-ablation of atrial fibrillation (13%, n=236) - Figure. Globally, the indications for cardiac CT were classified as appropriate in 64% of cases, inappropriate in 12%, and uncertain in 11%. A further 12% could not be classified according to the SCCT criteria. The most frequent reasons for inappropriate referral were an exercise ECG with low risk findings (6%, n=110), asymptomatic individuals with low or intermediate cardiovascular risk (2%, n=40), and symptomatic patients with coronary stenosis < 3mm in diameter (1%, n=21). There were no significant differences in the proportion of inappropriate tests in relation to referring physician's specialty and type of institution.

Conclusion: Even though there is room for improvement, only a small proportion of cardiac CTs were considered inappropriate, dismissing concerns that this test might be largely misused in clinical practice.

P4510 | BEDSIDE

Coronary CT angiography in patients with low-risk acute chest pain: quantitative analysis of plaque parameters

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Background: Coronary CT angiography (CTA) is recommended in the workup of patients presenting to the emergency department (ED) with low to intermediate risk acute chest pain.

Purpose: We analyzed CT data for quantitative plaque parameters between patients with non-obstructive and invasively confirmed obstructive coronary artery disease (CAD).

Methods: Coronary CTA data sets of consecutive 151 ED patients (mean patient age 51±14 years, 67% males) without known CAD presenting with acute chest pain in 5 (83%) patients FFR was performed in 22 patients (27 vessels) with FFRct ≤ 0.80 (Table). In 20 of these, 82Rb PET was performed (Table). Mean (range) FFRct in false positive vessels was 0.78 (0.74–0.80).

Conclusions: FFRct is an efficient gatekeeper to the cath lab in stable patients with intermediate coronary stenosis. FFRct and PET results show significant discordance. The relative diagnostic value of FFRct and conventional ischemia testing needs further delineation.

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Conclusion: Even though there is room for improvement, only a small proportion of cardiac CTs were considered inappropriate, dismissing concerns that this test might be largely misused in clinical practice.
pain but absence of both initial troponin elevation and significant ECG changes were retrospectively evaluated for quantitative coronary artery plaque analysis. Data sets were acquired on a dual source CT scanner (mean estimated effective radiation dose 5.2±4.7 mSv). CT data sets were visually assessed for significant stenoses (luminal narrowing >70%). If present, the patient was referred for invasive coronary angiography. Plaque composition (low-density non-calcified, non-calcified, calcified), remodeling index as well as contrast density difference (defined as the percentage decline in luminal contrast density over the lesion) were assessed using semi-automatic software (Autoplaq).

Results: A total of 504 vessels (2087 segments) were visually assessed. CAD was ruled out in 87 (58%) patients by CT. Non-obstructive CAD was present in 43 (28%) patients, whereas CT identified at least one significant stenosis in 21 (14%) patients. Further invasive angiography of CT-positive patients confirmed significant coronary stenoses in 20/21 patients. Revascularization was performed in all patients with invasively confirmed stenoses. Quantitative analysis revealed significantly increased non-calcified (271±280 vs. 447±287 mm³, p=0.024), low-density non-calcified (34±38 vs. 71±55.9 mm³, p=0.01) and total plaque volume (302±299 vs. 512±337 mm³, p=0.015), non-density non-calcified plaque burden (2.3±2.1 vs. 3.8±3.2, p=0.015) and a significantly higher maximal remodeling index (1.4±0.3 vs. 1.9±1.1, p=0.037) in patients with invasively confirmed obstructive CAD compared to non-obstructive CAD on a per-patient basis. In multivariable analysis, total low-density plaque burden (OR: 1.47, p=0.03) and quantitative stenosis (OR: 1.058; 95% confidence interval: 1.003 to 1.115; p=0.038) were significant predictors of PCI-related myocardial injury. CT lesion length (odds ratio: 1.476; 95% confidence interval: 1.476 to 34.544; p=0.015) and CT lesion length (odds ratio: 7.141; 95% confidence interval: 1.09–3.29) in FRS of 10–20%. The CAC distributions and CAD prevalence in various FRS groups were displayed. The benefit to lower risk populations of CAC score-based screening was also assessed. Methods and results: In total, 1,854 participants (aged 40–79 years) without history of CAD, stroke, or diabetes were enrolled. CAC scores of >100, and ≥200 were present in 33.8%, 8.2%, and 2.9% of the participants, respectively. The CAC scores rose significantly as the FRS grew more severe (P<0.001). The total CAD prevalence was 6.1%. The occult CAD prevalence in the FRS ≤5%, 6–10%, 11–20%, and >20% strata were 3.4%, 6.7%, 9.0%, and 11.6% (P=0.0001). Multivariable logistic regression analysis adjusting for body mass index, glucose, and white blood cell count, not only the intermediate and high risk groups but also the low risk (FRS <5%) group had significantly increased odds ratios for occult CAD compared to the very low-risk (FRS ≤5%) group. (1.83 [95% confidence interval, CI] 1.09–2.94 in FRS of 10–20%, 2.48 [95% CI 1.47–4.26] in FRS ≥20%) (1.83 [95% CI 1.09–2.94]) in FRS <5%, 1.09–20%, and 20% (n=891) (n=372) (n=366) (n=225)

OR [95% CI] for CAC score

0–5% (n=891) 6–10% (n=372) 11–20% (n=366) 20% (n=225)

0.83 [0.59–1.21] 1.12 [0.80–1.56] 1.60 [1.16–2.21] 2.30 [1.47–3.64]

Conclusion: The yield of screening for significant CAC and occult CAD is low in the very low risk population (FRS ≤5%) but it rises in low and intermediate risk populations.

P4514 | BEDSIDE
Noninvasive prediction of functional significance of coronary artery stenosis by coronary computed tomography measurements
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Background: Coronary computed tomography (CTC) can noninvasively identify the atherosclerotic coronary stenosis and plaque characteristics, however it may
lack detection of functional significance. Fractional flow reserve (FFR) determined by invasive angiography is useful in prediction of functional significant stenosis. **Purpose:** We investigated the relationships lesion morphologies assessed by CCT and FFR values. **Methods:** We assessed 58 coronary lesions with 54 patients undergoing CCT and invasive angiography with FFR measurement. Lesion length, minimum lumen diameter, (MLD), minimum lumen area (MLA), % area stenosis, lesion vessel area, plaque burden [vessel-lumen area]/vessel area > 100, remodeling index (RI), and minimum CT-density within the plaque at the culprit site were measured by CCT. Optimal cutoff values of CCT parameters for prediction of functional significant coronary lesions (FFR ≤ 0.75) were calculated. **Results:** FFR was < 0.75 in 12 lesions (20.7%). Lesions with FFR ≤ 0.75 showed smaller MLD (mm) (2.2 ± 0.7 vs. 2.5 ± 0.2, p = 0.16), MLA (mm²) (5.7 ± 3.0 vs. 6.9 ± 2.8, p = 0.25), larger plaque burden (%) (65 ± 17.0 vs. 56 ± 15.8, p = 0.12), larger RI (1.19 ± 0.33 vs. 0.98 ± 0.28, p = 0.06), and lower CT-density (HU) (29 (9–49) vs. 45 (31–63), p = 0.08) than those without cutoff. Cutoff values to predict FFR ≤ 0.75 were 1.9 mm for MLD, 3.5 mm² for MLA, 58.0% for plaque burden, 0.83 for RI, and 29HU for minimum CT-density. Multivariate analysis showed that MLD, 3.5 mm² (odds ratio 39.4, 95% confidence intervals 3.12–497.38, p = 0.005) and minimum CT-density < 29 HU identified by CCT (odds ratio 13.4, 95% confidence intervals 1.36–132.29, p = 0.03) were independent predictors for FFR ≤ 0.75. Diagnostic power of combination of smaller MLA, < 3.5 mm² and lower CT-density < 29 HU for predicting FFR ≤ 0.75 was 25.0% of sensitivity, 97.8% of specificity, 72.0% of positive predictive value, 83.3% of negative predictive value, and 82.8% of diagnostically accuracy. **Conclusion:** Noninvasive assessment by CCT measurements, not only lesion morphologies but also plaque quality, may be useful to identify functionally significant coronary lesions.

EXCITATION-CONTRACTION COUPLING AND CONTRACTILE REMODELLING

P4515 | BENCH Rosuvastatin attenuates the tgf-beta1-induced proliferation and differentiation of cardiac fibroblast through RUNX3 activation J.Y. Qian1, D.Y. Ren1, J.F. Xu1, Y.Y. Chen1, P. Yu1, M.Q. Fu1, Y.N. Song1, Y. Lou1, J.B. Ge1, 1Zhongshan Hospital, Fudan University, Cardiology, Shanghai, China, People’s Republic of; 2Zhongshan Hospital, Fudan University, Radiology, Shanghai, China, People’s Republic of

**Background:** Rosuvastatin has been reported to play a role in cardiac remodelling. However, little is known about the effect of rosuvastatin on CFs. **Purpose:** The study aimed to investigate the effect of rosuvastatin on the proliferation and differentiation of CFs induced by TGF-β1, and the potential role of RUNX3 in this process. **Methods:** CFs, isolated from Sprague-Dawley rats, were induced by TGF-β1 treatment for 24h. RUNX3 knock down or up-regulation in CFs was performed by small interfering RNA (siRNA) or lentiviral transfection (LT), respectively. CFs, with or without regulation, were cultured with rosuvastatin or PBS followed by TGF-β1 stimulation. The proliferation of CFs was analysed by the BrdU, MTT assays and flow cytometry. The differentiation of CFs was analysed by expression of α-smooth muscle-actin (α-SMA). **Results:** The proliferation of CFs induced by TGF-β1 was decreased by rosuvastatin treatment (p < 0.05). The expression of α-SMA was also inhibited by rosuvastatin (p < 0.05). The results were further confirmed by RNA interference (RNAi) or lentiviral transfection (LT), respectively. CFs, with or without regulation, were cultured with rosuvastatin or PBS followed by TGF-β1 stimulation. The proliferation of CFs was analysed by the BrdU, MTT assays and flow cytometry. The differentiation of CFs was analysed by expression of α-smooth muscle-actin (α-SMA). **Conclusion:** Rosuvastatin inhibits the proliferation and differentiation of CFs in response to TGF-β1 stimulation by activating the RUNX3 and repressing Akt expression, with the subsequent down-regulation of β-catenin/cyclin D1 cascade.

P4516 | BENCH Mitochondria play an important role in the regulation of the nuclear Ca transient C. Seidl, E. Ge, P. von der Mark, C. Gries, R. Jeschke, M. Pfeuffer, A. Greiner, T. Aicher, M. von Seidlein, F. Ungerer, M. Py, U. Frey, H. Gerber, J. Knöpfel, M. Kwon, M. Müller, H. Ruegsegger, M. Bornfleth, C. Naumann, K. Piechulla, K. Meier, University Hospital of Würzburg, Würzburg, Germany

**Background and purpose:** Cardiac myocytes release huge amounts of Ca for each contraction. In addition, Ca within myocytes is an important second messenger for important cellular processes as the regulation of nuclear gene transcription, apoptosis and mitochondrial metabolism. Mitochondria are able to take up Ca. Therefore, they are able to shape the cytosolic Ca transient. The amplitude of nuclear Ca transients is an important factor for the regulation of gene transcription. It consists of a passive component of Ca diffusion from the cytosol and an active component through Ca release in the nucleus via IP3 receptors. Here, we investigated whether mitochondria, by Ca buffering and shaping of the passive component of the nuclear Ca transient, are able to influence the nuclear Ca transient and thus nuclear gene transcription. To answer these questions mitochondrial, nuclear and cytosolic Ca was measured using confocal microscopy. **Results:** The treatment of electrically stimulated cardiac myocytes with blockers of mitochondrial Ca uptake (Ru360: mitochondrial Ca unporter (mCU), dantrolene: mitochondrial RyR blocker (mRyR1)) alone did not alter mitochondrial Ca content. Before, we were able to show that IP3 mediated Ca release from the SR resulted in an increase in mitochondrial Ca. Thus we stimulated the myocytes with the mRyR blocker (mRyR1). When Ru360 and dantrolene were added to ang II no increase in mitochondrial Ca concentration could be observed. In a next step the influence of this blocked mitochondrial Ca uptake on nuclear Ca concentration was examined by measuring nuclear and cytosolic Ca at the same time. Here, the addition of Ru360 and dantrolene to electrically stimulated myocytes treated with ang II resulted in an increase of cytosolic and nuclear Ca concentration. Interestingly when dantrolene was added, the nuclear Ca content increased over proportional compared to the cytosolic Ca concentration, indicating that mitochondrial Ca uptake through the mRyR1 is somehow relevant for the regulation of Ca distribution in the cytoplasm. **Conclusion:** Mitochondrial Ca uptake is an important factor for the fine tuning of the cytosolic Ca transient. For the regulation of the nuclear Ca transient, mitochondrial Ca uptake via the mRyR1 plays an important role.
transition (Endo-MT) contributes to organ fibrosis and BPM7 administration helped to preserve the expression of endothelial cells markers. Myocardial fibrosis is a crucial pathogenic factor during viral myocarditis (VMC) pathogenesis. This study was designed to analyze the role of Endo-MT during cardiac fibrosis in viral cardiomyopathy and to investigate whether BPM7 administration reduced myocardial fibrosis by inhibiting Endo-MT.

**Methods and results:** BALB/c mice were randomized into three groups: sham group, VMC group and VMC+BPM7 group. Impaired cardiac function and interstitial fibrosis were found in VMC model. Endo-MT was identified in CVB3-induced VMC model using confocal immunofluorescence staining, which showed co-localization between endothelial markers and mesenchymal markers. BPM7 treatment inhibited enlarged left ventricular diameters and improved cardiac function which presented as lower LV EDd and LV EDVs, as well as higher LVEF and FS (both p < 0.05). Virus replication and interstitial fibrosis in cardiac samples after CVB3 injection were surprisingly decreased by BPM7 intervention. Double immunofluorescence staining demonstrated that ameliorated myocardial fibrosis was consistent with the decrease expression of Endo-MT. Moreover, western blot displayed that both TGF-β and β-catenin signaling pathways were activated in VMC, which were downregulated after BPM7 supplement. CO-IP illustrated that CVB3-induced formation of a protein complex between β-catenin and smad3, which further promoted the Endo-MT in injury cardiac samples. BPM7 intervention attenuates Endo-MT by breaking down these protein complexes and then inhibits the downstream of β-catenin signalling pathway in VMC.

**Conclusion:** Endo-MT was crucial in CVB3 mediated myocardial remodeling and BPM7 attenuated cardiac fibrosis through inhibiting the interaction between smad3 and β-catenin during Endo-MT in viral cardiomyopathy. Conjoint activation of TGF-β and β-catenin pathway may coordinate induction of Endo-MT and promote myocardial fibrosis, which suggest a potential new therapeutic approach during CVB3 myocarditis.

### P4519 | BENCH

Human cardiac fibroblasts increase SR-dependency of induced pluripotent stem cell-derived cardiomyocyte calcium handling by modulating SR uptake and SERCA2a expression via direct physical contact

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**Introduction:** Cardiac fibroblasts can influence cardiomyocyte structure and function through direct physical interaction and/or by the secretion of soluble factors. Here we assess the relative importance of these different modalities of interaction in terms of their effects on cardiomyocyte electrophysiology.

**Methods:** Ventricular fibroblasts were isolated from the explanted hearts of diabetics (DC) patients (n=4) and cultured with human induced pluripotent stem cell-derived cardiomyocytes (iPS-CMs) at a ratio of 2:1 for 24 hours in three groups: iPS-CMs with fibroblast conditioned medium (CMed), co-cultured in transwells to allow bi-directional paracrine communication but prevent direct physical contact (CC), and iPS-CMs in direct contact with fibroblasts (DC). iPS-CMs alone were used as control. Ca2+ transients and action potentials were recorded optically using fluo-4 AM and di-8-ANEPPS. Data are presented as percentage change from control where appropriate.

**Results:** iPS-CM calcium transient duration was significantly reduced in DC vs control (−8.4±2.2% n=12 p < 0.05). iPS-CMs in DC displayed a greater dependence on SR uptake and SERCA2a expression via direct physical contact.

**Conclusion:** Endo-MT was crucial in CVB3 mediated myocardial remodeling and BPM7 attenuated cardiac fibrosis through inhibiting the interaction between smad3 and β-catenin during Endo-MT in viral cardiomyopathy. Conjoint activation of TGF-β and β-catenin pathway may coordinate induction of Endo-MT and promote myocardial fibrosis, which suggest a potential new therapeutic approach during CVB3 myocarditis.

### P4520 | BENCH

Reparative fibrosis is impeded in MK5 deficient mice following myocardial infarction

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**Background:** The adverse cardiac remodelling that occurs following left ventricular (LV) myocardial infarction (MI) is a complex process involving pathological changes in both cardiac and non-cardiac cells which contribute to the development of LV dysfunction and heart failure that develops after MI. As MK5 mRNA is highly expressed in heart and we have shown previously that reactive (interstitial) fibrosis is reduced in heterozygous MK5-deficient (MK5+/−) mice, MK5 may play a role in cardiac remodelling.

**Methods:** Twelve-week-old MK5+/− and wild-type littermate (MK5+/+) mice underwent ligation of the left anterior descending coronary artery (LAD). Sham mice underwent the identical procedure but the coronary artery was not occluded. LV structure and function were assessed before and 7 days post-LAD by transthoracic echocardiography (Echo). Scar size was assessed by both magnetic resonance imaging (MRI), before and 8 days post-LAD and Masson Trichrome staining. Mice were sacrificed 8 or 21 days post-surgery (n=4–34).

**Results:** Eight days post-LAD, survival rates for MK5+/+ and MK5+/− mice did not differ significantly. In contrast, survival rates did differ over 21 days: the median survival of MK5+/− mice was 9 days post-LAD. Echo revealed similar increases in LV end diastolic diameter, myocardial performance index, and wall motion score index in MK5+/− and MK5+/−/− mice compared to their respective sham. In the infarcted hearts, fibroblast to cardiomyocyte ratio was significantly reduced in MK5+/− compared to MK5+/−/− mice (30% vs. 22%). MRI indicated similar scar size in MK5+/− and MK5+/−/− mice 8 days post-MI. Histological analysis revealed a significant decrease in the percentage of infarction in MK5+/−/− mice compared to MK5+/−/− mice. Cardiomyocyte diameter and scar area did not significantly differ between the 2 ligated groups. Surprisingly, angiogenesis in the peri-infarct zone was significantly greater in MK5+/− compared to MK5+/−/− mice.

**Conclusion:** MK5 may play a role in scar maturation following myocardial infarction.

### P4521 | BENCH

VCP746: a cardioprotective adenosine receptor agonist with minimal haemodynamic effects


Adenosine receptor (AR) activation provides powerful cardioprotection. However, it is also associated with adverse effects in the form of profound heart rate (HR) and blood pressure (BP) reduction which has hindered the transition of AR agonists into the clinic. The aim of this study was to determine the effect of VCP746, a novel AR agonist on infarct size (IS), HR and BP and compare it to other adenosine agonists, 5′-N-Ethylcarboxamidoadenosine (NECA) and N6-Cyclopentyladenosine (CPA). Two animal models were used: 1) A Langendorff-perfused isolated rat heart model subjected to 30 min/60 min ischaemia/reperfusion (IR). Hearts were then incubated in 1% 3,3′,5-triphenyltetrazolium chloride (TTC) to determine IS. 2) An acute myocardial infarction (MI) rat model subjected to 30 min/120 min of IR. Hearts were then infused with 5% Evans Blue followed by incubation in 1% TTC to determine IS. IS was reduced in the isolated rat heart with VCP746 treatment (1 μM) and CPA (100 μM) at reperfusion compared to the vehicle-treated group (14.7±2.6% and 10.1±1.7% vs 32±2.4% of area at risk (AAR), respectively; n=5–6, P<0.05). HR in hearts treated with VCP746 at reperfusion were unaffected (205±3 vs 219±9 BPM; n=5, P>0.05), unlike in CPA-treated hearts (70±7 vs 219±9 BPM; n=5, P<0.05). In MI rats, IS was reduced following VCP746 (80 μg/kg) and NECA (10 μg/kg) treatment at reperfusion compared to the vehicle group (Table; n=4–8, P<0.05). The effect of VCP746 on HR and mean arterial pressure (MAP; Table; n=6–8, P<0.05 vs vehicle) while NECA significantly reduced HR and MAP (Table; n=6–8, P<0.05 vs vehicle). The results suggest that unlike NECA and VCP746, heart rate is not a limiting factor of effects that are cardioprotective, displaying a desired effect without the adverse effects. The infarct-sparking effect of VCP746 is also likely to be mediated through the A1AR.

**Effect of adenosine agonists and antagonist on infarct size and haemodynamics in MI rats**

<table>
<thead>
<tr>
<th>Vehicle</th>
<th>DPCPX (100 μg/kg)</th>
<th>VCP746 (80 μg/kg)</th>
<th>NECA (10 μg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IS (% AAR)</td>
<td>52.3±2.0</td>
<td>50.5±3.9</td>
<td>30.7±2.0 *</td>
</tr>
<tr>
<td>HR (BPM)</td>
<td>437±16</td>
<td>405±17</td>
<td>465±15</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>99±1.6</td>
<td>91.5±2.6</td>
<td>107±2.8</td>
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</tbody>
</table>

*P<0.05 vs vehicle; n=6–8; mean ± SEM.*
P4524 | BENCH
High-density lipoproteins increase myocardial salvage and attenuate microvascular obstruction by modulating toll-like receptor innate immune signaling

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Background: In the present study, we investigated the clinical and molecular effects of apoA1-rich HDL (aHDL) on a preclinical experimental model of acute myocardial infarction (MI).

Methods: Pigs were randomized to 2 intravenous infusions 3 days apart of aHDL (15mg/kg) or vehicle-saline. One day after the last dose all pigs underwent a 60 min closed-foreshortened coronary artery occlusion followed by reperfusion (exper- imental MI). Left ventricular ejection fraction (LVEF), and regional myocardial function (PCI's) were evaluated. LV diastolic function as assessed by 3T cardiac magnetic resonance imaging (CMR) 3 days thereafter. We evaluated myocardial neutrophil infiltration and peripheral blood mononuclear cells (PBMC)- and myocardial-toll-like receptor (TLR) activity.

Results: aHDL-recipient animals showed, as compared to vehicle, a 2-fold improvement in myocardial salvage index (0.43±0.04 vs 0.18±0.02; P<0.05) and 42% reduction in infarct size (13.8±1.3% vs 23.9±1% LV; P<0.05) despite comparable myocardial-at-risk (18.1%±1.4% vs 21.3%±1.4% LV). MVO was attenuated in aHDL-recipients (P<0.05 vs vehicle) and directly correlated with the extent of necrosis (P<0.05; R=0.63). LV volumes improved by 14% in aHDL-recipient animals (P<0.05 vs vehicle). HDL-infusion significantly reduced neutrophil recruitment to the infarcted myocardium which, in turn, was associated with the attenuation of myocardial TLR signaling (both, Myd88-dependent and TRIF-dependent pathways) and the prevention of MI-induced TLR activation in PBMC. aHDL also exhibited antioxidant effects and modulated the SAFE- and NF-kB signaling pathways.

Conclusion: In the onset of coronary ischemia, aHDL attenuates the deleterious effects of myocardial infarction by increasing myocardial salvage and improving cardiac perfusion. aHDL exerts cardiac immunomodulation by regulating neutrophil infiltration through TLR signaling.

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P4526 | BENCH
Cardioprotective effect of cpmg induction by sgc activator, bay60-2770, in ischemia-refusion injured rat heart

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Objective: Mitochondria play critical roles in both the life and death of cardiac myocytes. During ischemia and reperfusion (IR) injury, cGMP-mediated alterations of mitochondrial proteins by sgc activator have not been assessed up to now.

Methods: Ischemic reperfusion (IR) injured hearts have some limitations under the pathological conditions which are reduced NO generation and oxidized heme in sgc. To prove the cardioprotective effect of NO-independent and haem-independent sgc activator, which potentiates NO/CGMP signaling, we treated BAY60-2770 (4-(((4-carboxybutyl) (2-(5-fluoro-2-(4'-(trifluoromethyl) biphenyl-4-yl) methoxy) phenyl) ethyl) amino) methyl) benzoic acid) in IR injured rat heart. IR injury was established by occlusion of LAD for 40 min and reperfusion for 7 days, and the effect of sgc activator (5 mg/kg, Bay 60–2770) on myocardial protection in the IR injury was assessed by echocardiography and TCT staining.

To investigate the novel cardiac protective mechanism of sgc activator, 5 mM and 5 μM of Bay 60–2770 were perfused into isolated rat heart in Langendorf system. After 10 or 30 min reperfusion with BAY 60–2770, cGMP and cAMP concentration and PKG and GSK3β activation statuses were examined. In addition, 1 μM KTS823, 100 μM 5-HD, and 200 μM L-NAME were perfused with 5 mM Bay 60–2770 to explain the mechanism of sgc activator-mediated alterations of mitochondrial protein levels.

Results: In IR injured rat heart, sgc activator limits infarct size (53.0±11.3% in IR vs. 17.9±0.6% in Bay 60–2770 treated). Echocardiography shows that the reduced ejection fraction (89.5±2.4% vs. 77.3±6.8% in normal and IR hearts, respectively) by IR was recovered by sgc activator (84.4±2.2% vs. 85.6±2.4% in Bay 60–2770). Tissue samples from BAY 60–2770 (5 mM and 5 μM) perfused heart had cGMP levels about 2-fold higher than IR (17.2±5.7 μM and 5 μM in 5 mM vs. 38.49±10.95 fmol/mg tissue in 5 μM) without any alteration of cAMP concentration. PKG activity in myocardium after reperfusion was increased by sgc activator. The decreased protein level of CyP-D under BAY 60–2770 administration was recovered by KT-5823 in isolated myocardium.

Conclusion: Our results suggest that infarct size limitation by Bay 60–2770 was associated with elevated cGMP levels and further alteration of PKG-mediated mitochondrial protein statuses. Thus we propose that sgc activator protects mitochondria against IR injury.

P4527 | BENCH
Cardioprotective effects of inorganic phosphate in an ischemia-referession model

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Objectives: Ischemia-referession damage (IR) has been explained by overload of calcium (Ca2+) and overproduction of reactive oxygen species (ROS). Inorganic phosphate (P04), can complex Ca2+ and preserve cardiac function. We found biochemical evidences of protection at mitochondrial level and we decide to search if they were accompanied by improvement in clinical parameters like electric stability, myocardial mobility index, ventricular systolic function and survival.

Methods: We used 3 groups of 10 rats each (control, PO4 and non-PO4). PO4 group received 60μl of 10 mM PO4 five minutes before coronary occlusion. Electrical activity and haemodynamic stability were monitored. Echocardiographic studies were performed initially, 3 minutes after reperfusion and at 20 minutes. At the end of the study we collected the heart and through centrifugal differentiation, we obtained mitochondria. In them we measure free Ca2+, Ca2+ transport and lipoperoxidation.

Results: PO4 group had better survival (80% vs. 10%), mobility index during ischemia and 3 minutes reperfusion (2.71±0.756 vs. 1.50±0.837 and 4.40 vs. 1.67±1.19), and a better ejection fraction during ischemia, 3 min. and 20 min. af- ter reperfusion (62.1%±19.2 vs. 28.3%±14.2; 85.2%±6.3 vs. 43%±11.3 and 71.9%±31.8 vs. 25.7±9.38). We also found that free Ca2+ levels were similar between control and PO4 groups (196±27 nM and 179±58 nM) in contrast to non-PO4 where Ca2+ was higher (305±14 nM). Preserved function of Ca2+ transport and an almost absent lipoperoxidation were observed.

Conclusions: Pre-treatment with P04 decreases life threatening arrhythmias, mobility alterations and reperfusion damage. For the first time, it is demonstrated besides biochemical measurements its functional effects.

P4528 | BENCH
Urocortin-1 preserve XIAP and CD40-ligand to reduce ischemia-referession-induced cardiac myocyte apoptosis via the activation of ERK1/2 through EPAC

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Background: Urocortin-1 (Ucn-1) is a potent endogenous peptide that protects heart from ischemia and reperfusion (IR) injuries. Ucn-1 is known to improve post-ischemic cardiac performances, which include recovery of heart contraction, prevention from intracellular CA2+ overload and cardiac cell death. However, Ucn-1 role in the transcription of specific genes related to survival signaling pathway has not been fully defined.

Purpose: The aim of this study was to determine the pathways implicated in the improvement of cardiomyocytes survival induced by Ucn-1.

Methods: To determine hemodynamic parameters, rats hearts were perfused in isolated Langendorff system and were exposed to 40 min of ischemia followed by 60 min of reperfusion in the presence or not of Ucn-1. The signaling pathways involved in Ucn-1 effects were examined by the use of inhibitors of PKA, Epac and the Extra-cellular Signal–Regulated Kinases 1/2 (ERK1/2). Furthermore, we used isolated cardiomyocytes. Cardiomyocyte survival in Ucn-1 and ischemia reperfusion was followed by 3 h of reperfusion to study the cell survival and apoptosis. Annexin-V/PI staining, microarray, western blotting and qRT-PCR approaches were used to explore the implication of Epac, ERK1/2, BAD, CD40-ligand (CD40-lg) or X-linked inhibitor (XIAP) in Ucn-1 regulation of cardiac myocyte survival.

Results: We found that Ucn-1 application before ischemia and at the onset of reperfusion fully recovered heart contractility and prevented the increase of Left End Ventricular Diastolic Pressure (LVEDP). These beneficial protective effects were independent of protein kinase A (PKA) but were significantly reduced when hearts were co-treated with the inhibitors of Epac and ERK 1/2. Moreover, Ucn-1 protected cardiac myocyte from reoxygenation injury, as evidenced by the augmentation of cell survival and the decrease of cell necrosis. Ucn-1 stimulated the increase of the expression of BAD, CD40-lg and XIAP proteins that are implicated in apoptosis and cell survival. Finally, we determined that Ucn-1 regulated CD40-lg and XIAP through Epac and ERK 1/2 activation, meanwhile it preserved BAD expression independently of ERK 1/2 signaling pathway.

Conclusions: Our data confirm that Ucn-1 efficiently preserved hearts hemodynamics and cardiomyocytes from IR damage by regulation of the signaling pathways involved in cell survival and apoptosis which involve Bad, Epac and XIAP regulation.

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P4529 | BEDSIDE
The damaging nature of extracellular RNA in ischemia-referession injury: prevention of cardiomyocyte death and heart failure by RNAse1

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During acute myocardial infarction, cardiomyocyte death occurs and has a predominant impact on the quality of life and survival of patients suffering from coronary artery disease, the most eminent single cause of death in industrialized countries. Due to the occlusion of coronary vessels by arteriosclerotic plaque material, largely decreased oxygen supply (termed ischemia) of the myocardium determines the disease outcome. Due to reopening/reperfusion of stenosed vessels, a major organ damage remains. The initial mechanistic triggers of this myocardial ischemia/reperfusion (IR) injury remain largely unexplained. Here we show that factors from the damaged cardiac tissue itself, in particular extracellular vesicles (eRNA) and tumor necrosis factor-alpha (TNFα) contribute to IR injury. Following myocardial ischemia/reperfusion (IR) in mice or IR induced in the isolated Langendorf rat heart, increased eRNA levels were found together with cardiac injury markers. Likewise, eRNA was released from cardiomyocytes under

ECHO, EKG and free mitochondrial calcium
hypoxia and subsequently induced TNF-α liberation by activation of TNF-α converting enzyme (TACE) and provoked cardiomyocyte death. Conversely, TNF-α promoted eRNA release especially under hypoxia, feeding a vicious cell damaging cycle during I/R. Administration of RNase1 or TAPI (TACE-inhibitor) prevented cell death and myocardial infarction. Likewise, RNase1 significantly reduced TNF-α mediated mitochondrial permeability transition pores as well as oxidative damage in cardiomyocytes. Finally, a dramatic increase of endogenous vascular RNase1 in human subjects was achieved by inducing non-invasive intermittent limb I/R using an external occluder, thereby supporting the impact of the eRNA/RNase system in remote ischemic preconditioning.

Together, RNase1 as well as inhibition of TACE provide novel therapeutic regimen to interfere with the adverse eRNA-TNFα-ergic interplay and significantly reduce or avoid the adverse outcome of ischemic heart disease. The uncovered fundamental pathomechanisms are likely operative in other organs and tissues as well, such that the proposed interventions offer new concepts for general cyto-protection in medicine.

**P4530 | BENCH**

**Physical exercise exerts beneficial effects on walking capacity and polarization state of circulating monocytes and muscular macrophages in a mouse model of intermittent claudication**

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**Background and Introduction:** Physical exercise (PE) therapy is indicated to improve walking capacity in patients with intermittent claudication (IC) due to atherosclerotic stenosis of lower extremity arteries. The effect of PE on arterial stenosis on walking capacity is unknown.

**Purpose:** To determine protective effects of PE prior to peripheral arterial stenosis using a mouse model of IC.

**Methods:** Atherosclerotic C57BL6/J ApoE−/− mice were allowed free access to a voluntary wheel running (WR; daily average running distance: 4.2±1.6 km) or remained sedentary (SED) for 5 weeks before unilateral iliac artery ligation. Thereafter, the two groups were kept sedentary for 5 weeks. Maximal running distance and time until exhaustion were determined using a treadmill running test. Hindlimb perfusion was assessed using laser Doppler imaging. Real-time RT-PCR was used to determine macrophage phenotypes (pro-inflammatory M1 versus anti-inflammatory M2 macrophages) in hindlimb quadriceps muscle. Flow cytometry was employed to analyse blood circulating monocyte subsets (Ly6Chigh inflammatory monocytes versus Ly6Cloxidation resistant monocytes).

**Results:** Maximal walking distance and time were significantly improved by 23% and 13%, respectively, in WR mice compared to SED mice at 5 weeks post-arterial ligation. Compared to SED mice, ischemic hindlimb perfusion in WR mice was significantly increased at week 3 (+40%), week 4 (+50%) and week 5 (+28%) post-arterial ligation. In WR mice, mRNA expression of M2 marker CD206 was increased in ischemic muscle significantly increased (1.7-fold versus non-ischemic muscle at week 5 post-arterial ligation) whereas no significant change was observed in SED mice. M1 marker CD11c mRNA expression did not significantly differ between ischemic and non-ischemic muscle both in WR and SED mice. WR significantly increased the resident monocyte Ly6Cloxidation in the circulation (+45% versus SED mice at 5 weeks post-arterial ligation).

**Conclusion:** PE prior to peripheral arterial stenosis ameliorates impaired walking capacity subsequent to arterial stenosis. Underlying potential mechanisms include adaptation of the ischemic hindlimb perfusion and a positive effect on circulating monocytes and local muscular macrophages polarization state. Our findings support the role of PE in primary prevention of IC.

**METABOLISM AND METABOLIC SYNDROMES**

**P4531 | BENCH**

**N-acetylcysteine promotes adaptive cardiac remodelling through enhancing fatty acid oxidation in the murine heart**

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**Background:** Hearts under chronic pressure-overload stress undergo an initial remodelling that is adaptive however they eventually succumb to failure. The unbalanced ER-mediated energy extraction, opening of mitochondrial permeability transition pores as well as oxidative damage in cardiomyocytes. Finally, a dramatic increase of endogenous vascular RNase1 in human subjects was achieved by inducing non-invasive intermittent limb I/R using an external occluder, thereby supporting the impact of the eRNA/RNase system in remote ischemic preconditioning.

Together, RNase1 as well as inhibition of TACE provide novel therapeutic regimen to interfere with the adverse eRNA-TNFα-ergic interplay and significantly reduce or avoid the adverse outcome of ischemic heart disease. The uncovered fundamental pathomechanisms are likely operative in other organs and tissues as well, such that the proposed interventions offer new concepts for general cyto-protection in medicine.

**Purpose:** The aim was to identify Nox4-driven mechanisms that enhance adaptive cardiac remodelling processes.

**Methods:** To identify pathways that might be driving Nox4-dependent effects a proteomic screen of heart tissue from cardiac-targeted Nox4-overexpressing mice, Nox2-overexpressing mice and controls was undertaken using 2D-DIGE. This was complemented by 1H-NMR metabolomic analyses of heart tissue. Further studies were undertaken to explore the Nox4-dependent effects on substrate metabolism and bioenergetics in murine hearts using isolated working hearts and 31P-NMR. Finally endogenous Nox4-dependent effects on substrate handling were determined in cultured cardiomyocytes by perturbing the levels of Nox4 and examining extracellular flux with Seahorse XF24.

**Results:** Proteomic identified glycolysis and fatty acid oxidation as the most upregulated pathways altered by Nox4. Metabolomics also indicated significant differences in metabolites related to these pathways (e.g. 2.2 fold increase in acetyl/carnitine concentration, p=0.002). Nox4 hearts demonstrated a significantly increased capacity for FAO compared to wild-type hearts (3.6 fold increase, p=0.01), which was sustained under pressure-overload. Cardiac energetics under basal or pressure-overload indicated that a reliance on FAO was not detrimental to cardiac function. Extracellular flux analyses confirmed the Nox4-dependent effects in augmenting FAO in isolated cardiomyocytes.

**Conclusions:** Nox4 is important in modulating metabolism, specifically enhancing FAO in the murine heart. This may help to explain the cardioprotective effects of Nox4 but also provides insight into novel ROS-mediated mechanisms that can regulate metabolism.

**P4532 | BEDSIDE**

**Cystatin C is not causally associated with diabetes or the metabolic syndrome**

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**Background:** We recently reported a relationship between plasma levels of cystatin C and increased risk of incident diabetes (OR 1.71, 95% CI 1.13–2.59) as well as CVD (OR 1.75, 95% CI 1.12–2.74). The purpose of the present study was to investigate whether this association was consistent across different subgroups of the general population.

**Methods:** We studied the effect size of the strongest genome wide association study derived cystatin C SNP (rs13038305) on plasma cystatin C in the now completed MDC-CC-re-examination (n=3,385) and thereafter examined the association between plasma cystatin C as well as rs13038305 with incident diabetes (436 cases of diabetes and 2840 controls). The association of rs13038305 and incident MetS (610 cases of MetS and 2300 controls) was similarly investigated in the whole MDC-CC-re-exam. We also attempted to replicate our previously shown association of cystatin C with incident MetS in subjects from the MDC-CC-re-examination (147 cases and 709 controls) that were not included in our previous report.

**Results:** In the entire MDC-CC-re-exam, the age-adjusted OR was 1.09 (95% CI 0.84–1.43), p=0.647. In the replication cohort of MDC-CC-re-exam, the OR (95% CI) for incident MetS in subjects belonging to quartiles 1, 2, 3, 4 of plasma cystatin C was 1.00 (0.74–1.35), 0.95–1.35) and 1.05 (0.84–1.32), p=0.647, respectively.

**Conclusion:** We were able to replicate our previously shown association between high levels of cystatin C and increased risk of future development of MetS. However, a causal involvement of cystatin C in the aetiology of MetS or diabetes seems unlikely since genetic elevation of plasma cystatin C was not significantly related to incident these diseases.

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**P4533 | BEDSIDE**

**Platelet to lymphocyte ratio as a novel indicator of inflammation associated with the presence and severity of metabolic syndrome**

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**Background:** Metabolic syndrome (MetS) as a cluster of several cardiovascular metabolic components is rapidly growing public-health problem worldwide and significantly associated with poor cardiovascular outcomes. Increased visceral adiposity activates important pathways connecting low-grade chronic inflammation, oxidative stress and insulin resistance. Recently, platelet to lymphocyte ratio (PLR) has been evidenced as a novel indirect inflammatory marker. Therefore, for the first time, we aimed to investigate the association of PLR with both the presence and severity of MetS.

**Methods:** In this cross-sectional study, a total of 1146 participants were enrolled (n=539 with MetS and n=607 without MetS). MetS was defined according to NCEP-ATP III criteria. Independent predictors of MetS were determined by logistic regression analysis. PLR was calculated from complete blood count.

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**Ischaemia and protection / Metabolism and metabolic syndromes 779**

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Results: MetS (+) group revealed significantly higher PLR and C-reactive protein (CRP) levels as compared to MetS (−) group (p < 0.05). There was a graded relationship between number of MetS components and PLR (p < 0.05). Also, PLR was positively correlated with CRP level (r=0.163, p < 0.001). In multivariate regression analysis, PLR [1.121 (1.113–1.135), p < 0.001], CRP [1.044 (1.029–1.060), p < 0.001] and age [1.030 (1.017–1.043), p < 0.001] were remained as independent predictors for the presence of MetS.

Conclusion: Our findings showed that increased PLR was significantly associated with both the presence and severity of MetS which was linked to systemic inflammation on the basis of correlation between PLR and CRP. As PLR is an easily available, simple and cheap indirect indicator of inflammation, it can be used in clinical practice as a predictor of MetS.

P4534 | BEDSIDE
Increased serum YKL-40 is a novel marker of metabolic syndrome in adult patients
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Background: Metabolic syndrome (MS) is defined by a cluster of interdependent physiological, biochemical and clinical risk factors and linked to a state of chronic low grade inflammation. YKL-40 is known as an inflammatory glycoprotein which is secreted by various cell lines during inflammation. Thus, we aimed to assess the association of serum YKL-40 levels with the presence and severity of MS.

Methods: In this cross-sectional study, a total 190 consecutive patients (n=124 MS present and n=66 MS absent) were enrolled. MS was defined according to NCEP-ATP III criteria. Serum YKL-40 and hs-CRP levels were measured for all participants. Independent predictors of MS were determined by logistic regression analysis.

Results: Serum YKL-40, hs-CRP and white blood cell count were significantly higher in the MS present group (p < 0.05). There was a graded relationship between increasing number of MS components and serum YKL-40 level (p < 0.05). Also, serum YKL-40 level was positively correlated with hs-CRP level (r=0.431, p < 0.001) and white blood cell count (r=0.240, p=0.001). In multivariable regression analysis, YKL-40 was the best predictor for the presence (p < 0.001) and age (p=0.001) of MS. There was a graded relationship between increasing number of MS components and serum YKL-40 level (p < 0.001) and white blood cell count (p=0.001) were remained as independent predictors for the presence of MS. Those findings may implicate that, serum YKL-40 may be a novel and useful indicator for MS.

Conclusion: In this study, we demonstrated that serum YKL-40 level was significantly associated with the presence of MS. Those findings may implicate that, serum YKL-40 may be a novel and useful indicator for MS.

P4535 | BENCH
Factor Xa inhibits brown adipose tissue function and induces systemic metabolic dysfunction in obesity
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Brown adipose tissue (BAT) is a highly-vascularized organ abundant with mitochondria that produce heat through uncoupled respiration. Obesity causes BAT dysfunction, but the mechanism is largely unknown. We have recently reported that obesity causes capillary rarefaction and functional hypoxia in BAT, leading to a BAT “whitening” phenotype that is induced by mitochondrial dysfunction and lipid droplet accumulation, contributing to impaired systemic glucose metabolism. Coagulation factor Xa (FXa) is the activated form of FX and has a pivotal role for the regulation of coagulation system. There is evidence that FXa is involved in inflammatory responses, via the activation of its receptors, proteinase-activated receptor1 (PAR1) and PAR2. Increasing evidence shows that PAR1 contributes to tissue remodeling in various models such as liver fibrosis, restenosis and neointima formation in response to vascular injury, fibrotic lung disease, kidney fibrosis, and cardiac remodeling. Here we show the previously unknown role of FXa in promoting systemic metabolic dysfunction via the inhibition of BAT function in dietary obesity. We generated an obesity model by imposing a high fat high sucrose (HFHS) diet on C57BL/6Ncr mice. Mice fed the HFHS diet for eight weeks since four weeks of age showed a marked increase in circulating FXa level. To test the metabolic roles of FXa in obesity, we treated the mice with an FXa inhibitor. Treatment with the FXa inhibitor led to a non-significant reduction in body weight in both the chow and HFHS fed groups and improved systemic insulin resistance upon dietary obesity. The addition of FXa into brown adipose cell-line markedly increased mitochondrial reactive oxygen species (ROS) and reduced mitochondrial membrane potential. FXa treatment also inhibited mitochondrial respiration and induced apoptosis. The inhibition of PAR1 ameliorated FXa-induced mitochondrial ROS production. These results suggest that increased production of FXa associated with obesity promotes systemic metabolic abnormalities by inducing BAT dysfunction. The maintenance of BAT homeostasis via the inhibition of FXa-PAR1 signaling would become a new therapeutic target for obesity and diabetes.

P4536 | BENCH
The phosphodiesterase-5 inhibitor vardenafil protects against diabetic cardiomyopathy in type-2 diabetes mellitus
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Purpose: Diabetes mellitus (DM) is associated with a special heart disease, termed diabetic cardiomyopathy. The pathophysiological role of cyclic guanosine monophosphate (cGMP) signalling has been intensively investigated in DM. The phosphodiesterase-5 (PDE5) inhibitor vardenafil has been shown to exert cytoprotective effects. We investigated the effect of chronic inhibition of PDE5 by vardenafil in type-2 DM related cardiomyopathy.

Methods: For type-2 DM Zucker Diabetic Fatty (ZDF) mice, homozygous (fa/−) were used. Heterozygous (fa/+) or homozygous dominant (+/+) ZDF Lean (ZDLF) rats served as controls. Animals received either vehicle (ZDFL, ZDF) or 10mg/kg BW vardenafil per os (ZDFLVard, ZDFVard) from 7 to 32 weeks of age. Cardiac morphology was followed by echocardiography. Left ventricular (LV) function was assessed using a pressure-volume (PV) conductance microcatheter system. Gene expression analysis of atrial natriuretic factor (ANF; qRT-PCR), cardiomyocyte diameter/tibia length (CD/TL) and Masson’s staining (fibrosis score (FS)) were used to prove pathological myocardial hypertrophy.

Results: Cardiac hypertrophy (echocardiography: LV anterior wall thickness in systole (LVAVS): 2.81±0.1 mm; relative wall thickness (RWT): 0.49±0.02; LVmass/TL: 0.320±0.01 g/cm; CD/TL: 3.53±0.02 μm/m; ANF: 3.04±0.26 vs ZDFL (LVAVS): 2.53±0.04 mm; RWT: 0.43±0.02; LVmass/TL: 0.23±0.004 g/m; CD/TL: 3.09±0.02 μm/m; ANF: 0.92±0.17); p<0.05) and fibrotic remodelling (FS: 1.05±0.09 vs ZDFL (0.57±0.13); p<0.05) have been observed in ZDF. Drug treatment significantly decreased myocardial hypertrophy and fibrosis (LVAVS: 2.47±0.05 mm; CD/TL: 3.15±0.02; ANF: 1.39±0.21; FS: 0.59±0.08 vs ZDFP−0.05) in DM. PV analysis showed impaired diastolic function and increased cardiac stiffness (τ: 8.62±0.34 ms; slope of end-diastolic pressure volume relationship (EDPVR): 0.078±0.02 mmHg/ml vs ZDF (τ: 8.18±0.13 ms; EDPVR: 0.045±0.003 mmHg/ml); p<0.05) while contractility parameters and blood pressure remained unchanged in ZDF. Vardenafil improved diastolic parameters (τ: 8.62±0.34 ms; EDPVR: 0.078±0.02 mmHg/ml vs ZDF: p<0.05). Vardenafil did not have effect in ZDFL.

Conclusions: We reported that chronic administration of vardenafil prevents DM associated myocardial complications. PDE5 inhibition might be an important target to improve the cardiovascular outcome in diabetic patients in the future.
Peripheral gamma-aminobutyric acid (GABA) signaling in brown adipose tissue induces metabolic dysfunction in obesity

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Accumulating evidence suggests that adult humans possess active brown adipose tissue (BAT) that may contribute significantly to systemic metabolism because of its high energy consumption capacity. Recently, we demonstrated that metabolic stress induces BAT hyoxia, inhibits mitochondrial function and is causal for the development of BAT “whitening” and systemic metabolic dysfunction in murine obese models. Various neurotransmitters are known to be involved in the maintenance of BAT homeostasis. Among them, the gamma-aminobutyric acid (GABA) signaling in the central nervous system is well accepted to have anti-obesity effects through the activation of the sympathetic nervous system. Here we show the previously unknown role of peripheral GABA signaling in the development of systemic metabolic dysfunction in obesity.

We generated an obese model by imposing a high fat/high sucrose (HF/HFS) diet on C57BL/6NCr mice. Mass spectrometry analysis demonstrated a significant increase in the BAT GABA level in the dietary obese model. Addition of GABA into drinking water led to a marked increase of body weight, induced BAT whitening, on C57BL/6NCr mice. Mass spectrometry analysis demonstrated a significant increase of systemic metabolic dysfunction in obesity. Mitochondrial calcium is important for the maintenance of mitochondrial homeostasis, however calcium overload is reported to inhibit mitochondrial function. Treatment of BAT cells with GABA markedly increased mitochondrial calcium level, promoted the production of reactive oxygen species (ROS) and inhibited mitochondrial respiration. These results indicate that peripheral GABA contributes to the development of systemic metabolic dysfunction by inhibiting BAT function in obesity. The inhibition of peripheral GABA signaling would become a new therapeutic target for obesity and diabetes.

P4538 | BENCH
Chronic vagal nerve stimulation exerts glycemic control and cardioprotection via preventing cardiac mitochondrial dysfunction in obese-insulin resistant rats

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Background: Obese-insulin resistance exhibits not only adverse metabolic effects, but also cardiac dysfunction due to decreased parasympathetic activity, mitochondrial dysfunction, increased oxidative stress and apoptosis. Although an augmentation of parasympathetic activity by vagus nerve stimulation (VNS) exerts cardioprotection in chronic heart failure and myocardial infarction, the effect of VNS in obese-insulin resistant rats remains to be determined.

Purpose: We hypothesized that chronic VNS provides beneficial effects not only on glycemic control, but also on cardioprotection by exerting anti-apoptosis, anti-oxidative effect and cardiac mitochondrial protection.

Methods: Thirty-six rats were fed with high-fat diet for 12 weeks. Then, all rats were divided into Sham and VNS groups (n=18/group). VNS (20 Hz, 500-µs pulse width, 0.5-0.75 mA, 14-5 ON time and 48-5 OFF time) was applied for 12 weeks. Echocardiography, blood pressure and heart rate variability (HRV) were examined at 4, 8 and 12 weeks of VNS treatment. Blood samplings were collected for determining metabolic parameters. At the end, the heart was removed for determination of apoptosis and cardiac mitochondrial function.

Results: Chronic VNS for 12 weeks improved insulin sensitivity, increased %fraction showing decreased L/H ratio and reduced ROS production (Fig). VNS also reduced cardiac Bax/Bcl-2 ratio, and decreased cardiac mitochondrial ROS production, mitochondrial depolarization and swelling, compared with sham group.

Conclusion: Chronic VNS therapy exerts effective glycemic control and improves left ventricular contractile function via its ability to antagonize apoptosis, oxidative stress and cardiac mitochondrial dysfunction.

Acknowledgement/Funding: a NSTDA Research Chair Grant (NC), the Thailand Research Fund RTA5580006 (NC), BRG5780016 (SC), TRG5780002 (SK), CMU Center of Excellence Award (NC)

P4539 | BENCH
Intercellular between chromatom modifying enzymes SUV39H1, SRC-1 and JMJD2C triggers redox signalling and vascular dysfunction in obesity

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Background: Oxidative stress is a prominent feature of cardiometabolic disturbances leading to endothelial dysfunction and atherosclerosis. Understanding redox signalling in the context of metabolic disease is of paramount importance for the development of mechanisms-based therapeutic strategies. Adverse chromatin remodelling is emerging as a key driver of vascular damage and may play a role in this setting.

Purpose: In the present study we investigate whether epigenetic cues are involved in obesity-related vascular disease phenotype.

Methods and results: SUV39H1 knockout mice (SUV39H1−/−) and genetically obese mice (LepOb/Ob) were used for the study. Whole-body mitochondrial genome was isolated from 20 obese and 20 age-matched healthy subjects (age 48.5±9.6 years, p<NS, respectively). Expression profile of chromatom modifying enzymes was performed by real-time PCR array in SVFA, and expressed as fold change (FC) vs. controls. Mitochondrial density in BAT tissue was measured on H&E and endothelium-dependent relaxations to acetylcholine (Ach, 10−9 to 10−4 mol/L) were determined by ESR spectroscopy and organ chamber experiments, respectively. Chromatin immunoprecipitation (ChIP) was employed to study histone modifications. Mechanistic studies were performed in genetically obese mouse line (LepOb/Ob) and SUV39H1 knockout mice (SUV39H1−/−), according to the principles of laboratory animal care.

Results: Mitochondrial oxidative stress and endothelial dysfunction were observed in SVFA from obese as compared to controls. Vascular gene profiling of chromatom modifying enzymes revealed a significant dysregulation of methyltransferase SUV39H1 (FC=−6.7, p<0.01), acetyltransferase SRC-1 (FC=−3.0, p<0.01) and demethylase JMJD2C (FC=−2.7, p<0.01) in SVFA from obese as compared to controls. These changes favoured demethylation as well as increased acetylation at lysine 9 of histone 3 (H3K9), leading to chromatin accessibility and enhanced transcription of the mitochondrial adaptor p66Shc, a key driver of vascular oxidative stress. Interestingly, reprogrammung of SUV39H1, SRC-1 and JMJD2C in endothelial cells isolated from LepOb/Ob mice suppressed p66Shc upregulation and endothelial superoxide generation. By contrast, genetic deletion of SUV39H1 in mono-obese animals was associated with disturbed SRC-1/JMJD2C signalling, p66Shc overexpression and vascular oxidative burst.

Conclusions: We have identified a complex epigenetic machinery responsible for altered redox signalling in the vasculature of obese subjects. Our findings support the idea that targeting chromom remodelling may represent a novel strategy to reduce vascular disease burden in the setting of cardiometabolic disorders.

Acknowledgement/Funding: European Foundation for the Study of Diabetes (EFSDF)

P4540 | BENCH
The incretin hormone GIP is modulated by inflammatory stimuli and downregulated in critically ill ICU patients: central relevance of interleukin 1 beta

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Background: The incretin hormone GIP is modulated by inflammatory stimuli and known to act as regulator of glucose metabolism under inflammatory conditions. GIP is known to be released in response to endotoxin. GIP levels significantly increased in response to inflammatory stimuli leading to insulin secretion and prevention of hyperglycemia in context of critical illness. We here study the relevance of the other main incretin hormone glucose-dependent insulinotropic peptide (GIP) as a regulator of glucose metabolism under inflammatory conditions. GIP is known to be released in response to food intake from endocrine intestinal cells leading to glucose-dependent insulin secretion.

Methods and results: Low dose lipopolysaccharide (LPS) injection (100 μg/kg) - used as an inflammatory stimulus - time-dependently increased GIP secretion in C57BL/6J mice. Interestingly, this was only apparent at a low LPS dose (4.1 fold increase with 10 μg/kg; p<0.05) and lost with median LPS dosage (1.1 fold increase with 1 mg/kg; p=0.72) while high LPS concentrations led to a trend to wards decreased GIP levels (0.6 fold decrease with 2 mg/kg; p=0.2). To elucidate the relevant mechanisms we injected mice with inflammatory cytokines known to be released in response to endotoxin. GIP levels significantly increased in response to IL-1β (1.9 fold; p<0.01) and showed a trend for IL-6 (1.6 fold; p=0.16)

Conclusion: Chronic VNS therapy exerts effective glycemic control and improves left ventricular contractile function via its ability to antagonize apoptosis, oxidative stress and cardiac mitochondrial dysfunction.
P4541 | BENCH

The absence of Two-pore channels induce metabolic alterations at cardiac level

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Introduction: Two pore channels (TPCs) are potential calcium voltage ion channels activated by NAADP. There are two different subtypes in human and rodents: TPC1 and TPC2. Dysfunctional ion concentrations are deleterious to cardiac cells and are related with cardiac pathologies. However, little is known about the role of these new channels in the heart. In previous results we showed that fatty acid and are related with cardiac pathologies. However, little is known about the role of these new channels in the heart. In previous results we showed that fatty acid transport was altered in cardiac left ventricle of TPC1KO vs. wt mice.

Purpose: For maintaining a proper cardiac function a continuous production of energy is critical. Our aim is to go further into cardiac metabolic alterations in TPC1 and TPC1/2 KO mice vs. wt mice.

Methods: To identify the proteins deregulated by the lack of TPC1 and TPC1/2 we carried out a proteomic study in male left cardiac ventricles of TPC1 and TPC1/2 KO mice by LC-MALDI-TOF/TOF. We validated FABPs by western 2-DE. Finally, we performed a knockdown in neonatal rat cardiomyocytes with siRNA for TPC1, TPC2 and 1/2 and we measured glucose uptake.

Results: A LC-MALDI-MS was carried out in cardiac left ventricles of TPC1 and TPC1/2 KO vs. wt. A total of 108 proteins were found in TPC1 wt and KO mice; 22 unique were found in TPC1 KO mice, 15 unique in TPC1 wt and 71 in both conditions. In TPC1/2 KO vs. wt mice, 149 proteins were identified; 43 unique proteins were found in TPC1/2 KO; 98 common proteins between both conditions and 8 found only in TPC1/2 KO. The 2-DE western blot showed a decrease in FABP3 in left cardiac ventricles of TPC1 KO and 1/2 KO mouse (p<0.01) in comparison to healthy controls (p<0.001).

Conclusion: GIP provides a novel link between the immune system and the gut. Although GIP seems to hold minor relevance for the regulation of glucose metabolism under inflammatory conditions it acts as an immune-inflammatory modulator. This requires further characterization.

P4542 | BENCH

Teneligliptin ameliorates hypertensive cardiac remodeling via angiotensin-II-mediated cardiac-sodium-proton exchanger 1 pathway

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Purpose: Hypertension is primary cause of heart failure (HF). Several reports demonstrated the blood-pressure (BP)-lowering property of dipietyl peptide 4 (DPP4) inhibitors. We tested the effect of a new DPP4 inhibitor teneligliptin (TEN) on BP and HF using preclinical hypertensive HF models.

Methods: Spontaneously hypertensive rats (8-9 week-old male) and age-matched normotensive counterpart (WKY) were treated with TEN (10mg/kg/day) for 4 weeks. Hypertensive HF was evaluated in terms of BP, cardiac function, histological remodeling, and pulmonary congestion. Intracellular pH changes of cultured cardiomyocytes were monitored by its specific fluorescence indicator (pHrodo, Life Technologies) and live cell imaging using Confocal Scanning Unit (CSU X-1;Yokogawa Electric Corporation) and fluorescence microplate reader (Infinite, TECAN).

Results: Cardiac catheterization revealed that TEN ameliorated hypertension of SHRa−/− (Fig. 1). The maximum dP/dt of SHRa−/− was elevated (10452±539 for SHRa−/− and 5739±599 for WKY−/−), which was reduced by TEN (8033±656 in SHRa−/− without affecting heart rate. Diastolic indices (minimum dP/dt and tau) were ameliorated by TEN. SHRa−/− exhibited increase in heart and body weight (BW), ratio, left ventricular (LV) wall thickness, cardiomyocyte hypertrophy and fibrosis, which were attenuated by TEN. Elevated lung weight and BW ratio and circulating BNP level of SHRa−/− were ameliorated by TEN. Cardiac and circulating DPP4 activities of SHRa−/− were elevated, which was suppressed by TEN. Vasoconstrictor (A(+/-)at) of each aorta and heart remained unaffected by TEN. Circulating angiotensin-2 (AT-II) was elevated in SHRa−/−, which was suppressed by TEN without affecting ACE activity. Because DPP4 interacts with Na+/H+ exchanger (NHE)-1 and -3, and NHE-1 is related to hypertension and cardiac hypertrophy. In SHRa−/− heart, NHE-1 expression was elevated, which was decreased by TEN. Lastly, we measured intracellular pH changes and evaluated the impact of AT-II and TEN. Interestingly, AT-II (100nM) increased pH, which was partially restored by TEN (1microm).

Conclusion: TEN ameliorates hypertensive heart failure by normalizing ele-

P4543 | BENCH

The effects of age on ovine atrial conduction

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Background: The incidence of atrial fibrillation (AF) has a steep relationship with age, with prevalence in persons aged over 85 exceeding 15%. The susceptibility of the atria to fibrillation in the elderly is incompletely understood. Atrial conduction velocity (CV) has been shown to inversely correlate with vulnerability to AF. CV has also been reported to decrease with age. A determinant of CV is the peak sodium current INa. We investigated how CV and INa changed with age in a sheep model.

Methods: Young adult (~18 months) and aged (~8 years, last quintile of life) sheep underwent electrophysiological studies under general anaesthesia. A catheter with 32 bipolar electrode pairs recorded electrogams from the right atrium (RA) during stimulation at 3Hz. Paceremats were implanted and AF was subsequently induced using 90Hz burst pacing to the right atrium in conscious subjects. 6 lead ECGs were recorded at the time of surgery during sinus rhythm and were used to calculate p-wave duration. Animals were euthanized with Pentobarbital and myocytes were isolated from the left atrial appendage. INa was recorded using the whole cell patch clamp technique at room temperature with 3mM extracellular sodium.

Results: Aged sheep were more vulnerable to AF than young sheep in terms of the proportion of bursts that elicited AF (36.3±7.7% vs 22.4±3.9%, p<0.05). P-wave duration was 14% longer in aged animals (48.7±1.5ms vs 42.6±1.4ms, n=22, p<0.05). In contrast to other models of ageing, RA axial CV was increased by 36% in aged compared to young animals (1.0±0.04 ms vs 0.74±0.06 ms, n=11 animals, p<0.05). Circumferential CV showed similar changes. The anisotropic ratio (circumferential CV/axial CV) did not change with age. Increased CV was associated with a 29% age dependent increase in INa (26.5±2.5 PaF/P vs. 20.6±1.4 PaF/P, n=59 cells, 15 animals, p<0.05). There were no changes in the voltages of half maximal activation or inactivation, however INa recovered faster from inactivation in cells from aged animals (time constant of recovery 33.1±1.8 ms vs 24.9±2.3 ms, p<0.05).

Conclusion: Ageing was associated with increased vulnerability to AF and longer p-wave duration, suggesting a prolongation of atrial depolarization. Surprisingly, CV increased with age possibly due to increased INa. Increased CV in the aged atria could represent a physiological adaptation compensating for atrial dilatation.

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P4544 | BENCH

P4547 | BEDSIDE

P4546 | BEDSIDE

P4545 | BENCH

A role for tenascin-C in the development of pulmonary arterial hypertension

Background: Pulmonary arterial hypertension (PAH) is a severe and progressive disease entailing a deteriorating pulmonary vasculopathy with obstruction of small pulmonary arteries, smooth muscle cell hypertrophy and intimal fibrosis. It has been proposed that Tenascin-C (TnC), a key mediator of smooth muscle cell growth and survival is critically involved in the pathogenesis of PH. Aim of our study was to investigate the effect of TnC inhibition by direct gene manipulation on the development of PH.

Methods: We utilized mice with a homozygous TnC knock-out (TnC KO) and A/J wild types (WT). Both TnC KO and WT littermates were held in an environmental chamber with F1O2 of 10% or under normoxia for 4 weeks. We investigated the effect of TnC deletion and pharmacologic hypoxia on parameters of pulmonary vascular resistance such as right ventricular systolic pressure (RVSP) and right ventricular hypertrophy (Fulton Index/right to left ventricular ratio). To assess the degree of smooth muscle cell hyperplasia, alpha-smooth muscle actin antibody staining was performed.

Results: TnC KO mice showed significantly increased right ventricular pressures after 4 weeks under normoxic conditions, compared with wild type controls (15.2 vs. 21.95 mmHg, p < 0.001). Under 4 weeks hypoxic breeding TnC KO mice revealed significantly higher right ventricular pressures (27.3 vs. 34.9 mmHg, p < 0.001), and Fulton indices than controls (0.43 vs 0.50, p < 0.001). Under both normoxic and hypoxic conditions TnC KO mice revealed significant increased medial thickness (Fig.1).

Conclusion: TnC a extracellular matrix glycoprotein prominent during tissue remodelling and wound healing may play a pivotal role in the early pathogenesis of pulmonary hypertension.

Conclusion: Pulmonary pressures rise significantly with volume loading, even in healthy volunteers. The response in acute volume loading is different in pre- and post-capillary PH than other groups and CI increased more in control subjects.

Six out of 70 analyzed patients, 3 apparently normal at baseline and 3 considered having pre-capillary PH, were considered at risk for HFpEF after FCT due to a steeper increase in PAWP (> 10 mmHg increase reaching an absolute value > 20 mmHg).

Table 1. Difference between basal and FCT

<table>
<thead>
<tr>
<th>Normal</th>
<th>Post-FH</th>
<th>Pre-FH</th>
<th>p</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>ΔRAP (mmHg)</td>
<td>3±2</td>
<td>5±3</td>
<td>2±2</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>ΔPAWP (mmHg)</td>
<td>4±3</td>
<td>9±3</td>
<td>6±3</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>ΔMPAP (mmHg)</td>
<td>4±3</td>
<td>9±3</td>
<td>6±3</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>ΔCI (l/min/m²)</td>
<td>0.0±0.0</td>
<td>0.3±0.2</td>
<td>0.4±0.5</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>ΔDPG (mmHg)</td>
<td>-13±1</td>
<td>-2±1</td>
<td>15±5</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>ΔPVR (WU)</td>
<td>-1±1</td>
<td>0±1</td>
<td>-1±2</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Conclusions: Pulmonary pressures rise significantly with volume loading, even in healthy volunteers. The response in acute volume loading is different in pre- and post-capillary PH patients and allows unmasking patients at risk for developing HFpEF.

The trigger of pulmonary injury after balloon pulmonary angioplasty in patients with chronic thromboembolic pulmonary hypertension

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Purpose: We have been refining the procedure of balloon pulmonary angioplasty (BPA) for patients with chronic thromboembolic pulmonary hypertension (CTEPH) and thus, the incidences of complications were diminished. However, the mechanism of pulmonary injury after BPA is controversial; there are residual risks for complications related BPA.

Methods: We conducted a retrospective cohort study of patients with CTEPH undergoing BPA who were admitted to a high volume center of pulmonary hypertension in Japan between November 2012 and December 2013. Pulmonary injury after BPA was defined by newly appeared CT findings (GOO, consolidation and pleural effusion). We analyzed correlations between incidence of PI and procedural characteristics, pretreatment patient’s characteristics, and BPA related vascular injury (BR-VI): the angiographic findings of extravasation with pleural effusion). We analyzed correlations between incidence of PI and procedural characteristics, pretreatment patient’s characteristics, and BPA related vascular injury (BR-VI): the angiographic findings of extravasation with pleural effusion.

Results: We operated 297 procedures in 76 patients. The incidence of PI was 138 procedures (46.5%) and BR-VI appeared 51 procedures (17.2%). To compare procedures with PI and without PI, there was no significant difference in

Vascular remodelling / Chronic pulmonary hypertension
P454 | BEDSIDE
Clinical and echocardiographic characteristics of patients with pulmonary hypertension associated with heart failure with preserved ejection fraction or with pre-capillary pulmonary hypertension

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Background: Heart failure with preserved ejection fraction (HFpEF) is a frequent cause of pulmonary hypertension (PH) that may be difficult to differentiate from pre-capillary pulmonary hypertension (PrePH), particularly in elderly.

Conclusion: To simplifi ed clinical and echocardiographic characteristics that could help to differentiate PH-HFpEF from PrePH in current practice.

Methods: We reviewed data from 138 stable patients referred to the French PH referral center. PH-HFpEF was defi ned as mean pulmonary artery pressure (>25 mmHg) and mean pulmonary vascular resistance (>3 WU). Clinical and echocardiographic characteristics of 66 PH-HFpEF patients and 70 PrePH patients (group 1 and 4 of PH classifi cation) were compared.

Results: Compared with PrePH, PH-HFpEF patients were older (67±2 vs 61±17 years, p<0.01), had more frequent systemic hypertension (53% vs 20%, p<0.001) and diabetes mellitus (37% vs 13%, p<0.001), higher BMI (32.5±26.6 vs. 26.5±5, p<0.001) and higher prevalence of atrial fi brillation (16% vs 3%, p<0.001). No differences were observed in 6-minute walk distance and BPN levels. On RHC, PH-HFpEF had similar mPAP and PAWP as PH-PrePH. However, the heart rate was higher in PH-HFpEF. The right atrial pressure was higher in PH-HFpEF. The right ventricle area (155±5 vs 74±4 mmHg, p<0.001) and lower PVR (4.3±3 vs 73 WU). On echocardiography, PH-HFpEF patients had higher left ventricular mass index (89±35 vs 53±20 g/m², p<0.001), left atrial area (24.7±17 vs 17.5±5 cm², p<0.001) and E/e’ ratio (10.4±5 vs 8.5±5, p<0.05), and smaller right ventricle (RV) end-diastolic area (21.7±24 vs 24.8±0.01, p<0.001) and RV end-systolic area (14.6±8 vs 18.2±8 cm², p<0.001). There was no difference in right ventricle functional parameters (tricuspid annular plane systolic excursion, tricuspid S’ velocity and RV fractional area change).

Conclusion: To simplifi ed clinical and echocardiographic features (LV mass, LA area, end-diastolic and systolic RV area) may help physicians to identify PH-HFpEF from Pre-PH.

P4549 | BENCH
Percutaneous treatment of carbon dioxide mist attenuates the development of right ventricular dysfunction in monocrotaline-induced pulmonary hypertensive rats

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Background: Highly concentrated carbon dioxide (CO2) is useful for treating ischemic diseases. We have reported that treatment with a few micrometers of CO2 molecules, atomized by two fi dle nozzles (CO2 mist), offers a therapeutic benefi t in a rat model with heart failure due to myocardial infarction, as well as in a mouse model with peripheral arterial disease. In this study, we investigated whether this treatment could attenuate the development of right ventricular (RV) dysfunction in pulmonary hypertensive rats.

Methods: Six-week-old male Wistar rats were divided into three groups: one that received injected saline as control; one that received subcutaneous monocrotaline (MCT; 60 mg/kg) without treatment (PH-UT) group; and a third that received injected saline as control; a second that received subcutaneous monocrotaline (MCT; 60 mg/kg) with CO2 mist treatment (PH-CM) group. Western blotting revealed that the PAAT/PAET ratio, which is often used as an index of pulmonary hypertension, was signifi cantly decreased by MCT administration. Western blotting revealed that both RV phosphorylated endothelial nitric oxide synthase and heat shock protein 72 levels increased signifi cantly in the PH-CM group, compared to the PH-UT group.

Results: Percutaneous CO2 mist therapy may alleviate RV dysfunction in patients with pulmonary hypertension.

P4550 | BEDSIDE
Genetics of pulmonary arterial hypertension in a Spanish cohort. Preliminary results of the Spanish multicentric study of genetics of HPAP/PAH

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Purpose: To document the clinical and echocardiographic characteristics that could help to differentiate PH-HFpEF from PrePH in current practice.

Methods: 117 pt were studied: 104 with negative family story and 13 with positive family story. Mutations (mut) were found in 22 pt (18.6%) in BMPR2, 13 pt (11.0%) in KCNK3 and 15 pt (12.9%) in TBX4. After genetic analysis, 19 pt were attending 2 groups attending to family story and genetic fi ndings: PHAP group (no family story + no mut) and Heritable PAH group which included: PHAP with positive family story but no detected mut, PAH with positive family story with detected mut and sporadic cases with detected mut. Clinical data were obtained from Spanish Registry of PAH (REHAP).

Results: 117 pt were studied: 104 with negative family story and 13 with positive family story. Mutations (mut) were found in 22 pt (18.6%) in BMPR2, 13 pt (11.0%) in KCNK3 and 15 pt (12.9%) in TBX4. After genetic analysis, 19 pt were attending 2 groups attending to family story and genetic fi ndings: PHAP group (no family story + no mut) and Heritable PAH group which included: PHAP with positive family story but no detected mut, PAH with positive family story with detected mut and sporadic cases with detected mut. Clinical data were obtained from Spanish Registry of PAH (REHAP).

Conclusion: PHAP pt tend to be younger with slightly more severe hemodynamics, better 6MWT and less response in AVT. Prevalence of TBX4 and KCNK3 is low. BMPR2 mut were found in a smaller proportion of Heritable PAH than previously reported. Further research is needed to fi nd new PAH related genes that may play a role in Spain.

P4551 | BEDSIDE
Assessment of the exercise tolerance and oxygenation after balloon pulmonary angioplasty for patients with inoperable chronic thromboembolic pulmonary hypertension

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Background: Balloon pulmonary angioplasty (BPA) could be effective for inoperable chronic thromboembolic pulmonary hypertension (CTEPH). However, the assessment of exercise tolerance and oxygenation and respiratory function after BPA procedure is limited. The aim of this study was to evaluate the ef fi cacy of BPA in exercise tolerance, oxygenation and respiratory function after BPA procedure.

Methods: Consecutively 41 patients (12 male, 66±11.6 years old) who underwent BPA were enrolled. We evaluated hemodynamics, arterial blood and mixed venous oxygenation analysis with Swan-Ganz catheter, and respiratory function test before and after BPA, and 1 year-follow-up of 28 patients. Exercise tolerance of 6 minute-walk-distance (6MWD) and oxygen desaturation during 6MWD test were evaluated.
P4552 | BEDSIDE
Pulmonary hypertension in patients with dialysis: epidemiology and clinical impact
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Background: Previous papers reported that pulmonary hypertension (PH) was common and a predictor of mortality in patients with dialysis. However, there was no large-scale study evaluating by using right heart catheterization (RHC). Methods: We enrolled patient with dialysis who underwent elective RHC retrospectively. PH was defined as mean pulmonary arterial pressure ≥25 mmHg. Pre-capillary PH (group 5) and postcapillary PH (group 2) were defined as pulmonary arterial wedge pressure ≥15 mmHg and <15 mmHg, respectively. Patients who suspected of secondary PH were excluded. We assessed the prevalence and the prognostic impact of each PH in patients with dialysis.

Results: Eight hundred ninety patients were examined. Two hundred twenty eight patients (25%) had PH. The prevalence of group 5 was 48% (5) and group 2 was 180 patients (20%). Left ventricular ejection fraction (LVEF) was significant differences among the group (non-PH: 48±12%, group 5: 41±14%, and group 2: 40±14%, p for trend <0.001, respectively). During averaged 3.6 years follow-up, 179 patients died. Survival rate was significantly lower in patients with PH than those without (HR 2.26, 95% CI: 1.66–3.06, p=0.001). On multivariate analysis, both group 2 and group 5 were significant factors on mortality after adjusting for confounding factors such as LVEF and age (HR 2.18, 95% CI 1.08–3.98, p=0.004 and HR 1.83, 95% CI 1.22–2.71, p=0.030).

Conclusions: Present study suggested that PH was common, and both group 2 and group 5 PH were independent predictors of mortality in dialysis patients. PH patient with dialysis requires further intensive care and treatment.

P4554 | BEDSIDE
Common pitfalls in pulmonary hypertension diagnosis: the real-world application of ESC guidelines algorithm
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Background: Pulmonary hypertension (PH) diagnosis requires a demonstration of increase in mean pulmonary arterial pressure (PAP) ≥25 mmHg at rest, assessed by right heart catheterization. To date, comparative epidemiologic data regarding different PH groups are not available and real prevalence of PH in the general population is still unknown. Moreover, trans-thoracic echocardiography, despite being at the center of the diagnostic algorithm suggested by the ESC guidelines, still suffers from numerous issues in clinical practice.

Purpose: Our registry aimed to provide data regarding incidence and etiology of PH in a “real-world” unselected population referred to our Hospital. Moreover, we evaluated the implementation of echocardiographic screening for PH and the resulting diagnostic work-up in the everyday clinical practice of a regional hub centre.

Methods: Using our institutional database we evaluated retrospectively 13689 consecutive echocardiographic exams performed for any indication in our echo-lab between February 1st, 2013 and January 31th, 2014. For each exam we collected data regarding systolic PAP (PAPs) estimation (numeric, semi-quantitative or no estimation), and presence and severity of tricuspid regurgitation (TR). Subsequently, we analysed how many patients with high suspicion of PH (PAPs >50 mmHg or TR velocity >3.4 m/s) reached a final diagnosis during a 12-month follow-up.

Results: Among all collected exams, only 7059 (52%) reported a quantitative PAPs estimate. In 2903 (21%) exams we found a semi-quantitative PAPs estimation, 900 (7%) exams reported no PAPs estimation due to technical difficulties in founding TR, and 2827 (20%) mentioned no PAPs at all. In the group of patients with high echocardiographic likelihood of PH (n=517) only 346 (67%) were subsequently evaluated with pulmonary-angiography. In the same subgroup, specific laboratory screening tests were suggested as indicated: D-Dimers (67%), liver function (58%), thyroid function (13%), HIV (2%), connective tissue disorder (1%). Finally, only 63 (12%) patients reached a final diagnosis of PH: S (8%) in group 1, 37 (59%) in group 2, 13 (21%) in group 3, and 8 (13%) in group 4.

Conclusions: Despite PH is related to low survival rates and an overall bad prognosis, its incidence remains highly underestimated because PAPs estimation is far from optimal in everyday routine echocardiography. Moreover, only a minority of patients with likely PH follow an evidence-based diagnostic work-up, and even fewer reach a definitive etiologic diagnosis, and are thus treated accordingly.

AORTIC VALVE DISEASE I

P4555 | BEDSIDE
Comparing bone turnover biomarkers levels in aortic stenosis of bicuspid and tricuspid valve
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Background: Aortic stenosis (AS) remains the most frequent acquired heart valve disease. It is proposed that calcification of valve leaflets might have sim-
ilar pathways to skeletal bone formation. The aim of the study was to compare levels of bone turnover biomarkers in pts with bicuspid (BAV) and tricuspid (TAV) calcific AS and estimate their associations with bone mineral density (BMD).

Materials and methods: 129 pts with AS and peak aortic jet velocity more than 4.0 m/s; 78 pts with BAV (56±14.0 yrs; m: f 1:2.1) and 51 pts with TAV (62±17±0.9 yrs; m: f 1:1.2) were included. 31 healthy people as a control (57±30.8 yrs; m: f 1:1.1) were examined. Serum osteoprotegerin (OPG), sRANKL, vitamin D, osteopontin (OPN), C-terminal telopeptide of collagen I (CTX), C-terminal propeptide of procollagen type I (PICP) levels were estimated in all pts by ELISA. BMD of femur was investigated with dual energy X-ray absorptiometry.

Results: Pts with BAV and TAV were comparable for gender and ECHO parameters, but pts with TAV were older (p<0.001). Increased circulating OPG and sRANKL levels were revealed in pts with AS compared to healthy controls (Tab.1). Differences in PICP and CTX levels were significant (p<0.001). As similar in BAV and TAV groups. There wasn’t correlation between OPG/sRANKL and BMD because BMD wasn’t decreased. Vitamin D level was normal in all groups, but it was negatively correlated with OPG (p=0.04, p<0.002). We revealed also association between BMD, T-criterion and aortic valve pressure gradient (r=−0.28, p=0.04; r=−0.3, p=0.02 respectively). CTX level was positively correlated with aortic valve pressure gradient (r=0.56, p<0.001).

Table 1. Concentrations of biomarkers

<table>
<thead>
<tr>
<th></th>
<th>BAV</th>
<th>TAV</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>sRANKL</td>
<td>4.03±0.02**</td>
<td>4.50±0.05</td>
<td>3.66±0.02</td>
</tr>
<tr>
<td>OPG</td>
<td>6.64±0.4**</td>
<td>6.59±0.73**</td>
<td>4.84±0.32</td>
</tr>
<tr>
<td>OPN</td>
<td>6.67±1.36</td>
<td>45.82±1.94</td>
<td>35.69±1.85</td>
</tr>
<tr>
<td>CTX</td>
<td>34.67±7.22</td>
<td>40.62±1.38</td>
<td>43.01±13.23</td>
</tr>
<tr>
<td>PICP</td>
<td>0.36±0.03</td>
<td>0.28±0.01</td>
<td>0.36±0.05</td>
</tr>
</tbody>
</table>

P<0.007 vs control, *p<0.001 vs control.

Conclusion: Increased levels of bone turnover biomarkers were found in AS with BAV and TAV that confirm the common pathway of the heart valve calcification. Association of aortic valve calcification with bone resorption might be a potential target for therapeutic actions.

P4556 | BEDSIDE

Causes of death, mortality and evaluation of prognostic factors in patients with severe aortic stenosis in an aging society

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Background: Severe aortic stenosis (AS) is now predominantly a disease of the elderly, with significant mortality and morbidity. In order to investigate the burden of severe AS in the elderly population, we assessed mortality, causes of death, clinical event rates and prognostic factors of patients diagnosed with severe AS.

Methods: A total of 519 consecutive patients (mean age, 78±9 years) with severe AS in the current population, we assessed mortality, causes of death, and clinical events including aortic valve replacement, heart failure requiring admission, acute coronary syndrome and syncope, were measured as main outcomes.

Results: During a median follow-up of 3.5 years, 167 patients (32%) died; Overall survival rates at 1 and 3 years were 86% and 70%, respectively. Of all deaths, 101 (61%) were cardiovascular related and 56 (33%) were non-cardiovascular. Syncope occurred in only 18 (4%) patients, while heart failure requiring admission, acute coronary syndrome and syncope, were measured as main outcomes.

Conclusion: Severe aortic stenosis (AS) is now predominantly a disease of the elderly, with significant mortality and morbidity. In order to investigate the burden of severe AS in the elderly population, we assessed mortality, causes of death, clinical event rates and prognostic factors of patients diagnosed with severe AS.

P4557 | BEDSIDE

Impact of pulmonary arterial pressure on long-term survival in patients with aortic stenosis and preserved left ventricular ejection fraction

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Background: The prognostic impact of pulmonary arterial pressure (PAP) remains controversial in aortic stenosis (AS) and few studies focused only on patients with preserved left ventricular ejection fraction (LVEF). We therefore aimed to investigate the impact of PAP, derived from catheterization, on survival in severe AS with preserved LVEF.

Methods and results: Between 2000 and 2010, 749 patients (74±8 years, 57% of males) with preserved LVEF (<50%) and severe AS (valve area <1cm2) without other valvular heart disease underwent cardiac catheterization, including right heart hemodynamic assessment. Pulmonary hypertension (PH) was defined as mean PAP >25mmHg. Systolic and mean PAP were 34.5±12 and 21.9±9mmHg, respectively. Overall, 29% (n=215) of patients had PH, and these patients were significantly older, with lower LVEF and higher heart rate (all p<0.016) than those without PH. In addition, they more frequently had hypertension, diabetes, coronary artery disease (CAD) and chronic pulmonary disease (all p<0.043). Aortic valve replacement (AVR) was performed in 91% of patients and 30-day mortality was 4.3%, significantly higher in patients with PH (7.7% vs. 3.4%, p=0.014). In logistic regression analysis, after adjustment for age, gender, LVEF, CAD and mean transaortic pressure gradient, mean PAP was an independent predictor of increased 30-day mortality (odds ratio=1.06, 95% CI: 1.02–1.1, p=0.004). Overall long-term survival was significantly lower in patients with PH compared to those without PH with a hazard ratio of 2.7 with 95% CI: 1.2–7.6, P=0.019 adjusted for age, sex and censored at the time, if AVR was performed. TR grade was also a significant predictor of death on medical therapy, prior to AVR if performed with a hazard ratio of 2.7 with 95% CI: 1.2–7.6, P=0.0324.

Conclusion: In patients with moderate to severe TR, PH is associated with poorer functional capacity, worse left ventricular function, higher pulmonary pressures and more functional mitral regurgitation than patients with mild or no TR. Patients with higher grade of TR has worse survival on medical therapy that patients with mild or no TR. In patients with moderate AS, TR severity has survival significance and can be used, along with other established clinical and cardiac imaging criteria as a prognostic indicator to assist in patient selection for AVR.

P4558 | BEDSIDE

Impact of aortic valve disease I

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Background: We tested the hypothesis that tricuspid regurgitation (TR) is a surrogate marker of aortic stenosis (AS) severity, and specifically that TR severity correlated with established hemodynamic and exercise capacity variables, previously validated as reliable prognostic indicators of survival in moderate AS patients.

Purpose: To validate TR severity as a marker of medium term prognosis in patients with moderate AS, being evaluated for aortic valve replacement (AVR).

Methods: All patients with moderate AS with a valve area <1.5 cm2 seen over a five year period, who did not establish aortic valve replacement criteria including severe aortic valve replacement (AVR) and who underwent symptom limited exercise testing (CPX) to assess exercise capacity were included in this study. Patients with structural mitral or tricuspid valve disease were excluded.

We stratified patients by TR severity into 2 groups- trivial to mild TR versus moderate to severe TR. Differences in clinical variables, exercise capacity, echo parameters and outcomes by TR group were determined using t-tests and chi square tests as appropriate. Survival on medical therapy prior to AVR by TR grade was determined by Cox regression adjusted for age, sex and AVR.

Results: This study included 152 eligible patients. Patients with higher TR grade had worse exercise capacity (lower peak VO2 with a higher prevalence of VE/VO2 >35). Aortic valve area did not differ significantly between patient groups based on TR grade, but echo indices of LV performance were worse and pulmonary pressures were higher in patients with higher TR grades. There were 22 deaths (14%) over median follow-up = 3.3 years (IQR 2.3–4.0). The hazard ratio for death with higher TR grades was 3.0 with 95% confidence limits (CI) of 1.2–7.6, P<0.019 adjusted for age, sex and censored at the time, if AVR was performed. TR grade was also a significant predictor of death on medical therapy, prior to AVR if performed with a hazard ratio of 2.7 with 95% CI: 1.2–7.6, P=0.0324.

Conclusion: In patients with moderate to severe TR, PH is associated with poorer functional capacity, worse left ventricular function, higher pulmonary pressures and more functional mitral regurgitation than patients with mild or no TR. Patients with higher grade of TR has worse survival on medical therapy that patients with mild or no TR. In patients with moderate AS, TR severity has survival significance and can be used, along with other established clinical and cardiac imaging criteria as a prognostic indicator to assist in patient selection for AVR.
prognosis of these patients, AVR could be considered before the occurrence of severely elevated PAP.

P4559 | BEDSIDE
Assessment of myocardial deformation: predicting left ventricular dysfunction after surgery in patients with chronic mitral regurgitation

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Background: The development of postoperative left ventricular (LV) dysfunction is a frequent complication in patients with chronic severe mitral regurgitation (MR) and implies a poor prognosis. Assessment of myocardial deformation enables myocardial contractility to be accurately estimated. The aim of this study was to evaluate the predictive value of preoperative regional LV contractile function assessment using two-dimensional echocardiography–based multilayer speckle-tracking analysis in patients with chronic severe MR.

Methods: Forty-three consecutive patients with chronic severe MR scheduled for mitral valve replacement or repair were prospectively enrolled. Serial echocardiographic studies were performed before surgery, at 7 days follow-up and at least 3 months follow-up postoperatively. The conventional echocardiographic parameters were calculated. Global and regional LS were obtained quantitatively by 2D speckle tracking and automated function image (AFI) technique.

Results: The patients’ mean age was 51.7±14.3 years and 25 (58.1%) were male. In ROC curve analysis, the most useful cutoff value for discriminating between patients with LV remodeling and patients with LV no-remodeling in severe MR with normal LVEF was −20.5% of 2D mid-layer GLS (sensitivity 0.70, specificity 0.75). Patients were divided into two groups by the baseline global LS −20.5%. Preoperative speckle tracking–derived longitudinal strain values strongly predicted a postoperative LV remodeling or LV dysfunction. And, postoperative degree reduction of LVEDD might be additive predictive factor.

Conclusion: Speckle-tracking echocardiography can be used to predict a decrease in LV dysfunction after mitral valve replacement in patients with chronic severe mitral regurgitation. Postoperative degree reduction of LVEDD might be an additive predictive factor for postoperative LV dysfunction or remodeling. These might help prevent irreversible systolic dysfunction in the long term.

P4560 | BEDSIDE
Asymptomatic, severe degenerative mitral regurgitation: a step towards earlier detection of myocardial dysfunction

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Background: 2D speckle tracking echocardiography (2D-STE) has been used to appreciate left atrial mechanics in patients (pts) with severe mitral regurgitation (MR), while left ventricular (LV) deformation properties have not been studied extensively.

Purpose: The aim of the present study was to assess LV global longitudinal strain (LVGLS) in pts with normal ejection fraction (EF) and severe MR.

Methods: We studied 46 consecutive pts (52% men, with mean age 64±15 years) with asymptomatic, severe degenerative MR and normal EF and 30 healthy controls (53% men, with mean age 61±14 years). In addition to conventional echocardiographic measurements, global longitudinal strain of the LV (LVGLS) was estimated off-line from the three apical views by 2D-STE using EchoPac 110 workstation (GE Vingmed Ultrasound).

Results: The main results of our study are presented in Table 1. While pts with MR had increased EF compared to controls, they had impaired LVGLS, confirming the outstanding role of strain in the pathophysiological interpretation of cardiovascular diseases. It is impressive that although the increase of EF is a compensatory mechanism to MR, LVGLS unveils the indeed impaired systolic function of the LV, doubling actually the presence of the stage of compensated MR. Consequently, the impairment of the deformation mechanics of the LV in MR can possibly be used to detect latent myocardial dysfunction and to better define the perfect time to intervene, improving prognosis.

Table 1. Multivariate logistic regression analysis for determinants of postoperative LV remodeling

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds ratio (95% CI)</th>
<th>β Coefficient</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post OP LVEDD, mm</td>
<td>0.837 (0.647–1.083)</td>
<td>−0.178</td>
<td>0.172</td>
</tr>
<tr>
<td>Post OP EFa</td>
<td>1.055 (0.935–1.191)</td>
<td>0.054</td>
<td>0.385</td>
</tr>
<tr>
<td>Baseline mid-layer GLS</td>
<td>2.440 (1.259–4.729)</td>
<td>0.892</td>
<td>0.009</td>
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Conclusions: Speckle-tracking echocardiography can be used to predict a decrease in LV dysfunction after mitral valve replacement in patients with chronic severe mitral regurgitation. Postoperative degree reduction of LVEDD might be an additive predictive factor for postoperative LV dysfunction or remodeling. These might help prevent irreversible systolic dysfunction in the long term.

P4561 | BEDSIDE
Whole blood viscosity as an overlooked predictor of spontaneous echo contrast in patients with mitral stenosis

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Introduction: Spontaneous echo contrast (SEC) is specified with dynamic smoke-like appearance in transesophageal echocardiography (TEE) as a source of cardioembolism with prognostic importance. This entity arises from an interaction between red cells and plasma proteins, especially at low shear rates. Mitral stenosis (MS) serves a low velocity bloodstream milieu, facilitating SEC formation. Whole blood viscosity (WBV) can be calculated with confirmed equations from hematocrit and total plasma protein. We aimed to assess the relationship between WBV and SEC formation in MS.

Methods: 250 patients with MS who were performed TEE before mitral balloon valvuloplasty procedure between 2010 and 2015 were enrolled. SEC(+) group consisted of 152 patients (mean age 56.9±12.9 and 44.7% male) and SEC(−) group consisted 98 patients (mean age 55.3±13.2 and 42% male). WBV was derived from hematocrit and plasma protein concentration at low shear rate (LSR) (0.5 sec−1) and high shear rate (HSR) (208 sec−1) by validated formulas.

Results: SEC(+) patients had significantly higher WBV for both LSR (60.0±18.7 vs 62.6±19.1, P<0.001) and HSR (17.9±1.7 vs 16.7±1.3, P<0.001). Correlation analysis demonstrated a significant relationship between the grade of SEC and WBV for LSR (r=0.484, P<0.001) and HSR (r=0.463, P<0.001). A cut-off value of 72.3 for WBV at LSR has 73.5% sensitivity and 67.3% specificity for prediction of SEC (AUC: 0.748, P<0.001). A cut-off value of 17.0 for WBV at LSR has 72.5% sensitivity and 60.7% specificity for prediction of SEC (AUC: 0.699, P<0.001).

Table 1. Multivariate logistic regression analysis for determinants of postoperative LV remodeling

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Conclusions: WBV is a simple way of blood viscosity assessment. We have delineated a noteworthy relationship between SEC formation and WBV. Evaluation of WBV with this formula may guide us to risk stratification in patients with MS.

Discussion: WBV is a simple way of blood viscosity assessment. We have delineated a noteworthy relationship between SEC formation and WBV. Evaluation of WBV with this formula may guide us to risk stratification in patients with MS.

P4562 | BEDSIDE
The overlooked parameter of shear stress in mitral annular calcification: Whole blood viscosity

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Introduction: Endothelial insult prompted by an increased mechanical stress has been postulated as the initial step in the pathogenesis of mitral annular calcification (MAC). Increased whole blood viscosity (WBV), can aggravate endothelial disruption via enhanced mechanical stress. Therefore, we aimed to assess the relationship between MAC and WBV.
Methods: A total of 184 patients with MAC and 133 patients without MAC were enrolled in this study. WBV was calculated with a confirmed formulation by using hematoctrit and total plasma protein at low shear rate (LSR) and high shear rate (HSR).

Results: In patients with MAC, WBV values were significantly higher for HSR (18.0±4.0 vs. 17.2±5.0, p<0.001) and for LSR (78.0±14.2 vs. 61.9±17.1, p<0.001). At multivariate analysis, WBV for both shear rate was independent predictors of MAC. ROC curve, a cut-off value 70 of WBV at LSR has 83.7% sensitivity and 73.7% specificity (AUC: 0.785, p<0.001) and a cut-off value 17.5 of WBV at HSR has 79.6% sensitivity and 71.4% specificity (AUC: 0.761, p<0.001) for prediction of MAC.

Conclusion: As a major component of shear stress, WBV can be a useful and costless predictor of MAC. Further prospective studies are needed to prove the prognostic value of WBV in cardiovascular pathological conditions.

P4563 | BEDSIDE
Impact of leaflet/partial clip detachment on outcomes of repeat MitraClip therapy in high-surgical-risk patients
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Background and introduction: MitraClip (MC) implantation is a safe and efficacious percutaneous approach to treat significant mitral regurgitation (MR) in inoperable and high surgical-risk patients (pts). Failure of the index procedure or need for a second high-grade MR after a successful interventional may encourage investigators to attempt a repeat MC procedure.

Purpose: We sought to assess procedural details and outcomes of repeat MC therapy.

Methods: Of 410 high surgical risk pts initially treated with the MC at our institution, 17 in-house pts (4.1%) and 4 additional pts transferred from external institutions underwent repeat MC procedures. Mean age of the 21 pts (14 men [67%]) was 77 years; 15 pts (71%) had functional MR (FMR).

Results: Repeat procedures were performed 6.3 (median: range 0.7–34) months after the index intervention. At the time of the repeat procedure, leaflet tear along the edge of the clip (<) or partial clip detachment (PCD; n=3) was present in 8 patients (38%). Thirteen (62%) of the 21 repeat interventions were successful (discharge MR grade ≤2+), with a statistically significant difference in success rate observed between the 13 patients with intact leaflets at the time of the repeat intervention and the 8 patients in whom leaflet/PCD was present (11/13 [85%] vs. 2/8 [25%], respectively; p=0.0176). Thus, leaflet tear/PCD was strongly predictive of repeat procedural failure (odds ratio 16.5 [95% confidence interval [85%] vs. 2/8 [25%], respectively; p=0.0176). Thus, leaflet tear/PCD was strongly predictive of repeat procedural failure (odds ratio 16.5 [95% CI 8.5–32.7], p<0.001) were small, these differences would have influenced the choice of prosthesis size. In multivariate proportional-hazards models with a maximum of 3 covariates, only post-MC VCA >17 mm² (hazard ratio [HR] 4.45, 95% CI 1.97–10.0, p=0.0033) and impaired renal function (HR 4.14, 95% CI 1.97–8.69, p=0.002) prevailed as independent predictors of mortality.

Conclusions: In heart failure patients undergoing MC therapy for significant functional MR, post-MC VCA proved to be an intraprocedurally assessable parameter to guide interventional decision-making with respect to the patient’s long-term outcome. MC therapy should aim for a post-MC VCA ≤17 mm².

Acknowledgement/Funding: Ulrich Schaefer and Karl-Heinz Kuck have received research grants from Abbott Vascular, Inc.

P4564 | BEDSIDE
The prognostic significance of post-MitraClip vena contracta area in heart failure patients with functional mitral regurgitation
H. Alessandrini1, F. Kreidel1, M. Schlueter2, C. Frerker1, T. Thielen1, P. Wohlmuth1, U. Schaefer1, K.-H. Kuck1, 1 Asklepios Klinik St. Georg, Cardiology, Hamburg, Germany; 2 Asklepios proresearch, Hamburg, Germany

Background and introduction: In Europe, MitraClip (MC) implantation is performed in elderly patients with functional mitral regurgitation (FMR). MC intervention is strongly associated with procedural failure, whereas survival, at least in patients with FMR, is primarily affected by repeat procedural outcome.

Purpose: We aimed to analyse the impact of annulus measurements during systole or diastole on the choice of prosthesis size in a virtual model, assuming the Sapien3, ACURATE TA, and CoreValve as prosthesis.

Methods: We determined the effective annulus diameter size of patients with severe aortic valve stenosis scheduled for TAVI by computed tomography during systole (AnnSys) and diastole (AnnDia), as described previously. Patients were then virtually assigned to receive a prosthesis of specific size due to the manufacturer’s specifications. We analysed differences in the strategy to allocate the correct prosthesis size.

Results: In this single-centre registry, 696 patients were included. Although absolute differences in mean AnnSys (24.2±2.1 mm) and AnnDia (23.4±2.1 mm, p<0.001) were small, these differences would have influenced the choice of prosthesis size. Considering AnnSys as the valid annulus diameter compared with AnnDia resulted in the strategy decisions shown (Table 1).

Table 1

<table>
<thead>
<tr>
<th>Strategy decision</th>
<th>Sapien3</th>
<th>ACURATE TA</th>
<th>CoreValve</th>
</tr>
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<tbody>
<tr>
<td>No change [%]</td>
<td>75.4</td>
<td>59.2</td>
<td>70.0</td>
</tr>
<tr>
<td>Choice of larger size [%]</td>
<td>21.8</td>
<td>28.4</td>
<td>28.6</td>
</tr>
<tr>
<td>TAVI feasible [%] (AnnDia: annula too small)</td>
<td>0.1</td>
<td>8.0</td>
<td>0.1</td>
</tr>
<tr>
<td>TAVI not feasible [%] (AnnDia: TAVI feasible due to smaller annulus)</td>
<td>2.6</td>
<td>4.3</td>
<td>1.3</td>
</tr>
</tbody>
</table>

Conclusions: In our model in which patients referred for TAVI procedures were allocated to receive a transcatheter aortic valve prosthesis of a specific size, the decision to measure aortic annulus size during systole or during diastole would not only have had an impact on the choice of prosthesis size in more than 20% of patients but also on the judgement of whether TAVI would have been feasible. These results need to be verified in studies of on-going TAVI registries.

P4565 | BEDSIDE
Change in frailty status in octogenarians with severe symptomatic aortic stenosis after aortic valve replacement
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Background: Frailty has emerged as a measure of physiological reserves and as a predictor of mortality, prolonged hospitalization and readmissions after cardiac intervention.

Purpose: The aim of the study was therefore to observe change in frailty status six months after aortic valve replacement (AVR).

AORTIC VALVE DISEASE II

P4566 | BEDSIDE
Impact of computed tomography aortic annulus measurements during systole and diastole on prosthesis choice in patients undergoing transcatheter aortic valve implantation
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Background: Measurement of the aortic annular diameter in patients before transcatheter aortic valve implantation (TAVI) is crucial for the selection of the correct prosthesis size and interventional success rate. Cyclic changes during systole and diastole can result in significant differences in the annular diameter size.

Purpose: To analyse the impact of annulus measurements during systole or diastole on the choice of prosthesis size in a virtual model, assuming the Sapien3, ACURATE TA, and CoreValve as prosthesis.

Methods: We determined the effective annulus diameter size of patients with severe aortic valve stenosis scheduled for TAVI by computed tomography during systole (AnnSys) and diastole (AnnDia), as described previously. Patients were then virtually assigned to receive a prosthesis of specific size due to the manufacturer’s specifications. We analysed differences in the strategy to allocate the correct prosthesis size.

Results: In this single-centre registry, 696 patients were included. Although absolute differences in mean AnnSys (24.2±2.1 mm) and AnnDia (23.4±2.1 mm, p<0.001) were small, these differences would have influenced the choice of prosthesis size. Considering AnnSys as the valid annulus diameter compared with AnnDia resulted in the strategy decisions shown (Table 1).

Table 1

<table>
<thead>
<tr>
<th>Strategy decision</th>
<th>Sapien3</th>
<th>ACURATE TA</th>
<th>CoreValve</th>
</tr>
</thead>
<tbody>
<tr>
<td>No change [%]</td>
<td>75.4</td>
<td>59.2</td>
<td>70.0</td>
</tr>
<tr>
<td>Choice of larger size [%]</td>
<td>21.8</td>
<td>28.4</td>
<td>28.6</td>
</tr>
<tr>
<td>TAVI feasible [%] (AnnDia: annula too small)</td>
<td>0.1</td>
<td>8.0</td>
<td>0.1</td>
</tr>
<tr>
<td>TAVI not feasible [%] (AnnDia: TAVI feasible due to smaller annulus)</td>
<td>2.6</td>
<td>4.3</td>
<td>1.3</td>
</tr>
</tbody>
</table>

Conclusions: In our model in which patients referred for TAVI procedures were allocated to receive a transcatheter aortic valve prosthesis of a specific size, the decision to measure aortic annulus size during systole or during diastole would not only have had an impact on the choice of prosthesis size in more than 20% of patients but also on the judgement of whether TAVI would have been feasible. These results need to be verified in studies of on-going TAVI registries.
Methods: In this observational prospective cohort study including patients at 80+ with severe symptomatic aortic stenosis (AS) accepted for transcatheter aortic valve implantation (TAVI) or surgical aortic valve replacement (SAVR), frailty status was assessed one day prior to and six months after AVR using the Study of Osteoporotic Fracture (SOF) Frailty Index. Patients were categorized as robust, pre-frail or frail accordingly. EuroScore was used to determine operative risk and Charlson Comorbidity Index to measure comorbidity. The McNemar-Bowker Test of Symmetry was used to investigate whether AVR could change frailty status in the total study population.

Results: In all, 143 patients were included, mean age 83 years (SD 2.7). Thirty-four percent were robust, 27% pre-frail and 39% frail. There was no significant difference in frailty status between treatment groups (p = 0.11) or between sexes (p = 0.88). Frail patients were in a higher New York Heart Association (NYHA) function class II (p = 0.03) and had higher S-ProBNP (p = 0.04). No significant differences were detected in EuroScore (p = 0.07), Charlson Comorbidity Index (p = 0.12) or in aortic valve area (p = 0.78). The proportion of patients who improved their frailty status was 34% whereas 18% changed for the worse. However, no significant overall change was observed (p = 0.16).

Conclusion: No significant change was observed in overall frailty status after six months, but our findings show that frailty is a dynamic syndrom; an important finding from a clinical perspective which must be further studied.

P4567 | BEDSIDE
The opening of aortic valve during exercise is a key to prevent development of aortic insufficiency among those with closed aortic valve at rest during ventricular assist device support
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Background: We previously demonstrated that the opening of native aortic valve (AV) at rest was a sufficient condition to prevent development of aortic insufficiency (AI) during left ventricular assist device (LVAD) support. However, clinical impact of native AV opening during exercise in patients with closed native AV at rest remained unknown.

Methods: We enrolled 37 patients whose native AV remained closed at rest at 3 months after CF LVAD implantation, and followed them at our institute between 2006 and 2014.

Results: Of them, 7 patients (19%) who had achieved the opening of native AV during cardiopulmonary exercise testing at the 3rd months (the opening group, Fig A), had better tolerability than improved LV contractility during exercise over those with closed native AV irrespective of exercise (the closed group) (p = 0.05 for all). The opening group suffered no AI at the 6th months (Fig B), and had higher readmission-free ratio due to cardiovascular events over the closed group during 2-year study period (100% vs. 56%, p = 0.005).

Conclusion: The opening of native AV during exercise was sufficient condition to prevent development of AI in patients with closed native AV at rest. Aggressive cardiac rehabilitation to improve exercise tolerability may have a prophylactic impact on development of AI accompanied by better quality of life during CF LVAD treatment.

P4568 | BEDSIDE
Long term survival after aortic valve replacement: role of European and American guidelines adherence
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Background: ESC and ACC/AHA guidelines recommend aortic valve replacement (AVR) with class I indication only for patients with symptomatic severe aortic valve stenosis (SSAVS) and asymptomatic patients with depressed left ventricle ejection fraction (LVEF < 50%).

Purpose: We examined the influence of International guidelines adherence on long term survival.

Methods: 604 patients underwent isolated AVR for SAVS between January 2001 and December 2012. The population was first divided in two groups based on preoperative LVEF (≤ or ≥50%). A second step analysis was performed based on presence or absence of symptoms (NYHA ≤ 1 or ≥II respectively).

Results: Median follow-up time was 5.75 years (3.24–8). Patients with LVEF ≤50% presented higher long term mortality (p = 0.015). Presence of symptoms had a not a significant negative impact on mortality (p = 0.201) (panel A). The combined analysis (panel B) showed that preserved LVEF is a protective factor for mortality in asymptomatic patients (class IIb) and asymptomatic patients with reduced LVEF presented higher risk of mortality (HR 1.32, CI 95%, 0.12–14.17). LVEF did not play any role in mortality for symptomatic patients (class Ia) (HR 0.41, CI 95%, 0.18–0.95). At multivariate analysis the independent risk factors for death were age (HR 6.46, CI 85%, 2.22–18.76) and presence of atrial fibrillation (HR 1.07 CI 95%, 0.57–2.04) or new permanent pace-maker (HR 1.21, CI95%, 0.44–3.32) at discharge.

Conclusions: Current international class Ia indications for symptomatic patients guarantee a good long term survival. Class Ia indications for asymptomatic patients with reduced LVEF are associated with poor long term survival. Present findings suggest the need of critical revision of surgical indications for this specific group of patients.
P4570 | BEDSIDE
Echocardiographic and MRI assessment of myocardial strain and strain rates using speckle tracking and feature tracking in asymptomatic aortic stenosis
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Background: Myocardial deformation analysis allows detection of subclinical myocardial dysfunction, which may have prognostic value in aortic stenosis (AS). Speckle tracking Echocardiography (STE) is the most widely used technique for strain assessment, while Feature tracking (FT) is a novel technique on magnetic resonance imaging (MRI).

Purpose: To compare MRI-FT and STE in patients with AS and healthy controls (HC).

Methods: 138 Patients with asymptomatic moderate-severe AS and 23 controls underwent STE/MRI on the same day. Only patients with full STE and MRI datasets were included. Measurements included global longitudinal peak systolic strain (PSS), peak systolic strain rate (PSSR) and peak early diastolic strain rate (PEDSR). Agreement was assessed with t-tests, correlation and intra-class correlation coefficients.

Results: 72 AS patients (age 65±12.9 years, 72% male, aortic valve area 1.15±0.34 cm², mean pressure gradient 34.47±12.24 mmHg) and 16 HC (mean age 68±8.24 years, 75% male, mean AVA 3.49±0.86 cm²) were included. There was no significant difference in PSS between the two groups, but with poor agreement. There was a significant positive bias for FT strain rates which was particularly marked for peak early diastolic strain rate with poor agreement between techniques. This finding likely results from poor speckle tracking during diastole.

Conclusions: Myocardial strain and strain rates measured with FT and STE in asymptomatic patients with AS have poor agreement even in patients with good echocardiographic images. Further work is required to determine whether MRI measured strain/strate can be useful in the management of asymptomatic patients with AS.

Acknowledgement/Funding: National Institute Health Research, Universities Hospitals of Leicester, Cardiovascular Biomedical Research Unit Glenfield Hospital

P4571 | BEDSIDE
The relationship between aortic valve weight and hydraulic load in patients with severe isolated aortic stenosis who underwent surgical aortic valve replacement
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Background: Aortic valve calcification (AVC), and the hydraulic vascular load both play important roles in defining global LV afterload in aortic stenosis (AS). We sought to determine the magnitude of vascular load and its relationship with AVC in severe AS.

Methods: Of 719 pts with isolated severe AS who underwent surgical AVR between 2010–2014 and had AV weight, 649 (age = 76±9 yrs, 59% men, mean AVA = 0.33±0.09 cm², EF = 56±12%, AV weight = 2.46±1g) had complete hemodynamic profile. Systemic vascular resistance (SVR), systemic arterial compliance (PSS), and global LV afterload (ZVA) could be measured in 276 pts. 4 hemo-dynamic subgroups were analyzed using cut points of stroke volume index (SVI) and mean gradients (MG) of 35 ml/b/m² and 40 mm Hg, respectively. Normal flow/high gradient (NF/HG) and low flow (LF/HG) groups had the highest valves, whereas the LF/HG group had the worst vascular indices in both unadjusted (table) and adjusted models.

Conclusions: F FT is modestly associated with SAC. 2. Pts with LF/HG have the worst vascular profile which may contribute to a decline in stroke volume and adverse postoperative outcomes.

P4572 | BEDSIDE
Pre-procedural dual antiplatelet therapy and bleeding events following transcatheter aortic valve implantation (TAVI)
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Introduction: TAVI is associated with bleeding that increases mortality. Little is known about pre-procedural dual antiplatelet therapy (DAPT) use and its impact on hemostasis.

Purpose: We sought to determine the frequency, predictors and bleeding risk in patients receiving DAPT before TAVI.

Methods: Three-hundred-and-three (n=303, 76±6±7 years, 49% female, EuroScore 23.1±16.9) consecutive patients were prospectively analyzed and followed for in-hospital events. According to pre-procedural ant platelet status population was divided into 2 groups: patients receiving aspirin and clopidogrel (DAPT) and those on aspirin only or no antiplatelet therapy (noDAPT).

Results: Pre-procedural DAPT was used in 139 cases (46%). Previous PCI (OR 4.8 [2.8–8.3]; p<0.0001), implantation of self-expandable prostheses (OR 2.1 [1.2–4]; p=0.007) femoral access (OR 2.2 [1.1–4.5]; p=0.026) and platelet count (OR 1.006 [1.002–1.01]; p<0.002) were independent predictors of pre-procedural DAPT. No difference was observed in the rates of any bleeding (23% in DAPT vs. 24.4% in noDAPT, p=0.930) or major/life-threatening bleeding (12.2% in DAPT vs. 14.7% in noDAPT, p=0.715). Propensity-score matching analysis did not alter the results. GFR ≥30 ml/min was the strongest predictor of bleeding (OR 4.3 [1.9–9.9]; p<0.0005). There was a trend towards lower frequency of MI and stroke/TIA in DAPT as compared with noDAPT (3.6% vs 9.8%; p=0.082).

Conclusions: Pre-procedural DAPT is frequent and does not increase short-term bleeding complications following TAVI. Possible impact of DAPT use before TAVI on ischemic complications needs to be investigated in larger populations.

Acknowledgement/Funding: Supported by unrestricted Grant from the Polish Ministry of Science and Higher Education (No. N402 4400 33)

P4573 | BEDSIDE
Aortic anatomical parameters do not predict procedural success in patients undergoing transcatheter aortic valve implantation
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Objectives: The aim of our study was to assess whether anatomical parameters predict procedural success in patients undergoing transcatheter TAVI.

Methods: 296 consecutively patients suffering from severe, symptomatic aortic stenosis underwent multislice computed tomography (MSCT) before TAVI. Anatomical parameters were assessed qualitatively and quantitatively: annulus dimensions (maximum and minimum diameter, perimeter, area, ellipticity index), aortic annulus calcification, of the left ventricular outflow tract (LVOT), aortic annulus (AA), and aortic valve (AV) were measured by two blinded investigators.

The primary endpoint of our study was device success in accordance with the VARC-2 criteria defined as absence of procedural mortality, correct positioning of the prosthetic heart valve into proper anatomical location, and function of the prosthetis itself (no prosthetis-patient mismatch, mean pressure gradient <20mmHg, peak velocity <3m/s, no moderate or severe paravalvular aortic re- gurgitation (AR)) plus the absence of stroke.

Results: 296 patients (age 81±16 years, 54% male, left ventricular ejection fraction 51.7± 14.4%, EuroSCORE II 5.5 [3.4–11.2%] underwent transcatheter TAVI at our institution.

Device success was achieved in 253 patients (85.5%); 4 peri-procedural deaths, 5
strokes, 13 valve-in-valve procedures due to misplacement of the first prosthesis, and 21 patients with moderate paravalvular AR. The Rosenhoeck score and semi-quantitative assessment of LVOT and AA calcifications did not show any relationship to the occurrence of more than mild paravalvular AR or procedural success. Mass and volume of LVOT and AV calcifications were associated with the occurrence of paravalvular AR immediately after deployment of the transcatheter heart valve but not with the final result after corrective measures such as postdilation (Figure) and did also not show any relationship to procedural success.

The annulus dimensions and consecutively the cover index (but not the AA annulus (P=0.277) were the only parameters that were associated with more than mild paravalvular AR: perimeter (79.2±8.4 vs. 73.6±6.4 mm; P=0.005), area (480.5±99.0 vs. 421.7±73.4 mm²; P=0.01), ellipticity index (1.32±0.10 vs. 1.29±0.11; P=0.01), and cover index (9.1±1.9 vs. 7.5±9.5%; P<0.001).

Conclusions: Anatomical parameters except for the dimension of the aortic annulus and the degree of oversizing reflected by the cover index do not predict the occurrence of paravalvular AR or procedural success in patients undergoing transcatheter aortic valve implantation.

P4574 | BEDSIDE
Additional value of exercise-stress echocardiography in asymptomatic patients with aortic valve stenosis
Aims: Usefulness of exercise-stress echocardiography for risk stratification of asymptomatic patients with aortic stenosis (AS) is still debated (Class IIIb recommendation). The exercise-induced increase in transvalvular gradient has been proposed as a parameter of the center for factor but data are scarce. We sought to evaluate the additional prognostic value of echocardiographic parameters during exercise-stress echocardiography.

Methods: In this observational prospective study, we enrolled all consecutive asymptomatic patients with moderate/severe AS and normal ejection fraction who underwent an exercise-stress echocardiography at our institution. Clinical and echocardiographic data at rest and at peak exercise were collected. The composite primary outcome variable was the occurrence of AS related events (symptoms or heart failure related to the AS or cardiovascular death during follow-up).

Results: Among the 121 patients enrolled, 35 (29%) had an abnormal exercise test (occurrence of symptoms or abnormal blood pressure profile during exercise) and were operated on within the following weeks. Eighty-six patients (mean quartiles; age 67 [57–75] years, 68 male, mean gradient 46 [35–52] mmHg, aortic valve area 0.87 [0.62–1.11] cm²) had a normal exercise test and 34 (48%) reached the clinical endpoint during follow-up (17.5 [10.9–36.4] months). The proposed threshold of 18 mm Hg mean gradient increase had no prognostic value. In multivariate analysis, rest mean gradient (p=0.001; HR 1.07 [1.03–1.11]) but not exercise-induced increase mean gradient (p=0.4; HR 0.69 [0.29–1.65]) were predictive of outcome.

Conclusion: Exercise-induced increase in mean gradient was not predictive of outcome in patients with normal exercise-test. Our results raise questions regarding the additional value and therefore the use of exercise-stress echocardiography for risk stratification of asymptomatic patients with AS.

AORTIC VALVE INTERVENTIONS
P4575 | BEDSIDE
Improved management of left-sided infective endocarditis not accompanied by lower mortality
T. Sevilla1, P.E. Garcia Granja1, J. Lopez Diaz1, I. Vilaçoça2, C. Ortiz Bautista1, C. Olmo1, C. Ferrera2, I. Gomez1, J.A. San Roman1,1 University Hospital of Valladolid, ICICOR, Valladolid, Spain;2 Hospital Clinic San Carlos, Madrid, Spain
Introduction: Despite continued progress in the management of infective endocarditis (IE) this entity continues to have an in-hospital mortality of 20–30% which has remained steady over the past 2 decades. Objectives: The aim of this study is to determine if there is a relationship between a worsening epidemiological profile and the lack of improvement in mortality rates over the past 18 years in IE.

Methods: We prospectively collected all IE episodes diagnosed in three tertiary hospitals from 1997 to 2014. A global cohort of 969 left-sided IE episodes was generated. Predictive accuracy of the model and validation was measured (ROC area under the curve: 0.805). This model was applied to the second and the third periods. Expected mortality for the second period (2003–2008) according to the model was 32.1% whereas observed mortality in the cohort was 28.1% (12.5% of reduction). Expected mortality for the third period (2009–2014) was 30.7% and observed mortality was 27.4% (11.3% of reduction).

Conclusions: Although the crude in-hospital mortality rate of IE has remained unchanged over the past 18 years, there has been a reduction in observed mortality compared to the expected mortality according to the prognostic risk profile of the patients.

P4576 | BEDSIDE
Changes in clinical, epidemiological and prognostic profiles in native left-sided infective endocarditis without underlying heart disease
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Introduction: Native left-sided infective endocarditis (NSLIE) in patients without underlying heart disease has increased in the last decades, and their clinical, epidemiological and early prognostic profile can be changed.

Methods: Our aims are to compare NSLIE profile between patients with UHD and without (NUHD) underlying heart disease and 2) to describe changes in this profile in NUHD patients.

Results: From 1997 to 2014 a consecutive series of 254 patients diagnosed with NSLIE was analyzed. An anatomical classification of UHD (n=145) vs NUHD (n=109) was based on echocardiographic findings. Then, we compared changes that have occurred in NUHD patients from 1997 to 2000 (n=26) and from 2001 to 2014 (n=83).

1) The proportion of NUHD was significantly higher in the 2001–2014 period (54.2% vs 25.7%, P<0.001). The mean age was 53±5.18 years in the UHD group and 56±4 years in NUHD, P=0.2. There was no significant difference in the valve affected, but the size of endocardial vegetations was greater in NUHD than in UHD group (13.6±4mm vs 11.6±4mm, P=0.01). NSLIE caused by Streptococcus viridans was more frequent in the UHD group (34% vs 17.6%, P=0.004), but Enterococcus spp and Staphylococcus aureus were responsible for 23.1% and 20.4% in the NUHD group, respectively. The NUHD group had a more frequent history of intravascular catheter (12% vs 3%, P=0.009), liver disease (15% vs 3%, P=0.001), immunsuppressive condition (8% vs 0.6%, P=0.002), neoplasia (9% vs 2%, P=0.018) and diabetes mellitus (7% vs 1.3%, P=0.021). There were no differences in the development of complications or early surgery rate. Early mortality rate was similar (29% in the NUHD group and 21% in the UHD group, P=0.145). 2) NUHD group: the mean age was higher in the 2001–2014 period (60±15 years vs 41±21 years, P=0.001), and the size of endocardial vegetations was also greater (13±4mm vs 10.7±3mm, P=0.003). There were no significant differences in microbiology (Enterococcus spp 25% in both periods, Staphylococcus aureus 30% in both periods and 17% in 2nd period vs 1st period, P=0.131); and Streptococcus viridans 7% in 1st vs 20% in 2nd, P=0.152, or in risk factors. However, in 2001–2014 there was further development of cardiac complications (72% vs 35%, P<0.001), septic shock (29% vs 4%, P=0.008), a higher elective rate of surgery (48% vs 15%, P=0.004) and early mortality rate (38% vs 15%, P=0.033).

Conclusions: NSLIE in patients without underlying heart disease has great clinical severity because of their age and the high prevalence of comorbidities, and it has a similar short-term prognosis for those patients with previous valvular disease.

P4577 | BEDSIDE
A new gatekeeper for prevention of in-hospital mortality in infective endocarditis: platelet to lymphocyte ratio
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Background: Risk stratification constitutes for an important step in management of patients with infective endocarditis (IE) due to significant morbidity and mortality despite diagnostic and therapeutic improvements. Recently, platelet to lymphocyte ratio (PLR) has been defined as a novel indirect marker of inflammation and it has been significantly associated with adverse outcomes. We hypothesized that an increased PLR on admission would predict in-hospital mortality in patients with IE.

Methods: In this prospective study, a total of 120 consecutive patients with definite IE were enrolled. Clinical, echocardiographic and laboratory parameters were recorded. The outcome measure was in-hospital death from any cause. Independent predictors of in-hospital mortality were determined by Cox regression analysis.

Results: In-hospital mortality was observed in 28 (23.3%) patients. Patients in in-hospital mortality revealed a higher PLR (414.2±403.3 vs 208.3±33.1). CRP and white blood cell counts as compared with those survived (p<0.05). In ROC curve analysis, using a cut-off level of 207.5, on admission PLR level predicted in-hospital mortality with a sensitivity of 64%, specificity of 85%, and an area under the ROC curve of 0.85 (95% CI 0.77–0.92). The PLR cut-off level of 207.5 was confirmed as a significant predictor of in-hospital mortality in these patients.
Conclusion: Our study findings showed that on-admission PLR value well predicted in-hospital mortality in IE. Thus, the PLR, as a simple, easy to use and promising biomarker, help us in identification and risk stratification of high-risk IE patients for early aggressive management strategies to prevent in-hospital mortality.

P4578 | BEDSIDE
The impact of a second mitral valve surgery after repairing a rheumatic mitral valve
Background: The repair of rheumatic mitral valves (MV) is not consensus based, on the less favourable reports concerning the immediate rate and shorter durability of mitral valve repair (MVR).

Purpose: We purposed to analyse MV reoperations in this setting and the impact of a second mitral valve intervention after repairing a rheumatic MV.

Methods: From January 1992 to December 2012, 1491 patients with isolated rheumatic MV disease (tricuspid regurgitation admitted) and without previous MV intervention, were submitted to MV surgery, of which 1201 had MVR (80.5%). There were 136 reoperations during follow-up (124 had MVR and 8 replacement in the first surgery). The causes of reoperation were ascertainment and survival (Kaplan-Meier) was further analysed to compare the patients who needed a second surgery with those who did not (log-rank).

Results: The mean age was 60.6±10.5 years, female gender prevailed (73%), the mean age was 60.6±10.5 years, female gender prevailed (73%), the majority of patients were in NYHA class III-IV (63.3%), 52.8% were in atrial fibrillation (AF).

Conclusions: Despite the higher number of reoperations in the MVR patients, the survival free of reoperation (p=0.214). The mean time from MVR to reoperation was 10±5.3 years. In 20%

P4580 | BEDSIDE
How accurate are cardiologists at detecting aortic and mitral murmurs? a reality check on auscultation skills in the era of transcatheter interventions
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Background: Recent dramatic breakthroughs in the transcatheter treatment of aortic and mitral valve disorders have offered amazing new therapies to patients. However, to fully benefit from these procedures, patients need their cardiologist to detect their valve problem in a timely manner. We wanted to test cardiologists’ auscultation skills at detecting common aortic and mitral murmurs.

Purpose: To assess the skill of cardiologists in detecting basic and advanced aortic and mitral murmurs.

Methods: A total of 1098 cardiologists volunteered to undergo a test of their auscultation skills at an annual cardiology meeting (American College of Cardiology). Cardiologists chose to be tested on a set of basic murmurs including Aortic Stenosis, Mitral Regurgitation, Mitral Stenosis, Tricuspid Regurgitation and Aortic Regurgitation. Cardiologists could choose to be tested on both modules. After a pre-test, all subjects listened to 400 repetitions of each murmur while viewing cardiac images including phonocardiograms relevant to that lesion. The training time averaged 90 minutes for each set of murmurs. Immediately following the training, there was a posttest of the respective murmurs in a randomized order. The test murmur samples were from different patients than the training murmur samples.

Results: On the basic murmurs, 980 cardiologists scored 47.6±12% on the pretest which increased to 88.4±15% on the posttest (p<0.001, paired t-test).

Conclusions: Cardiologists’ auscultation skills on both basic and advanced murmurs are alarmingly low. These skills are crucial for patients to fully benefit from the amazing advances in transcatheter treatments for valvular heart disease. However, these auscultation skills improve dramatically following intensive repetition training in a short time frame.

P4579 | BEDSIDE
Inter-rater variability in reporting screening echocardiograms for rheumatic heart disease in high risk populations
Background: The repair of rheumatic mitral valves (MV) is not consensus based, on the less favourable reports concerning the immediate rate and shorter durability of mitral valve repair (MVR).

Purpose: To purposed to analyse MV reoperations in this setting and the impact of a second mitral valve intervention after repairing a rheumatic MV.

Methods: From January 1992 to December 2012, 1491 patients with isolated rheumatic MV disease (tricuspid regurgitation admitted) and without previous MV intervention, were submitted to MV surgery, of which 1201 had MVR (80.5%). There were 136 reoperations during follow-up (124 had MVR and 8 replacement in the first surgery). The causes of reoperation were ascertainment and survival (Kaplan-Meier) was further analysed to compare the patients who needed a second surgery with those who did not (log-rank).

Results: The mean age was 60.6±10.5 years, female gender prevailed (73%), the majority of patients were in NYHA class III-IV (63.3%), 52.8% were in atrial fibrillation (AF).

Conclusions: Despite the higher number of reoperations in the MVR patients, the survival free of reoperation (p=0.214). The mean time from MVR to reoperation was 10±5.3 years. In 20%...
(TAVI) as well as increasing demand for intervening severe aortic valve and coronary artery diseases, there is significant interest in evaluating outcomes of aortic valve replacement (AVR) with or without ‘+/-’ concurrent coronary artery bypass grafting (CABG), particularly in high-risk patients to inform decision-making for modality of intervention.

Purpose: We reviewed the characteristics and outcomes of octogenarians undergoing isolated AVR and AVR+CABG at our centre.

Methods: All patients 80 years of age or older undergoing AVR +/- CABG at our City Hospital during 2005–2012 were included, and their characteristics and outcomes collected for analyses.

Results: There were 93 and 104 octogenarians respectively undergoing isolated AVR and AVR+CABG with mean follow-up of 4.4±2.2 years and 4.1±2.3 years. On average 10 more cases of AVR +/- CABG per year were performed from 2010 onwards. AVR was started at our centre. AVR+CABG patients have significantly higher proportion with history of myocardial infarction, left main and three vessel disease (all P<0.005), higher average CCS and NYHA class (both P<0.001), impaired renal function (P=0.019), higher STS score (6.9% vs 4.9%, <0.001) and longer cardiopulmonary bypass and cross-clamp time (both P<0.001) compared to AVR. They also had significantly higher rate of operative mortality (6.7% vs 0.0%, P=0.015) and prolonged ventilation 24 hours (23.1% vs 10.7%, P<0.001), but similar late mortality (P=0.195). Survival at 1, 3 and 5 years were 94.6%, 82.6% and 73.0% for AVR and 91.3%, 86.1% and 67.6% for AVR+CABG.

Conclusion: AVR+CABG had significantly higher but acceptable operative mortality in octogenarians similar to other studies and age-groups. These factors are important for the consideration of patients undergoing AVR +/- CABG or TAVI +/- percutaneous coronary intervention, where age alone should not exclude someone from undergoing cardiac surgery.

P4582 | BEDSIDE
Impact of direct transcatheter aortic valve implantation on final device position and paravalvular leak. Is it beneficial?


Background: Transcatheter aortic valve implantation (TAVI) may be limited by paravalvular leak (PVL) related to malpositioning of the bioprosthesis. Balloon aortic valvuloplasty (BAV) prior device implantation is often used. The potential effect of BAV in the implantation depth (ID) and consequently in post-TAVI PVL is not known.

Purpose: We compared patients in whom BAV was performed prior to device implantation in the same session during TAVI, with those that BAV was not used. ID and PVL was evaluated.

Methods: We studied 191 consecutive patients who underwent TAVI by two interventionalists. The one is using direct TAVI while the other is using BAV prior to implantation, as default strategies. There were 147 patients (78 males; 81±5 years) with BAV (group 1) and 44 patients (22 males; 79±8 years) without BAV (group 2). Metric pigtail was used for calibration during aortography. Initial (stage 1), immediate before release (stage 2) and after release (stage 3) ID of the prosthesis was recorded in non-coronary cusp (NC) and left coronary cusp (LC). PVL was evaluated by angiography. In all patients the CoreValve was used.

Results: Baseline clinical characteristics were comparable between the BAV and no-BAV group. In group 2, ID at NC increased from stage 1 to stage 2 to stage 3 (4.5mm±1.8SD to 7.4mm±2.7SD to 8.2mm±5.2SD, respectively), (repeated measures ANOVA, p<0.001). In group 1, ID at NC increased from stage 1 to stage 2, but decreased from stage 2 to stage 3 (3.5mm±1.9SD to 7.2mm±2.9SD to 7.3mm±4.5SD, respectively), (repeated measures ANOVA, p<0.001). Thus, when we compared the difference of the ID (stage 3-stage 2) between group 1 and group 2, we found significant increase in depth in group 2 (~0.77mm±4.2SD) vs significant decrease of the ID in group 1 (0.55mm±2.4SD), (p=0.033). These differences were not detected at LC. In a linear regression the absence of BAV prior to device implantation was the only predictor for greater ID after device release. In addition, PVL of grade II immediately post implantation was less in group 2 vs group 1 (6.8% vs 20.4%, p=0.036, respectively), probably as a result of close contact between the device and the aortic cusps.

Conclusions: The absence of BAV prior to device implantation, lead to a deeper position, probably by restricting the corrective manipulations. However PVL is less. The exact mechanism is not known and further studies are needed to explore these findings.

P4583 | BEDSIDE
Treatment of post procedural aortic regurgitation in transcatheter aortic valve replacement patients


Background: Post procedural aortic regurgitation (AR) is a prevalent adverse outcome of transcatheter aortic valve replacement (TAVR), which has significant impact on mortality.

Purpose: Our goal was to evaluate methods of treatment of post-procedural AR in TAVR patients.

Methods: We categorized patients with AR—mild following valve deployment to 3 groups consisting of balloon post-dilatation only, second valve deployment and medical therapy only.

Results: Among 649 patients undergoing TAVR, we identified 96 (15%) patients with AR—mild following deployment, of whom 69 (72%) were treated with balloon expandable device. Treatment groups were balloon post-dilatation in 40 (42%), second valve implantation in 9 (9%) among which 5 patients were treated with balloon post-dilatation prior to the second valve deployment, and medical therapy in 47 patients (49%). Reduction of AR to mild and below was noted in 59% and 89% of the re-ballooning group and second valve group, respectively, while no reduction was noted in the medical therapy group. Mortality rates at 1-year tended to be lower in patients with re-intervention compared with medical therapy (25% vs. 43%, χ2=0.08), and lower in patients with low AR severity compared with moderate and above (28% vs. 39%, p<0.01).

Conclusions: Re-ballooning or second valve implantation successfully reduces severity of AR in TAVR patients and should be sought diligently in order to improve survival rates.

P4584 | BEDSIDE
Safety of transcatheter aortic valve implantation in patients with pure native aortic valve regurgitation

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Transcatheter Aortic Valve Implantation (TAVI) has become an alternative to surgical treatment in patients with severe aortic stenosis and high surgical risk, however, in patients with native and inoperable severe aortic regurgitation remains limited. The aim this study was to evaluate the use of TAVI in patients with pure native aortic valve regurgitation and comparing them with patients with aortic stenosis.

Methods: From April 2008 to December 2014, the CoreValve prosthesis (Medtronic, USA) was implanted in 10 consecutive high-risk surgical patients with symptomatic severe aortic regurgitation (AR) and in 431 patients with aortic stenosis (AS).

Results: The mean age and logistic EuroSCORE were similar in both groups (AVR vs. AS) 72±9.4 vs. 79±6.8 years, p=0.993 and 15.3±8% vs. 17.7±12, p=0.552 respectively. There were significant differences in measurement of anulus and ascending aortic size (24.5±1.7 vs. 22.1±1.8 mm, p=0.001 and 15.3±8% vs. 17.7±12, p=0.005, respectively). Implantation of a TAVI was performed successfully in all patients with AR and the post-procedure aortic regurgitation grade was: absent in 5 patients, moderate in 4 patients, and moderate-severe in one patient.

Conclusions: The NYHA functional class improved from 3.2±0.6 to 1.6±0.5 and remained stable at one year. The mortality at 30 days was 10% in patients with AR compared to 3.7% in patients with AS, p=0.307 and there was no significant differences with late mortality (11.2% vs. 15.2%, p=0.738) after a mean follow-up of 30.5±20 months. The patients with AR had more acute kidney injury after procedure and lower occurrence of new onset left bundle branch block than patients with AS (40% vs. 15.3% [OR=3.68 (95% CI 1.01–13.4), p=0.037] and 11.1% vs. 47.8%, [OR=0.96 (95% CI 0.92–0.99) p=0.030], respectively.

Conclusions: TAVI with the CoreValve prosthesis for patients with aortic regurgitation and a high surgical risk is a safe and efficient option resulting in a medium-term clinical improvement.
PERICARDIAL AND MYOCARDIAL DISEASE, TUMOURS, OTHER

P4585 | BEDSIDE
Layer-specific strain in diabetic patients with normal ejection fraction using speckle tracking imaging
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Objectives: Preclinical left ventricular systolic dysfunction was documented in diabetes mellitus (DM) patients with normal ejection fraction (EF). The aim of this study is to quantitatively assess whether there is any difference in GLS and GCS of three-layers of cardium between DM patients and normal subjects using speckle-tracking imaging.

Methods: Fifty-seven DM patients and 60 matched controls were studied. All subjects have normal EF (<55%), GLS and GCS of three-layer cardium were assessed using layer-specific speckletracking echocardiography.

Results: GLS of three-layer cardium in DM patients are lower than those of normal control (DM vs normal, endo-GLS: −23.62±3.16 vs −25.06±2.85, P < 0.05; mid-GLS: −20.80±2.86 vs −22.15±2.59, P < 0.05; epi-GLS: −18.37±2.69 vs −19.63±2.40, P < 0.05). GCS of endo- and mid-cardium in DM patients are lower than those of normal controls (DM vs normal, endo-GCS: −29.31±5.31 vs −34.61±5.07, P < 0.05; mid-GCS: −17.93±3.57 vs −20.70±3.03, P < 0.05). GCS of three-layer cardium is the highest at the apex and the lowest at the base.

Conclusion: GLS of three-layer cardium may be a sensitive indicator of early left ventricular systolic dysfunction in DM patients with normal EF. GLS decreases in three-layer cardium, while GCS decreases only in endo-cardium and mid-cardium in DM patients.

P4586 | BEDSIDE
Anakinra: an emerging option for refractory idiopathic recurrent pericarditis: a systematic review of published evidence
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Purpose: Accumulating evidence suggests idiopathic recurrent pericarditis as a disease of probable autoimmune origin, and thus anakinra, an interleukin-1 inhibitor, could be of benefit.

The goal of this systematic review was to assess the efficacy and safety of anakinra in patients with idiopathic recurrent pericarditis published up to October 2014 in several databases. All references found, upon initial assessment at title and abstract level for suitability, were consequently retrieved as full reports for further appraisal.

Methods: Studies reporting the use of IVIG for the treatment of recurrent pericarditis and published up to December 2014 were searched in several databases. All references found, upon initial assessment at title and abstract level for suitability, were consequently retrieved as full reports for further appraisal.

Results: Among the 18 citations retrieved, 17 reports (4 case series and 13 single-case reports, with an overall population of 30 patients with 20 males and mean age 27 years) were included. The mean disease duration was 14 months and the mean number of recurrences before IVIG was 3. IVIG were prescribed after failure of other therapeutic attempts including at least NSAID, colchicine and corticosteroids. Approximately 47% of patients had idiopathic recurrent pericarditis, 10% had an infective cause, and the remainder a systemic inflammatory disease. Nineteen out of the 30 patients (63.3%) were on corticosteroids at IVIG commencement. IVIGs were generally administered at a dose of 400–500 mg/kg/day for 5 consecutive days for one cycle and with possible repeated cycles according to the clinical response. Complications were uncommon (headache in approximately 3% of cases) and not severe or life-threatening. After a mean follow-up of 71 months, namely 33 months after completion of all cases after the first IVIG cycle, and 6.6% after subsequent cycles. At the end of follow-up, 22 of the 30 patients (73.3%) were recurrence-free and five patients (16.6%) were on corticosteroids.

Conclusions: IVIG are rapidly acting, well tolerated, and efficacious steroid-sparing agents in refractory recurrent pericarditis after failure of conventional therapies.

P4587 | BEDSIDE
Lipoprotein-associated phospholipase A2 (Lp-PLA2), a vascular inflammation marker, is frequently increased in patients presenting with acute pericarditis
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Introduction: Lp-PLA2 plays a causal role in the development of atherosclerosis and contributes to plaque instability through pathways related to non-systemic inflammation. Lp-PLA2 concentration in healthy controls is 163±43 ng/ml and 235 ng/mL is used as a cutoff value for clinical decision. So far, Lp-PLA2 levels were not reported among acute pericarditis (AP) patients.

Hypothesis: Levels of Lp-PLA2 in AP, a nonvascular inflammation, should be normal. Lp-PLA2 was measured in 35 patients with AP presenting with chest pain, ST elevation and increased Troponin I (Tnl).

Results: Patients aged (mean±SD, median): 37±14±2.2, 32 years, respectively. 90% were males. Mean (SD), median and range of Lp-PLA2 were 247 (66), 237, 139–408 ng/ml, respectively. Abnormal Lp-PLA2 level (greater than 235ng/ml) was present in 51% of cases.

Conclusions: We demonstrated that Lp-PLA2 is increased in AP patients and its level correlates with systemic markers of inflammation and necrosis suggesting that this enzyme is not exclusively associated with vascular/unstable plaque inflammation.

P4588 | BEDSIDE
Intravenous human immunoglobulins for refractory recurrent pericarditis: a systematic review of all published cases
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Purpose: Refractory recurrent pericarditis is a major clinical challenge after colchicine failure, especially in corticosteroid-dependent patients. Human intravenous immunoglobulins (IVIG) have been proposed as possible therapeutic options for these cases. The goal of this systematic review is to assess the efficacy and safety of IVIG in this context according to published studies.

Methods: Studies reporting the use of IVIG for the treatment of recurrent pericarditis were published up to December 2014 were searched in several databases. All references found, upon initial assessment at title and abstract level for suitability, were consequently retrieved as full reports for further appraisal.

Results: Among the 18 citations retrieved, 17 reports (4 case series and 13 single-case reports, with an overall population of 30 patients with 20 males and mean age 27 years) were included. The mean disease duration was 14 months and the mean number of recurrences before IVIG was 3. IVIG were prescribed after failure of other therapeutic attempts including at least NSAID, colchicine and corticosteroids. Approximately 47% of patients had idiopathic recurrent pericarditis, 10% had an infective cause, and the remainder a systemic inflammatory disease. Nineteen out of the 30 patients (63.3%) were on corticosteroids at IVIG commencement. IVIGs were generally administered at a dose of 400–500 mg/kg/day for 5 consecutive days for one cycle and with possible repeated cycles according to the clinical response. Complications were uncommon (headache in approximately 3% of cases) and not severe or life-threatening. After a mean follow-up of 71 months, namely 33 months after completion of all cases after the first IVIG cycle, and 6.6% after subsequent cycles. At the end of follow-up, 22 of the 30 patients (73.3%) were recurrence-free and five patients (16.6%) were on corticosteroids.

Conclusions: IVIG are rapidly acting, well tolerated, and efficacious steroid-sparing agents in refractory recurrent pericarditis after failure of conventional therapies.

P4589 | BEDSIDE
Cardiac assessment of patients with familial amyloid polyneuropathy
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Background: Familial amyloid polyneuropathy (FAP) is an autosomal dominant disease, caused by a mutation in the transthyretin gene. It is characterized by a wide heterogeneity of genotypes and predominantly neurological and cardiac phenotypes.

Purpose: The purpose of this study was to assess cardiac involvement in a group of patients with FAP.

Material and methods: Forty five consecutive patients with genetically verified FAP were prospectively included in the study. All patients were referred to our center because of signs and symptoms of peripheral polyneuropathy. Cardiac assessment included a clinical examination, electrocardiography (ECG), echocardiography (ECHO). The mean age (range) of the patients was 58±6.8 years (42–72 years), 26 of them were male. The following mutations were isolated - G129G36 in 35 patients, Val30Met in 5, Ser77Pro in 4 and Ser23Pro in one patient.

Results: Cardiac involvement was evident on echocardiography in all patients. There was a significant increase in left and right ventricular wall thickness

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(septum=18.1±3.4mm, posterior wall=17.1±2.5mm, right ventricular free wall=8.1±2mm). A varying degree of diastolic dysfunction was found – mild in 17 (37.8%) patients, moderate in 10 (22.2%) and severe in 18 (40%) patients. Reduced LV ejection fraction was found in 8 (17.8%) patients. Significantly reduced mitral annular myocardial velocities (s′a=−5.9±2.1 cm/s, e′a=−5.8±1.7 cm/s) were registered. Pericardial effusion was evident in 14 (31.1%) patients. Pathologic ECG was present in 40 (88.9%) of the evaluated patients and the most common findings were low voltage in 16 (35.6%), A-V block first degree in 12 (26.7%), left anterior fascicular block in 12 (26.7%), pathological Q wave in 13 (28.9%) patients.

Conclusion: Cardiac involvement was found in all evaluated patients at the time of diagnosis, but peripheral neuropathy was more common presenting condition. Cardiac assessment is an important part of the evaluation of patients with suspected FAP and the presence of some typical features on Echo and ECG may warrant genetic analysis and lead to diagnosis.

**P4590 | BEDSIDE**

Comparative assessment of right ventricular outflow tract (RVOT) dimensions by echocardiography and magnetic resonance tomodraphy in arrhythmogenic right ventricular cardiomyopathy (ARVC)

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ARVC is an inherited disease that accounts for up to 25% of sudden cardiac deaths in young individuals. Hence, an early diagnosis is essential to prevent fatal outcome. According to the 2010 Task Force criteria, 6, in transhoschoric echocardiography (TTE), a diagnostic criterion is met if RVOT dilation in addition to RV wall abnormalities is present. Recent studies questioned the diagnostic performance of TTE in comparison to cardiac magnetic resonance (CMR). Therefore, we investigated the reproducibility of TTE and CMR RVOT measures in patients with ARVC.

**Methods:** Besides the TTE RVOT measurements of the TFC (RVOT-PLAX-RVOT 1, Fig. 1a; and RVOT-PSAX-RVOT 2, Fig. 1b), we assessed additional end-diastolic RVOT measures. These included the RVOT diameter in prolongation of M-Mode for the aorta and LA in PLAX (RVOT3, Fig. 1a), the RVOT diameter in prolongation of M-Mode for the Teichholz calculation of LVEF (RVOT 4, Fig. 1a), and the distal RVOT diameter right below the pulmonary valve (RVOT5, Fig. 1c).

**Results:** These are preliminary results from ongoing studies. Up to now, in 24 patients with a definite, borderline or possible ARVC diagnosis, CMR and TTE were performed. Significant differences between CMR and TTE were found for RVOT2 (p<0.011) and RVOT5 (p=0.002). RVOT 1 and RVOT4 exhibited the highest correlation (r=0.88 each), compared to RVOT3 (r=0.80). The best agreement between TTE and CMR was found for RVOT 4.

**Conclusions:***

The presence of IQRS on 12-lead ECG is associated with LGE on CMR and may warrant further evaluation for better risk stratification in patients with HCM.

**P4591 | BEDSIDE**

Fragmented QRS complexes in patients with hypertrophic cardiomyopathy: a marker of myocardial fibrosis detected by cardiac magnetic resonance imaging with gadolinium enhancement

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**Background:** Fragmented QRS complexes (IQRS) have been shown to be a sign of myocardial fibrosis/scarring and subsequent depolarization abnormality in patients with dilated cardiomyopathy, cardiac sarcoidosis and repaired cardiac tetralogy.

**Purpose:** The aim of this study was to evaluate the association between the IQRS and the late gadolinium enhancement (LGE) on CMR in patients with HCM.

**Methods:** The 12-lead ECGs of 191 patients with HCM who underwent CMR with gadolinium were analysed for the presence of IQRS. IQRS was defined as an additional deflection on the beginning or top of R wave (R′), or notching/fragmentation in the nadir of the R or S wave in 2 contiguous leads. Patients with typical bundle branch block pattern and with QRS >120 ms (n=31) were excluded from analysis.

**Results:** Of the remaining 160 patients, 64 (40%) had IQRS on 12-lead ECG and 102 (63.8%) had LGE on CMR. Patients with and without IQRS were of similar gender (69% vs. 73% respectively, p=0.52) and age (56±16 vs. 57±14 years respectively, p=0.78). LGE was significantly more prevalent in patients with IQRS complexes than patients without IQRS complexes (n=47, 73% vs. n=55, 57%, p=0.037). The positive predictive value of IQRS for LGE on CMR was 73.4%, with a specificity of 70.6%, sensitivity of 46% and negative predictive value of 42.7%. Patients with IQRS had also longer QRS duration (101±16ms vs. 92±13ms, p=0.001) indicating depolarization abnormality/delay in these patients.

**Conclusions:** These are preliminary results from an ongoing study. Up to now, 24 patients with a definite, borderline or possible ARVC diagnosis, CMR and TTE were performed. Significant differences between CMR and TTE were found for RVOT2 (p<0.011) and RVOT5 (p=0.002). RVOT 1 and RVOT4 exhibited the highest correlation (r=0.88 each), compared to RVOT3 (r=0.80). The best agreement between TTE and CMR was found for RVOT 4.

**Figure 1:** LGE on CMR and IQRS complexes

Conclusions: The presence of IQRS on 12-lead ECG is associated with LGE on CMR and may warrant further evaluation for better risk stratification in patients with HCM.

**P4592 | BEDSIDE**

Prognostic significance of non-dilated left ventricular size and mitral regurgitation in patients with end-stage phase of hypertrophic cardiomyopathy

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**Background:** Although a subtype of hypertrophic cardiomyopathy (HCM), end-stage phase of HCM characterized by left ventricular (LV) systolic dysfunction, has been reported to have a poor prognosis, some patients with end-stage HCM survive for a relatively long period. In patients with LV systolic dysfunction, degree of LV dilatation and functional mitral regurgitation (MR) are generally thought to be important predictors of poor prognosis. However, there has been little information on the relations among LV size, presence of MR and prognosis in end-stage HCM patients.

**Purpose:** The aim was to determine whether echocardiographic assessment of LV size and MR provides incremental prognostic information for those patients.

**Methods:** We studied 31 consecutive patients with end-stage HCM.

**Results:** During a follow-up period of 5.6±2.4 years, there were 13 HCM related deaths (cardiovascular survival rate of 84% at 5 years from diagnosis of end-stage phase). When the patients were divided into two groups by LV size at diagnosis of end-stage HCM: a non-dilated LV group (LV end-diastolic diameter (LVEDD) <50 mm, n=9) and a dilated LV group (LVEDD ≥50 mm, n=22), clinical course in the non-dilated LV group was significantly worsened. As for the clinical impact of MR, no patient in the non-dilated LV group showed significant MR and 7 of the patients with dilated LV size showed significant MR during follow-up. Once significant MR was reached, HCM related deaths were significantly more frequent in patients with MR (Figure: HCM related deaths according to LV size and presence of significant MR).

**Conclusions:** Patients with end-stage HCM, particularly those with less LV dilatation at diagnosis of end-stage phase and with significant MR during follow-up, had a poor prognosis.
P4594 | BEDSIDE
Cardiac MRI characterization of phospholamban R14del-related cardiomyopathy
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Background: The Dutch R14del founder mutation in the gene encoding for phospholamban (PLN) causes dilated and/or arrhythmogenic cardiomyopathy and is associated with increased risk of malignant ventricular arrhythmias and heart failure.

Purpose: To study ventricular function, and extent and localization of fibrosis using cardiac magnetic resonance imaging (CMR) with late gadolinium enhancement (LGE) in PLN R14del mutation carriers.

Methods: Contrast CMR studies of a representative sample of 196 mutation carriers were obtained by comparing the heart rate (HR) during the 1 study: before administration of atropine (0.02 mg/kg) and during the 10 study: after atropine. The same number of controls were obtained. A hypervagotonic BD was defined if after administration of atropine (0.02 mg/kg) the patient showed normalization of all parameters. The mean age at the time of the first examination was 145.9. During this period, 49 (68.1%) had normalization of SN function and AV conduction, lack of normalization of parameters after atropine (group B); 4 of them required pacemaker implantation. A comparison of different variants of the hypervagotonic binodal dysfunction (BD) in children. Comparison of different variants of the binodal dysfunction
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Purpose: This study aimed to assess the results of the natural course and comparison of the features of variants of the hypervagotonic binodal dysfunction (BD) in children.

Methods: We enrolled 72 consecutive pediatric patients, who at the first examination were diagnosed with hypervagotonic BD. BD included: combined sinus node dysfunction (SND): sinus bradycardia, sinoatrial block, sinus arrest with escape ectopic rhythm, and/or increasing the sinus node recovery time (SNRT) and/or ectopic rhythm, and/or increasing the sinus node recovery time (SNRT) and/or increasing the AV conduction, lack of normalization of parameters after atropine (group B); 4 of them required pacemaker implantation. A comparison of the different variants of the binodal dysfunction

Results: Sixteen patients were operated on for pulmonary venous stenosis (7), residual ASD or partial PVR (5) and vena cava stenosis (4). Twelve late deaths occurred (6.7%). 5 from non cardiac causes and 7 due to pulmonary veins stenosis. Survival was 80%, 75%, 70% and 65% at respectively 1 year, 10 years, 20 years and 40 years of FU. Survival was significantly lower in infracardiac type (p=0.0017). Overall 131 patients survived of whom 84.7% are in NYHA class I with none ongoing cardiac medication. Pulmonary pressure levels range within normal value in 109 cases (83%), grade I PHT persists in 9 (7%).

Conclusion: Overall late outcomes of patients with TAPVR is favourable, and the infracardiac type is associated with the lowest survival rates. Pulmonary veins stenosis is a rare but life-threatening late complication.
um HR: 80.69±4.07 (group A); 70.00±10.34 (group B) (p=0.035). After atropine: the mean HR: 107.5±24.89 (group A); 100.95±10.97 (group B) (p=0.024); minimum HR: 105.6±23.72 (group A); 93.5±11.26 (group B) (p=0.016); maximum HR: 116.5±26.05 (group A); 101.95±10.97 (group B) (p=0.012). Duration SNRT before atropine: 1272.78±303.3 msec (group A); 1560.08±275.84 msec (group B) (p=0.04). We have not received significant difference in duration of the interval PQ, QRs, SNRT after atropine, cSNRT, WP.

Conclusions: Among children with hypervagotonic BD progression of the disease is observed in 21% of the children. All children need following examination in order to determine the progression of the disease.

P4597 | BEDSIDE
Clinical and echocardiographic predictors for the recurrence of subaortic stenosis
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Introduction: Obstruction of the left ventricular outflow tract (LVOT) and resultant sub-aortic stenosis (SAS) may represent an acquired condition since it is rarely recognized during the newborn period, but is common in later life. Recurrence of SAS after corrective surgery, requiring reoperation, occurs in up to 55% of patients. Conflicting data exist regarding the predictors of reoperation of SAS after surgical resection.

Purpose: This study aimed to determine predictors for the recurrence of SAS requiring repeat surgery after initial surgical resection.

Methods: Demographic, clinical, anatomical pre- and post-operative echocardiographic characteristics of 93 consecutive paediatric and adult patients with SAS were reviewed. Parameters were compared between two groups: those who underwent repeat resection and those who did not. Multivariate regression analysis was used to determine the predictors of the recurrence of SAS requiring reoperation. Receiver operator curve analysis was utilised to determine the sensitivity and specificity of prediction of the need for re-operation.

Results: Thirty seven patients (39.8%) required reoperation for recurrent SAS. These patients underwent initial operation at a younger age (5.3±10.0 vs 11.6±15.7, p=0.001) than those without reoperation. Preoperatively they had lower left ventricular ejection fraction (67.6±9.5% vs 73.6%±7.5%, p=0.007) and fractional shortening (FS) (33.5±9.0 vs 39.0±9.4, p=0.027), steeper aorto-valvular angle (130.5±8.5° vs 136.1±8.3°, p=0.006) and smaller mitral valve anulus diameter (15.6±5.9mm vs 20.2±6.4mm, p=0.003). They had a shorter distance between the point of obstruction of the LVOT and the aortic valve annulus both in systole and diastole (4.9±2.3mm vs 6.9±4.4mm, p=0.008 and 4.5±2.8mm vs 6.7±4.2mm, p=0.006). Post-operative residual SAS with higher peak and mean trans-aortic gradients (28.7±15.1mmHg vs 20.0±10.5mmHg, p=0.003 and 15.5±8.3mmHg vs 10.2±5.7mmHg, p=0.002) was more common in patients with recurrence. The FS (beta=−0.124, p=0.044), the aorto-ventricular angle (beta=−0.436, p=0.001) at baseline and the presence of residual SAS post-operatively (beta=−4.900, p=0.001) predicted the recurrence of SAS with 94.4% sensitivity and 88.9% specificity (AUC: 0.970, 95% CI: 0.893–0.997, p=0.001).

Conclusions: Requirement for reoperation in patients with SAS may be predicted by pre-operative echocardiographic factors which include LV function and geometry, and post operative residual obstruction.

P4598 | BEDSIDE
Relation between soluble suppression of tumorigenicity 2 (sST2) and brain natriuretic peptide (BNP) in healthy pediatrie subjects: from birth through adulthood
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Background: Although heart failure (HF) is not clinically evident until adulthood, the burden of asymptomatic disease is significant, thus an accurate and early biomarkers for HF in children is needed. Soluble suppression of tumorigenicity 2 (sST2) is a marker of cardiac stretch. It is used to predict adverse outcome, death and HF in adult healthy population. The reliability and role of sST2 during growth is not yet defined.

Purpose: The aim of this study was to measure circulating levels of sST2 in healthy subjects as a function of age, from birth up to adulthood. Moreover, brain natriuretic peptide (BNP) measurement in parallel with sST2 could offer further insight into its role in cardiac physiology.

Methods: Plasma sST2 and BNP were measured in 131 healthy subjects (% males) divided according to age into 5 groups: 28 newborns (0–3 days), 22 neonates (3–30 days), 24 infants (1–12 months), 31 toddlers (1–2 years), 30 adolescents (13–18 years), and 25 adults (>18 years).

Results: sST2 was present in peripheral circulation of all age-groups (Fig A). Newborns showed higher sST2 compared to the other groups (p<0.0001, Fig A).

No sST2 variation was observed throughout the puberty up to adulthood. BNP exhibited the same trend during growth, showing a significant relation with sST2 (r=0.614, p<0.0001) (Fig B).

Conclusions: In healthy subjects, sST2 levels were high during the first 3 days of life and do not vary as a function of age. These data are of pivotal importance for the possible use of sST2 in paediatric practice. In addition, the strong correlation with BNP suggests for sST2 a role in physiology and development of heart.

P4599 | BEDSIDE
It is the time to reconsider the evolution of preexcitation syndrome in children?

Background: With the development of ablation techniques, the natural follow-up of preexcitation syndrome (PS) became difficult to assess. Several studies in children have reported a spontaneous disappearance of PS in children <12 years (y) with a long accessory pathway (AP) effective refractory period (ERP), but stability in children >12 y or with inducible SVT and short AP-ERP. The purpose of the study was to collect the data of untreated children with a PS, studied 2 times at least one year apart and assess the evolution.

Methods: 2 baseline electrophysiological studies (EPS) were performed within 1 to 25 years of one another (mean 7±5 y) in 41 children/teenagers, 19 boys, 22 girls, aged initially from 2 to 19 years (12±4), with overt PS. First EPS (EPS1) was indexed for sympcope (n=4), atrioventricular reentrant tachycardias (AVRT) (n=18) or for asymptomatic PS (n=19). The protocol was similar, performed in control state (CS) and after isoproterenol.

Results: At EPS2, among patients studied for sympcope at EPS1, 1 has still sympcope, 2 have AVRT, 1 is asymptomatic. Among children with AVRT at EPS1, 15 (84%) have still AVRT, 2 are asymptomatic and 1 presented with rapid AF (maignant form). Among asymptomatic children, 14 (74%) remain asymptomatic, 2 have AVRT, 3 have sympcope. AVRT occurring in initially asymptomatic children or children with initially sympcope occurred in 2/4 with inducible AVRT at EPS1. The fastest rate conducted by AP tended to be less rapid at EPS2 in CS and after isoproterenol than at EPS1 but differences were not significant (181±75bpm vs 190±63 in CS) (0.6) (198±82bpm vs 239±82 after isoproterenol) (0.88). AP has lost anterograde conduction in 6 children with initially long AP-ERP after a mean follow-up of 7±5 years. Most children with spontaneous or inducible AVRT’s at the first evaluation still have inducible AVRT’s at the second evaluation. AP-ERP did not increase significantly. Therefore, long-term follow-up is required in the paediatric population with a PS.

P4600 | BEDSIDE
Follow-up of children and teenagers with paroxysmal supraventricular tachycardia but without preexcitation syndrome
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Background: Paroxysmal supraventricular tachycardia (SVT) is considered as benign if ECG in sinus rhythm (SR) is normal, but its occurrence in children/teenagers is always associated with an anxiousness of parents, child and doctors. The purpose of study was to report the clinical and electrophysiological data of children with SVT, their follow-up and management.

Methods: 162 children and teenagers aged from 5 to 19 years (mean 15±3) with normal ECG in SR (n=55) and in AF (n=107) were studied for spontaneous SVT. Transesophageal electrophysiological study was systematic. Children were followed from 1 month to 13 years (mean 2.15±2.6 years).

Results: SVT was poorly-tolerated in 27 patients (17%). SVT was related to atr-
P4601 | BEDSIDE
Solute suppression of tumorigenicity 2 (sST2) time-course in pediatric patients with heart failure supported by ventricular assist device implant
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Background: VAD utilization is increasing in children with heart failure (HF) unresponsive to medical therapy allowing for bridge to transplantation. Circulating biomarkers have an important role in the diagnosis and prognosis of HF in adults, with early indications for their use in pediatric population. Solute suppression of tumorigenicity 2 (sST2) is considered an emerging marker of cardiovascular stress with clinical value for predicting HF in adults.

Purpose: The aim of this study was to evaluate in pediatric patients whether sST2 is associated with the presence of HF and if its plasma levels are modified after VAD therapy.

Methods: A group of 9 pediatric patients submitted to VAD implant [5±3.7 (mean±SD) months, 5 males, 14±7 LVEF%, Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) profiles 1/2] were studied. Indications for support was idiopathic dilated (7 patients) and non compaction cardiomyopathy (2 patients). A group of 90 healthy age- and sex-matched children were used as controls (73±7.7 months, 56% males). sST2 plasma levels were measured by a dedicated ELISA before (day 0) and at 4 hrs, 1, 3, 7, 14, and 30 days after LVAD implant.

Results: Before VAD implant, sST2 levels are highest in HF compared with healthy children (p<0.0001 newborns vs. children, Fig A). After device implantation, sST2 plasma levels significantly increased during first day and returned to pre-implant values in 3 days (Fig B).

sST2 in HF pediatric patients

Conclusion: In pediatric population, circulating levels of sST2 were associated with presence of HF and were modified by LVAD implant. These data stimulate to evaluate the impact of inflammatory signals on patient outcome, suggesting a role for sST2 in a more integrated management of HF in children.

P4602 | BEDSIDE
Double outlet right ventricle with non-committed ventricular septal defect
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Objective: The management of Double Outlet Right Ventricle (DORV) associated with anatomically non-committed Ventricular Septal Defect (NCVS) constitutes a surgical challenge. The limits for, and the specific outcomes after anatomical versus univentricular repair still remain to be established.

Background: Between 1993 and 2013, 93 patients presenting with DORV/NCVSD and 2 adequately sized ventricles were included into the study at two centers forming the National Referral Center. The selection criteria included the absence of outflow tract VSD: 21 inlet (4 complete atrio-ventricular septal defect (AVSD)), 9 muscular and 5 perimembranous. RVOTO was present in 18/35 (51%). Twenty patients had undergone 25 initial palliative procedures.

Results: Anatomical repair by means of intraventricular baffle construction was performed in 23 (Group I) at a median age of 10.5 months. VSD was surgically enlarged in 11 (48%). An associated RVOT reconstruction was required in 11 and Arterial Switch Operation (ASO) was done in 5. The remaining 12 patients underwent univentricular palliative repair (Group II). There were 4 hospital deaths (11.4%); 3 in Group I and one in Group II (p=0.06). 8/20 survivors of group I patients underwent 13 reoperations after a median delay of 24 months, with subaortic stenosis being the main cause for reoperation (16%). There was one late death in group 2. At last visit, all survivors were in NYHA class I-II. Ten years actuarial survival rate and freedom from reoperation were respectively 74.7±5% and 58±5% in Group I and, 80±7% and 71±7% in Group II. Univariate analysis showed that AVSD and/or isolated mitral cleft were associated with death (p=0.04) and need for reoperation (p=0.038).

Conclusions: Despite the need for complex procedure and the high incidence of reoperation for subaortic obstruction, our results suggested the long-term advantages of anatomical repair in DORV with NCVS. The presence of associated AVSD and/or isolated mitral cleft was the only risk factors for mortality and reoperation.

P4603 | BEDSIDE
Risk stratification and outcome in patients with coronary artery lesions caused by kawasaki disease
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Outcome in patients with coronary artery lesions (CAL) caused by Kawasaki disease (KD) depends on coronary artery aneurysm (CAA) characteristics in the acute phase (A) and in the post-inflammation phase (B). Risk stratification in patients with CAL in the acute phase and in the post-inflammation phase is important for clinical management.

Methods: We reviewed the outcome and incidence of cardiac events in 214 patients (159 male 55 female) who had CAL an initial coronary angiogram within 100 days of the acute onset between 1978 and 2011. We divided the patients into the following groups: Group I: patients with CAA <6.0 mm when BSA >0.50” in the acute phase. In the patients with bilateral large CAA, at least one optimal coronary revascularization was conducted. Group II: patients with CAA ≥6.0 mm when BSA ≤0.50” or <6.0 mm when BSA >0.50”. Further, we classified between either bilateral group or unilateral group, adopting the laterality of the maximum CAA to decide the respective group, and between either body surface area ≤0.50 or >0.50. Cardiac events (CE) included death, acute myocardial infarction (MI) and coronary artery revascularization. CE free rates were analyzed by Kaplan-Meier method.

Results: The follow-up period in respective groups were 18±10, 16±8 and 11±7 years (mean±SD). Cardiac events occurred in 43 pts as shown here by groups. About half of which related to MI. Coronary artery revascularization was undertaken in about 70%. The 25-year CE free rate in respective groups based on the diameter and the laterality of the maximum CAA is shown in Table. The 25-year cardiac events free rate

n (pts) BSA ≤0.5 0.5 < BSA BSA ≥0.5

Bilateral Unilateral Bilateral Unilateral

L 98 50% 86% 30% 75%
M 59 50% 75% 100% 100%
S 57 100% 100% 100% 100%

BSA, body surface area.

Conclusion: CE in patients with CAL caused by KD can occur, in the case with the “maximum CAA diameter ≥6.0 mm when BSA ≤0.50” and “the maximum CAA diameter ≥6.0 mm when BSA >0.50” in the acute phase. In the patients with bilateral large CAA, incidence of cardiac events was more frequent than in pts with unilateral large CAA. At least one optimal coronary revascularization would improve the outcome for such patients.

P4604 | BEDSIDE
Possible mechanism of coronary calcification in chronic-phase Kawasaki disease
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Background: Kawasaki disease (KD) is a systemic vasculitis prevalent in infants and sometimes complicates coronary artery lesions (CALs). It has been well known that coronary calcification is common in chronic patients with CALs but, nevertheless there are still many unclear points regarding the mechanism and clinical significance of it. Recently, it has been reported that vascular calcification is an active, regulated process similar to osteogenesis, relating to the chronic...
inflammation and oxidative stress. Therefore, vascular calcification also promote bone resorption and decrease bone mineral density (BMD). In this study, in KD, we evaluated the possible implication of significant calcification prevalence in CALs to the long-term prognosis.

Methods: We included 48 patients with a history of KD (age: 16.9±6.2 year-old). The breakdown was 19 patients without CALs and 29 with CALs; 16 without calciﬁcation and 13 with calcification on multi-detector computed tomography. We measured %FMD as an endothelial function marker and hs-CRP as an inﬂammatory marker, serum hydroperoxide and urinary 8-OHdG as oxidative stress markers. Patients in CAL(+) group took no medicine and those in CAL(-) group were under antplatelet and/or anticoagulant therapy, particularly, those with calcification were additionally administrated statin or ARB.

Results: Values of %FMD in CAL(+) group were signiﬁcantly lower compared with those of CAL(-) group (p=0.05), and values of hs-CRP were signiﬁcantly lower than those without calcification (p=0.05). Values of hs-CRP and %FMD in CAL (+) group were signiﬁcantly lower than those in CAL(-) group (p=0.05). 8-OHdG values as oxidative stress marker in CALs (+) group were signiﬁcantly lower than those in CAL(-) group (p=0.05). The BMD in CAL(+) group tended to be lower with the age-matched reference values (88.1±7.1% of normal).

Conclusions: In KD chronic stage, the decreased %FMD may be an essential condition to occur coronary calcification. Decreased BMD in patients with coronary calcification suggested the possible relation of vascular calcification and ostetogenic process in KD. Similar to the general mechanisms of arterial calcification. The discrepancy in endothelial dysfunction, inﬂammation and oxidative stress in this study may suggest that it is necessary to consider some novel therapy for improved prognosis of KD patients.

P4605 | BEDSIDE New concept for left ventricular training in corrected transposition of the great arteries: the double switch operation
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Purpose: Patients with corrected transposition of the great arteries (cTGA) beyond the newborn age need a left ventricular (LV) training to undergo a double switch operation (DS) (atrial plus arterial switch operation). A new approach with pulmonary arterial banding (PAB) and atrioseptectomy to increase pre- and afterload is presented. It is evaluated in regards of effectivity, numbers of re-operations necessary and the outcome of DS.

Methods: We report on six consecutive patients with cTGA to be trained for DS using this enhanced LV training (eLVT). Five patients had conventional PAB before, but did not reach a sufﬁcient gradient across the banding. All six patients underwent eLVT as the last procedure to reach DS.

Results: Five of six patients underwent successful DS at in mean 1.2 years after enhanced LV training (eLVT). The postoperative period was short and uneventful in all patients with a total ventilation time of 24 hours, stay on ICU of 3 days and only one episode of inotropic support. Over the whole follow up period of 1.5 years (7.2 patient years) un restricted cardiac function and biventricular circulation, no additional arrhythmics episodes and regression of tricuspid valve regurgitations were observed.

Conclusion: With the eLVT re-PAB operations can be reduced and DS performed at low risk and short periods on intensive care units. If it is equally efﬁcient in patients older than 12 years, has to remain open. Long term follow-up is still needed and results from other centres are essential to underline the beneﬁt of this procedure.

P4608 | BEDSIDE Outcome of bialloack taussig shunt placement without patient ductus arteriosus ligation in neonates with pulmonary atresia
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Background: Modified Blalock Taussig Shunt (mBTS) placement has been a life-saving palliative surgical intervention in neonates with congenital heart disease who lack adequate pulmonary blood flow. There is currently no general consensus about the ligature of associated patient ductus arteriosus (PDA) during the procedure.

Purpose: The purpose of the study was to describe the outcome of mBTS without PDA ligation in patients with pulmonary atresia.

Methods: A retrospective chart review was done on all neonates diagnosed with pulmonary atresia at a median of 2 years period. Inclusion criteria included newborn infants with age of 26 days or less diagnosed with pulmonary atresia who underwent mBTS placement without PDA ligation. Infants with pulmonary atresia but without associated PDA and those with associated major aortopulmonary collateral arteries (MAPCAs) were excluded from the study. Outcomes were incidence of pulmonary overcirculation, low diastolic blood pressure, ductus occlusion and death in the early post-operative period.

Results: A total of 29 charts were reviewed and 3 were excluded. 2 were excluded due to the presence of MAPCAs and 1 due to absence of PDA. 26 patients met the study criteria. The age of the patients ranged from 2 to 20 days with gestational age of 32 to 39 weeks. Their birth weights ranged from 1.8 kg to 3.8 kg. Shunt size ranged from 3 mm to 4 mm. 2 (7%) patients developed persistent low diastolic blood pressure (less than 25 mmHg) post operatively that required subsequent PDA ligation. Both patients were delivered at the gestational age of 32 weeks with birth weights of 1.8 kg and 1.9 kg. 3 (11%) patients developed shunt occlusion within the first week of surgery. All 3 were placed on Prostaglandin E1 to keep their ductus arteriosus patent before undergoing stent angioplasty. There were 2 (7%) deaths as a result of shunt occlusion 6 weeks after surgery.

Conclusion: Modified BTS without PDA ligation in neonates who have pulmonary atresia and birth weight less than 2 kg is associated with increased incidence of low diastolic pressure. Failure to ligate PDA during mBTS placement is not associated with increased incidence of early shunt occlusion and is beneficial in selected patient management. A prospective study with calcification and in patients who develop early shunt occlusion with Prostaglandin E1 to maintain the ductus arteriosus patent before further intervention.

BIOMARKERS: INSIGHTS INTO THE HEALTH OF PATIENTS AND POPULATIONS

P4607 | BEDSIDE Prognostic value of profound iron deficiency in patients with Coronary Artery Disease - establishment of a new functional definition of iron deficiency in the AtheroGene Study
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Introduction: Iron deﬁcient heart patients see improvement with intravenous supplementation. Traditionally, diagnosis of iron deﬁciency has been based on the assessment of low transferrin saturation (Tsat) and reduced serum ferritin. However, these standard measures of iron status seem unreliable, especially in acute clinical settings. There are pathophysiological premises that soluble transferrin receptor (sTfR) and, in particular, circulating hepcidin, which orchestrates systemic iron metabolism, could be more sensitive alternatives for iron deﬁciency diagnosis. In this study, we aimed to evaluate the prognostic value of a new hepcidin-based definition of iron deﬁciency in cardiovascular disease.

Methods: Levels of hepaticin, ferritin, sTfR, iron and transferrin were measured at baseline in 1,303 patients with acute coronary syndrome (ACS) and 2,022 patients with stable angina pectoris (SAP). Functional iron deﬁciency was deﬁned as a concomitance of depleted body iron stores (demonstrated as low-soluble hepcidin) and insufﬁcient iron levels in metabolizing cells (demonstrated as high-soluble sTfR). Serum hepaticin was measured using a newly available ELISA (DRG). Serum sTfR was measured using an immunomassay (Roche Cobas). Main outcome measures were cardiovascular mortality and nonfatal myocardial infarction (MI).

Results: During a median follow-up of 4.6 years, 5.5% of all subjects died. Both, low hepaticin and high sTfR predicted higher mortality rates, even after adjustment for all significant predictors in univariate models. When the traditional definition of iron deﬁciency and the new functional definition were included in one Cox proportional hazard model, only iron deﬁciency defined based on serum hepaticin and sTfR remained a signiﬁcant predictor of 30-day and long-term mortality in patients with coronary artery disease. Hazard ratios (HR) in the Cox model were 2.48, 95% CI 1.2–5.3, in a multivariate model, when preserved iron status was set as standard. In addition, the new deﬁnition was a powerful predictor of the combined endpoint cardiovascular death and MI (HR 1.85, 95% CI 1.1–2.6; p=0.019 in CAD, and HR 1.85, 95% CI 1.1–2.6; p=0.039 in ACS). Finally, addition of functional iron deficiency clearly improved various model performance measures, including c-statistics (AUC: 0.778).

Conclusions: A functional deﬁnition of iron deﬁciency based on a concomitance of low-serum hepaticin and high-serum sTfR more accurately allows identifying patients with a particularly poor outcome. These results will impact the paradigm of iron supplementation in cardiovascular disease.

P4608 | BEDSIDE Association between plaque vulnerability and omega-3 polyunsaturated fatty acids in normal low-density-lipoprotein cholesterol patients with coronary artery disease
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Objective: The aim of this study was to evaluate the relationship between omega-3 polyunsaturated fatty acids (n3PUFAs) and coronary plaque vulnerability in normal low-density-lipoprotein (LDL) cholesterol patients with coronary artery disease.

Background: Recent reports suggest that lower serum n3PUFAs is a new risk factor for coronary artery disease.

Methods: Consecutive normal LDL cholesterol patients with stable anginapectoris (n=100) without any lipid lowering therapies were divided into two groups based on the presence of in vivo thin cap fibroatheroma (TCFA) in the de novo target
vessels assessed by the combined use of virtual histology intravascular ultrasound and optical coherence tomography.

**Results:** Eicosapentaenoic acid (EPA)/arachidonic acid (AA), docosahexaenoic acid (DHA)/AA and (EPA+DHA)/AA ratio were significantly lower in patients with in vivo TCFAs than patients without in vivo TCFAs (0.30 [0.26–0.37] vs 0.48 [0.33–0.58], 0.86 [0.73–0.94] vs 0.98 [0.82–1.16] and 1.16 [0.95–1.24] vs 1.46 [1.13–1.64], P < 0.05). Although percent necrotic core volume was significantly higher in the definite TCFA group (23.5% [21.7 to 25.1] vs 20.3% [16.2 to 22.8], P < 0.01), there was no significant correlation with laboratory data. On the other hand, EPA/AA, DHA/AA and (EPA+DHA)/AA ratio were positively correlated with thinnest fibrous cap thickness (r = 0.75, P < 0.01; r = 0.43, P < 0.01; and r = 0.66, P < 0.01).

**Conclusion:** Low EPA/AA, DHA/AA and (EPA+DHA)/AA ratio might be associated with coronary plaque vulnerability even in patients with a normal LDL cholesterol level.

**References:**

1. Unoki T, Takagi D, Suzuki M, Akiro T, Akiro Y, Shinozaki T, Abe M, Akao K, Hasegawa H, Wada H. On behalf of the ANOX study investigators. National Hospital Organization Yokohama Medicine Center, Yokohama, Japan; National Hospital Organization Sendai Medical Center, Sendai, Japan.

**P4610 | BEDSIDE**

**Objectives:** To investigate the novel biomarker copeptin in patients presenting to a hospital with the primary complaint of acute breathlessness.

**Methods:** This study group is a prospective, ED based population of 364 consecutive patients presenting to a hospital with the primary complaint of acute breathlessness. Copeptin measurements were made on a BRAHMS Kryptor analyser. Serum creatinine was measured by routine hospital core biochemistry system.

**Results:** Copeptin was detectable in 46/150 samples (31%). The median value was 7.4 pmol/L (interquartile range: 5.6–10.3). The 99th percentile level was 16.4 pmol/L. Median serum creatinine was 85 pmol/L (IQR: 77–90; n=150). The 99th percentile level was 115 pmol/L. The median age of the breathless cohort was 73 (IQR: 63–81; 42% female). In total, 6.9% of the 364 patients met the criteria for AKI. Copeptin levels in AKI patients were higher than non-AKI (AKI (n=25) median 14 pmol/L (IQR: 110–196) vs. non-AKI median 14 pmol/L (IQR: 77–116, P < 0.001). Creatinine was also higher in AKI than non-AKI individuals (median AKI = 142 pmol/L, IQR: 110–196 vs. non-AKI median 96 pmol/L, IQR: 82–116, P < 0.001). Assessment of presentation creatinine to diagnose presentation or impending AKI arranged a ROC AUC of 0.79 (95% CI 0.69–0.88, P < 0.001) at a cut-off value of 15 pmol/L. In comparison, presentation copeptin generated an AUC of 0.810 (95% CI: 0.734–0.886, P < 0.001) at a cut-off value of 18.5 pmol/L. Adding creatinine to copeptin produced an AUC = 0.856 (95% CI: 0.787–0.926) which was significantly better than creatinine alone (P = 0.048).

**Conclusion:** Addition of copeptin significantly improved creatinine based detection of AKI in a group of ED breathless patients at the time of presentation. Further studies of the utility of copeptin to assist AKI detection in larger, more general risk populations are warranted.

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**References:**

1. Tsuchioka T, Takagi D, Suzuki M, Akiro T, Shinozaki T, Abe M, Akao K, Hasegawa H, Wada H. On behalf of the ANOX study investigators. National Hospital Organization Yokohama Medical Center, Yokohama, Japan; National Hospital Organization Sendai Medical Center, Sendai, Japan.
nificantly correlated with Ln-SAA-LDL (P<0.0005), but not with other biomarkers. Furthermore, stepwise multivariate regression analysis, including possible confounders and these biomarkers, revealed that Ln-SAA-LDL, but not other biomarkers, was an independent determinant of Ln-Gensini score (P=0.004).

Conclusions: Serum levels of SAA-LDL, but not VEGF-C, VEGF-A, sVEGF-2, or AT-LDL were independently associated with the presence and severity of CAD. The follow-up data of the ANOX study will provide evidence for the predictive values of these biomarkers independent of known risk factors and the severity of CAD at the baseline.

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P4612 | BEDSIDE
Combining B-type natriuretic peptide and high-sensitivity cardiac troponin I in the evaluation of patients with suspected inducible myocardial ischemia


Background: The diagnosis and prognosis of coronary artery disease currently relies on imaging procedures, which are facing concerns due to their high costs and potential risks. Considering this, an easy to use, widely available and cost-effective gatekeeper is of great clinical importance. Previous studies showed high-sensitivity cardiac troponin I (hs-cTnI) and B-type natriuretic peptide (BNP) are independently associated with myocardial ischemia. Therefore their combination additionally to clinical judgment might fill this role.

Methods: 1421 consecutive patients referred to rest/bicycle myocardial perfusion SPECT were recruited. We included patients who undergoing exercise stress tests with or without stress testing. Blood samples were drawn before, immediately after and two hours after stress testing. Clinical judgment was assessed using a visual analogue scale before and after stress testing. The diagnostic end-point of myocardial ischemia was evaluated by myocardial perfusion SPECT and coronary angiogram, if available. Areas under the receiver operating characteristics curves (AUC) were constructed and compared. Prognostic endpoints (death, myocardial infarction, revascularization) were determined by 2 year follow up. Cox regression was used to assess for independence of predictors.

Results: Diagnostic setting: Myocardial ischemia was found in 605 (42.6%) of all patients. Levels of hs-cTnI and BNP were significantly higher in patients with inducible myocardial ischemia at all time points (p<0.01 for all). BNP and hs-cTnI were associated highly significant with presence of exercise induced myocardial ischemia in univariate and multivariate regression (BNP p=0.008, hs-cTnI p<0.001). When combining both biomarkers with the clinical judgment, BNP did not provide a significant advantage to the AUC (0.73 without vs 0.74 with BNP).

In all analysis addition of biomarkers markedly improved the AUC compared to clinical judgment alone (p<0.05 for all).

Prognostic setting: Median duration of follow up was 754 days and at 720 days the combined endpoint was reached in 300 (21.9%) of patients. Cox proportional hazards analysis showed BNP and hs-cTnI were independent relevant predictors of death, myocardial infarction and revascularization. For calculation of the hazard ratio, biomarkers were log-transformed and yielded a HR 1.56 for BNP and 2.35 for hs-cTnI.

Conclusion: BNP provided additional value to hs-cTnI and clinical judgment for prognosis, but not for diagnosis, in patients referred to evaluation of suspected exercise induced myocardial ischemia.

P4613 | BENCH
Lack of effect of higher dose vitamin D supplements on systolic blood pressure and arterial stiffness measure in older people after 12 months of treatment. Results of BEST-D trial

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Background: Low plasma levels of 25-hydroxy vitamin D (25(OH)D) are associated with higher risks of cardiovascular disease (CVD). Before planning a large trial of vitamin D to assess effects on CVD outcomes, we conducted a pilot study of vitamin D3, 50 μg vitamin D3 or placebo. The primary assessment compared plasma 25(OH)D levels at 12 months between the two active doses. Secondary assessments included the effects of any dose of vitamin D versus placebo on systolic blood pressure (SBP), aortic pulse wave velocity (PWVaco) and augmentation index (Aix), assessed using the Arteriograph (Tensiomed), and stiffness index (SI) and reflection index (RI), assessed using PulseTrace PC242, at baseline and at 12 months.

Results: Mean (SD) baseline age was 72 years (6), 51% were male and the mean systolic blood pressure (SBP) was 131 (SD 19). Treatment with either dose of vitamin D was associated with a doubling in mean (SE) plasma 25(OH)D levels (119 [1.7] vs 53 [2.4] mmol/L, P<0.0001), but had no significant effect on mean levels of SBP or any of the measures of large or small arterial stiffness after 12 months (Table).

Effects of vitamin D supplements

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<thead>
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<th>Treatment</th>
<th>SBP (mmHg)</th>
<th>PWV (m/s)</th>
<th>AI (%)</th>
<th>SI (m/s)</th>
<th>RI (m/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin D (n=204)</td>
<td>132 (1.0)</td>
<td>10.0 (0.1)</td>
<td>37 (0.9)</td>
<td>9.4 (0.2)</td>
<td>67 (1.7)</td>
</tr>
<tr>
<td>Placebo (n=101)</td>
<td>132 (1.6)</td>
<td>10.1 (0.1)</td>
<td>37 (1.4)</td>
<td>9.5 (0.1)</td>
<td>66 (2.3)</td>
</tr>
</tbody>
</table>

Mean (SE)

Acknowledgement/Funding: British Heart Foundation

P4614 | BEDSIDE
Impact of exercise training on dipeptidyl peptidase 4 and its relation to endothelial biomarkers in patients with stable coronary artery disease

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Background: Dipeptidyl peptidase 4 (DPP4) is known to be present in many tissues, including endothelium and its effects go beyond metabolic aspects. DPP4 seems to exert many functions on cardiovascular system and it was shown that the inhibition of DPP4 activity may improve cardiovascular profile. This finding opens new possibilities for treatment of cardiovascular diseases by using thera-peutic options which may reduce DPP4 activity.

Purpose: To investigate the effects of regular exercise training on DPP4 and relationship between changes in DPP4 and circulating blood markers of endothelial function (nitric oxide (NOx), and Xanthine Oxidase (XOD), in patients with stable coronary artery disease (CAD).

Methods: 42 subjects: 23pts with stable CAD (CAD group; 55±26.8 years, 14men) and 19 healthy controls (C group; 55;±16.0 years, 11 men) were studied. At baseline in all pts doses of vitamins, DPP4, NOx and XOD by peripheral vein sampling, were evaluated and exercise test was performed. After the initial study, all patients underwent a supervised 3 weeks exercise training at residential center, and after that period values of DPP4, NOX and XOD as well as exercise tolerance were determined again.

Results: Baseline value of DPP4 was significantly higher in CAD than in C group (P=0.008). After 3 weeks of exercise training DPP4 decreased significantly in CAD group (from 792.0±260.08 to 573.11±173.63 μL/g, P<0.0005), as well as XOD (P=0.0005), while NOX increased (P=0.025). Exercise capacity (METS) at baseline were significantly lower in CAD than in C group (P=0.016), and it significantly increased in CAD group after exercise period (P<0.0005). A positive correlation in difference achieved during exercise period was found between increase in NOx level and decrease in XOD (r=0.841, P<0.0005), between decrease in NOx and decrease in DPP4 (r=0.713, P<0.0005) and between NOX increase and increase in METs (r=0.893, P<0.0005). Also, positive correlation in difference achieved during exercise period was found between decrease in XOD and decrease in DPP4 (r=0.581, P=0.004), between decrease in XOD and increase in METs (r=0.719, P<0.005) and between decrease in DPP4 and increase in METs (r=0.719, P<0.005).

Conclusion: In pts with stable CAD regular exercise training leads to significant reduction of DPP4 and restoration of endothelial function which is expressed through significant increase of NOX and decrease of XOD. There is a positive correlation between increase in NOX and decrease in DPP4 and between decrease in XOD and decrease in DPP4.

P4615 | BENCH
Determination of the 99th percentile value for high-sensitivity cardiac troponin T and I

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Background: High-sensitivity cardiac troponin T (hs-cTnT) and I (hs-cTnI) in a large well-phenotyped healthy reference population.

Introduction: The 99th percentile upper reference limit of high-sensitivity cardiac troponin (hs-cTn) of healthy reference population is commonly used for diagnosis of myocardial infarction. These limits differ substantially between high sensitive troponin T (Roche) and I (Abbott) assays (14 ng/l versus 26 ng/l, respectively). It is unclear whether this divergence stems from cohort variation from which they were derived, or reflect intrinsic assay differences. We performed a side by side comparison of sex- and age-specific 99th percentile upper reference limits for hs-cTnT and hs-cTnI in a large well-phenotyped healthy reference population.
Methods: The healthy reference population for the present study was derived from the first 3,451 participants in The Maastricht Study (TMS), an extensively phenotyped population based cohort. The healthy reference population was defined by excluding individuals with diabetes mellitus, a clinical history for known cardiovascular disease by questionnaire, N-terminal pro-B-type natriuretic peptide > 125 ng/l or estimated Glomerular Filtration Rate < 60/min/1.73m². Non-parametric analysis were performed to determine 99th percentile values of hs-Ctn.

Results: From TMS cohort, a total of 1,803 individuals were included in the healthy reference population. Six hs-Ctn values according to Dixon’s outlier detection method, leaving 1,797 individuals for the analyses. Overall 99th percentile upper reference limit of hs-Ctn (cTnT and hs-Ctn) was 15 (95% CI, 14–16) ng/l and 19 (95% CI, 18–22) ng/l, respectively. The 99th percentile of hs-Ctn was 20 (95% CI, 19, 21–23) ng/l and for women 12 (95% CI, 10, 13–15) ng/l. The 99th percentile of hs-Ctn was 20 (95% CI, 19, 21–23) ng/l and for women 12 (95% CI, 10, 13–15) ng/l. The 99th percentile of high sensitivity hs-Ctn group increased with age, and most prominent in the stratum ≥ 65 years.

Conclusion: 99th percentile values for hs-Ctn assays are strongly sex- and age-dependent. Side by side comparison reveals remarkably similar 99th percentiles upper reference limits for the high sensitive troponin T and I assay, which is in contrast with current clinical practice. Clinical validation studies are needed to investigate whether the sex- and age-specific cut-off values outperform fixed cut-off values for diagnosing myocardial infarction.

P4616 | BEDSIDE
Red cell distribution width as a novel predictor for the clinical outcomes in patients with paroxysmal atrial fibrillation

Background: High red cell distribution width (RDW) values have been shown to be associated with poor long-term clinical outcomes in patients with cardiovascular disease. Also, RDW was associated with incidence of atrial fibrillation. However, little is known about the impact of RDW on the prognosis in patients with paroxysmal atrial fibrillation (AF).

Purpose: We aimed to evaluate relationship between RDW values and clinical outcomes in patients with paroxysmal AF.

Methods: We analyzed 567 patients who were newly diagnosed as paroxysmal AF. Clinical outcomes were analyzed after median 4.8 (3.4–6.9) year follow-up. Progression of AF was defined as paroxysmal AF at enrollment becoming persistent AF at 1-year follow-up. The composite clinical outcomes were defined as the composite of death, hospitalization due to heart failure, new onset stroke. Bleeding events were composed of major and minor bleeding. The relationship of RDW with clinical outcome or bleeding events was analyzed using continuous or categorical variables as quartiles: < 12.8, 12.8–13.2, 13.3–13.8 and ≥ 13.9.

Results: A total of 147 (25.9%) patients progressed to persistent AF. Patients with highest RDW quartile were oldest and more frequent history of heart failure. Progression into persistent AF was increased in a stepwise manner as an increment of RDW (16.4% vs. 22.2% vs. 32.1% vs. 35.6%, linear p = 0.024) and bleeding events (adjusted OR 1.57, 95% CI 1.16–2.12, p = 0.004). The relationship of RDW with the composite of death, hospitalization due to heart failure, new onset stroke was 30 ng/L (CV 10%). A total of 2185 pts had cTnI values < 10 ng/L, thus fulfilling the inclusion criteria of this study. All pts were followed for up to 4 years with a median follow-up of 3.2 yrs, 507 of the 2185 pts had died. Pts with cTnI values < 10 ng/L had a significantly better survival than pts with cTnI values ≥ 10 ng/L (p < 0.01 between groups).

Results: The 2185 pts were divided into two groups. Group I: cTnI values < 10 ng/L (n = 453), and group II: cTnI values 10–30 ng/L (n = 1732). Group II pts were older with a mean (SD) age of 65 (16) yrs vs 55 (16) yrs in group I (p < 0.0001) and also had more cardiovascular risk factors and co-morbidity. After a median follow-up of 3.2 yrs, 507 of the 2185 pts had died. Pts with low cTnI values < 10 ng/L had a significantly better survival than pts with cTnI values of 10–30 ng/L (p < 0.0001; Figure). When performing an age-adjusted log-rank test of survival, however, this significance disappeared (p = 0.08).

Conclusion: This study demonstrates that plasma MIF values are elevated in response to myocardial ischaemia and may be a useful diagnostic biomarker.

Acknowledgement/Funding: NH & MRC of Australia

P4618 | BEDSIDE
Long-term mortality in hospitalized patients with cardiac troponin values below the 99th percentile
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Background: An increased cardiac troponin (cTn) concentration is defined as a value exceeding the 99th percentile of a normal reference population. This discriminatory value is designated as the decision limit for the diagnosis of myocardial infarction (MI). The prognostic use of cTn values below the decision limit, however, has not been studied in hospitalized patients (pts).

Purpose: To assess the prognostic usefulness of cTnI values below the decision limit in hospitalized pts without acute MI.

Methods: During 2010 a total of 3762 consecutive, hospitalized pts with a suspected acute MI had cTnI measured. The upper reference limit for the assay used was 30 ng/L (CV < 10%). A total of 2185 pts had cTnI values < 30 ng/L, thus fulfilling the inclusion criteria of this study. All pts were followed for up to 4 years with a median follow-up of 3.2 yrs, 507 of the 2185 pts had died. Pts with cTnI values < 10 ng/L had a significantly better survival than pts with cTnI values of 10–30 ng/L (p < 0.0001; Figure). When performing an age-adjusted log-rank test of survival, however, this significance disappeared (p = 0.08).

Conclusion: This study demonstrates that plasma MIF values are elevated in response to myocardial ischaemia and may be a useful diagnostic biomarker.

Acknowledgement/Funding: NH & MRC of Australia

P4617 | BEDSIDE
Macrophage migration inhibitory factor (MIF) levels in the blood rise in response to myocardial ischaemia evoked by an exercise stress test
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Background: Recent studies have demonstrated that macrophage migration inhibitory factor (MIF) plasma levels rise early in the course of myocardial infarction. The purpose of the study was to determine whether myocardial ischaemia without infarction is also associated with elevated cTnI values even in pts without acute MI.

Methods: The study cohort comprised patients referred for evaluation of possible myocardial ischemia by either stress echocardiography or nuclear perfusion studies. Blood samples were obtained before and at 5 and 15 minutes after exercise. All samples were kept on ice until centrifugation and stored at ~80°C prior to analysis for MIF (ELISA, R&D Systems, ng/ml), TroponinT (Tn, electrochemiluminescent immunoassay, Roche, μg/l) and hsCRP (immunoturbidimetric assay, Abbott Architect, ng/ml). Subjects with exercise induced regional wall motion abnormality or reversible perfusion defect were classified as positive whilst those without such changes and without ecg changes were classified as negative. Results are mean±sd, unless stated otherwise.

Results: There were 19 positive (83±10.6 years, 5 stress echo) and 64 negative (62±25±10.6 subject). There were no differences in baseline CPR (2.7±2.0, 4.3±2.7, 8.3±3.4 and 5.2±2.5) between positive and negative cases. There were no changes with exercise for Tn or CPR in either group. In contrast there was significant rise in plasma MIF following exercise in the positive but not the negative group (Fig). The figure shows mean (±sem) change from baseline at 5 and 15 min for positive (black bar) and negative subjects. *, ** signify p < 0.05, < 0.01 between groups.

Conclusion: This study demonstrates that plasma MIF values are elevated in response to myocardial ischaemia and may be a useful diagnostic biomarker.

Acknowledgement/Funding: NH & MRC of Australia
Paroxysmal versus non-paroxysmal atrial fibrillation in Europe: the EORP-AF General Pilot Registry


Background: Atrial fibrillation (AF) has different presentations (first detected, paroxysmal, persistent, permanent), with uncertain impact on outcome.

Objective: To investigate clinical presentation, management and outcome of paroxysmal and non-paroxysmal AF within EORP-AF General Pilot Registry.

Methods: Overall 2589 patients with available 1-y follow up data were evaluated according to AF type.

Results: Patients with paroxysmal AF (26.8%) were younger, had lower prevalence of heart disease (particularly valvular) and major co-mordibilities, as well as lower CHADS2, CHA2DS2VASc and HAS BLED scores. Patients with first detected AF (29.9%) had characteristics similar to persistent AF patients (25.9%), but lower use of oral anticoagulants, if indicated. Patients with persistent AF represented 17.4% of the cohort. At 1 year, the rate of stroke/TIA and thromboembolism was low (0.6–1.0%) and did not differ between paroxysmal and non-paroxysmal AF. All-cause mortality was higher in non-paroxysmal vs. paroxysmal AF (Log rank test, p=0.0018) (Figure). On multivariable analysis, the OR for paroxysmal vs. non-paroxysmal AF, however, the higher mortality risk became non-significant (OR 0.948, 95% CI 0.547–1.642, p=0.8477) after adjustment for clinical variables known to potentially affect the outcome.

Conclusions: In a real-world observational registry, patients with non-paroxysmal AF have a worse outcome, in terms of all-cause mortality, which was related to a more severe clinical risk profile. The risk of stroke at 1 year was relatively low, perhaps reflecting the high rates of anticoagulation use in this cohort.

P4620 | BEDSIDE
Beyond Framingham risk equations: how can cardiovascular risk be estimated when treatment changes over time?

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Background: Among people without cardiovascular (CV) disease, prescribing decisions for lipid- and blood-pressure-lowering medications often depend on estimates of CV risk from tools such as the Framingham equations or SCORE charts, using risk factors measured at baseline. However, many patients receive new or changing treatments (eg. statins) during follow-up, raising questions about the validity of contemporary data to create risk tools for primary prevention. We investigated the impact on effect estimates (hazard ratios, HR) of updating treatment at baseline.

Methods: Using a large primary care database of routine CV risk assessments, we investigated the impact on effect estimates (hazard ratios, HR) of updating treatments (eg. statins) during follow-up, raising questions about the validity of contemporary data to create risk tools for primary prevention. We investigated the impact on effect estimates (hazard ratios, HR) of updating treatment at baseline.

Results: Of 132,235 subjects with updated LLT data (55% men), 2,802 (2%) experienced a CV event within 291,278 person-years. Among men, the HR for LLT at baseline was 1.26 (95% CI 1.14 to 1.40). Among women, the HR for LLT at baseline was 0.89 (95% CI 0.77 to 1.02), and as an updated covariate was 1.14 (95% CI 1.00 to 1.30).

Conclusions: In CV risk estimation, the apparent effect of treatment such as LLT is significantly different when models use treatment at baseline compared to as an updated covariate. A limitation of these models currently is that they are not adjusted for a change in cholesterol ratio during follow-up, which may influence the HR of LLT as an updated covariate. Further research should resolve which methodology will produce valid risk models and hence optimal prescribing decisions.

Acknowledgement/Funding: Health Research Council of New Zealand, Heart Foundation of New Zealand

P4621 | BEDSIDE
The added value of a combined genetic score as cardiovascular risk predictor in a Portuguese population with intermediate risk according to the European score

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Background: Cardiovascular risk stratification has included traditional cardiovascular risk factors including tobacco, cholesterol and blood pressure adjusted to age and sex. The utility of genetic risk scores (GS) as predictor of cardiovascular risk remains inconclusive.

Aim: We intended to evaluate the ability of a multiloci genetic score (GS) within the intermediate risk subgroup, defined by the European score, to add predictive power for the development of coronary arterial disease (CAD).

Methods: Study of 609 individuals with 59±4.3 years considered at intermediate risk by the European score (score 2 and < 9). The multifactorial and multiloci genetic score was determined in the whole population after genotyping with specific primers. A GS based on 29 genes associated with atherosclerotic disease in general and coronary heart disease was created. Multivariate analysis and respective ROC curves and area under curve (AUC) were performed using the traditional risk factors (TRF). The analysis was repeated, adding the previous GS.

Results: By multivariate analysis GS was an independent predictor for DAC (OR−2.19; 1.47 to 2.95, p < 0.0001), arterial hypertension (OR−2.72; 1.50 to 4.97; p = 0.0001), arterial hypertension (OR−2.97; 2.06 to 4.28; p < 0.0001) and smoking (OR−2.07; 1.21 to 3.56, p < 0.0001) were also independent predictors for CAD. AUC increased from 0.70 to 0.72 after adding GS to the AUC obtained for TRF.

Conclusions: In our population the GS increased the predictive value of TRF in the subgroup of patients at intermediate risk by the European Score. The predictive value of TRF is lower in patients with higher GS. In this subgroup the inclusion of genotyping may be considered for better stratification of cardiovascular risk.

P4622 | BEDSIDE
Validation of SAME-TT2R2 score for predicting poor anticoagulation in a prospective real world cohort of atrial fibrillation patients initiating Vitamin K antagonists

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Background: Among patients that were admitted to hospital, as this would influence achievement of stable anticoagulation. Patients that were admitted to hospital, as this would influence achievement of stable anticoagulation.

Aim: We intended to evaluate the ability of a multiloci genetic score (GS) within the intermediate risk subgroup, defined by the European score, to add predictive power for the development of coronary arterial disease (CAD).

Methods: Study of 609 individuals with 59±4.3 years considered at intermediate risk by the European score (score 2 and < 9). The multifactorial and multiloci genetic score was determined in the whole population after genotyping with specific primers. A GS based on 29 genes associated with atherosclerotic disease in general and coronary heart disease was created. Multivariate analysis and respective ROC curves and area under curve (AUC) were performed using the traditional risk factors (TRF). The analysis was repeated, adding the previous GS.

Results: By multivariate analysis GS was an independent predictor for DAC (OR−2.19; 1.47 to 2.95, p < 0.0001), arterial hypertension (OR−2.72; 1.50 to 4.97; p = 0.0001), arterial hypertension (OR−2.97; 2.06 to 4.28; p < 0.0001) and smoking (OR−2.07; 1.21 to 3.56, p < 0.0001) were also independent predictors for CAD. AUC increased from 0.70 to 0.72 after adding GS to the AUC obtained for TRF.

Conclusions: In our population the GS increased the predictive value of TRF in the subgroup of patients at intermediate risk by the European Score. The predictive value of TRF is lower in patients with higher GS. In this subgroup the inclusion of genotyping may be considered for better stratification of cardiovascular risk.

P4619 | BEDSIDE
Improving risk scores in the real world 803

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Improving risk scores in the real world 803
with acenocoumarol in our out-patient anticoagulation clinic. Based on our study inclusion/exclusion criteria, only 459 patients (64% of the whole cohort) entered the final analysis: 222 (47%) male, median age 76 (interquartile range, IQR 70–82); median (IQR) CHA2DS2-VASC score was 4 (3–5) and median (IQR) HAS-BLED score was 3 (2–3). Median (IQR) SAME-TT2R2 score was 2 (1–2). At 6 months, the mean ± standard deviation (SD) TTR at was 64±17% overall, and 248 patients (54%) had a TTR value >65%. Patients with a SAME-TT2R2 score 0–1 had a median TTR of 67±18% whereas in patients with a SAME-TT2R2 score ≥2, was 61±16%, p = 0.001. The odds ratio (OR) for having a low TTR value was 2.29 (95% CI 1.43–3.6, p = 0.001) for those patients with a SAME-TT2R2 score ≥2.

Conclusions: In a prospective real world AF cohort of patients initiating oral anticoagulation with acenocoumarol, we have validated the clinical value of the SAME-TT2R2 score, for the identification of which patients would have poor quality anticoagulation. Thus, rather than imposing a “trial of VKA” for such patients (and exposing such patients to thromboembolic risks), we can a priori identify those patients who can (and cannot) do well on a VKA. Such patients would benefit from additional strategies for improving anticoagulation control with VKA or alternative oral anticoagulant drugs.

P4623 | BEDSIDE
External validation of prediction models for the diagnosis of coronary artery disease
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Maastricht University Medical Centre (MUMC), Cardiology, Maastricht, Netherlands; 2 Erasmus Medical Center, Clinical Epidemiology and Radiology, Rotterdam, Netherlands; 3 Erasmus Medical Center, Cardiology, Rotterdam, Netherlands; 4 Maastricht University, Epidemiology, Maastricht, Netherlands; 5 Maastricht University Medical Centre (MUMC), Clinical Epidemiology and Radiology, Rotterdam, Netherlands; 6 Erasmus Medical Center, Cardiology, Rotterdam, Netherlands; 7 Maastricht University Medical Centre (MUMC), Clinical chemistry, Maastricht, Netherlands

Background and introduction: Prediction models for estimating probability of coronary artery disease (CAD) are crucial in guiding decision making in patients presenting with chest pain. The Diamond and Forrester prediction model was developed in a high-risk population referred for invasive coronary angiography and was expected to overestimate the probability of CAD within low-risk populations. Current European Society of Cardiology guidelines on stable CAD recommends use of a revised version of the Diamond Forrester model.

Purpose: We performed an external validation on previously published prediction models developed for estimating the probability of CAD in low-risk populations.

Methods: We analyzed 1,506 patients, referred from a cardiology outpatient department for coronary CT-angiography (CCTA). Inclusion criteria where: age ≥40 and stable chest pain. Scans were performed between December 2007 and December 2012 using 64-slice multidetector (Brilliance 64; Philips Healthcare) or a dual-source CT-scan (Somatom Definition Flash, Siemens). CAD was defined as ≥1 vessel with ≥50% luminal stenosis on CCTA. Three prediction models were calculated: 1. basic model: age, sex, chest pain symptoms, 2. clinical model: basic model + diabetes, hypertension, dyslipidemia, smoking, 3. extended model: clinical model + coronary calcium score. Diagnostic performance of the prediction models were quantified by calculating the area under the receiver operating characteristic curve (c-statistic). Calibration was assessed using calibration-in-the large and calibration plots.

Results: The area under the receiver operating characteristic curve was 0.69 (95% CI: 0.67–0.72) for the basic model; 0.70 (95% CI: 0.68–0.73) for the clinical model; and 0.86 (95% CI: 0.84–0.88) for the extended model. Calibration-in-the large showed that the average predicted probabilities of the prediction models were lower to the observed probability of obstructive CAD but were comparable for patients presenting with typical chest pain. The calibration plots showed some underestimation of the prediction models.

Conclusions: Updated prediction models, developed for low-risk populations, show a more accurate estimation of the likelihood of CAD than the commonly used Diamond and Forrester model.

Acknowledgement/Funding: Not applicable

P4624 | BEDSIDE
ACCURACY OF STATIN ASSIGNMENT ACCORDING TO THE EUROPEAN VS. AMERICAN GUIDELINES - A CORONARY CT ANGIOGRAPHY STUDY

Introduction: The American scientific societies (AHA/ACC) have issued new guidelines on the assessment of cardiovascular (CV) risk and the initiation of statin therapy. The aim of this study was to compare the accuracy of the ESC and AHA/ACC guidelines in assigning statins to patients with higher risk features on coronary CT angiography (CCTA).

Methods: We assessed 327 patients (181 men, age 59±9 years) undergoing CCTA for true coronary artery disease (CAD). Patients -40 or >75 years old, with diabetes or known CV disease were excluded. The burden of coronary atherosclerosis was assessed by the coronary artery calcium score (CACS) and the presence of obstructive CAD (stenosis ≥50%).

Results: The median risk of events was 9.7% according to the AHA/ACC calculator, and 2.6% according to the European SCORE (fatal events only). Compared to SCORE, the AHA/ACC calculator showed greater discriminatory power for identifying patients with CACS >300 (C-statistic: 0.74 (95% CI 0.67–0.82) vs. 0.69 (95% CI 0.61–0.78), p=0.008). The proportion of patients who would be treated with statins according to the ESC guidelines was numerically higher than according to the AHA/ACC recommendations (69% vs. 61%, p=0.060). For patients with higher-risk findings on CCTA, the likelihood of receiving statins was similar with both guidelines (p=NS). Patients with low risk findings (CACS = 0 and no visible plaques) were more likely to receive statins if managed according to the European guidelines.

Conclusions: This global GRS, mainly in its extreme values, allows the prediction of the probability of the development, or not, of CAD and also allows that the genetic risk have similar weight to one of the traditional risk factors.
on the predictors for stroke and death in ‘real-world’ AF patients are limited, especially from large prospective Asian population cohorts.

**Purpose:** The aim of this study is to investigate the predictors and risk model for stroke and death in the Fushimi AF Registry.

**Methods:** The Fushimi AF Registry is a community-based prospective survey designed to enroll all of the AF patients. The inclusion criterion for the registry is the documentation of AF on a 12-lead electrocardiogram or Holter monitoring at any time, and there are no exclusion criteria. We started to enroll patients from March 2011, and follow-up data were available for 3,304 patients by the end of July 2014 (median follow-up period 741 days). We explored the predictors for composite endpoint of ‘death, stroke, and systemic embolism’ (SE) during follow-up period in 1,553 patients not receiving oral anticoagulants (OAC) at baseline. The model for predicting death/stroke/SE was determined by the cumulative numbers of risk factors which were significant on multivariate analysis.

**Results:** The mean age was 73.2±12.5 years, and 679 (44%) patients were female. The mean CHADS2 and CHA2DS2-VASc score were 1.76 and 3.08, respectively. Cumulative events during follow-up were as follows: stroke in 60 (4%), death in 231 (15%), respectively. On multivariate analysis, advanced age (<75 years) (hazard ratio (HR): 1.68, 95% confidence interval (CI): 1.24–2.28), previous stroke/SE/transient ischemic attack (HR: 1.65, 95% CI: 1.23–2.29), previous stroke/SE/transient ischemic attack (HR: 1.65, 95% CI: 1.23–2.23), heart failure (HR: 1.61, 95% CI: 1.18–2.17), chronic kidney disease (HR: 1.53, 95% CI: 1.16–2.02), and anemia (HR: 2.36, 95% CI: 1.75–3.12) were independent predictors for death/stroke/SE. A risk model based on these 6 variables could stratify the incidence of death/stroke/SE in patients without OAC, as well as those with OAC in our registry, with a high predictive value (C-indexes 0.75 in patients without OAC, and 0.70 in patients with OAC).

**Conclusion:** Advanced age, previous stroke/SE/transient ischemic attack, heart failure, chronic kidney disease, and anemia were independently associated with the risk of death/stroke/SE in “real-world” non-anticoagulated Japanese patients. The inclusion criterion for the registry is the documentation of AF on a 12-lead electrocardiogram or Holter monitoring at any time, and there are no exclusion criteria. We started to enroll patients from March 2011, and follow-up data were available for 3,304 patients by the end of July 2014 (median follow-up period 741 days). We explored the predictors for composite endpoint of ‘death, stroke, and systemic embolism’ (SE) during follow-up period in 1,553 patients not receiving oral anticoagulants (OAC) at baseline.

**Acknowledgment/Funding:** Boehringer Ingelheim, Bayer Healthcare, Pfizer, Bristol-Myers Squibb, Aestellas Pharma, AstraZeneca, Daiichi-Sankyo, Novartis Pharma, MSD

**P4627 BEDSIDE**

**Accuracy of 10-year-risk calculation for first atherosclerotic cardiovascular event from new pooled cohort equations and WHO risk calculation in EGAT population**

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**Background:** Currently, the American College of Cardiology (ACC)/American Heart Association (AHA) recommended using Pooled Cohort Equations to estimate cardiovascular (CV) risk in Thai population. The World Health Organization (WHO) also issued guidelines for assessment and management of cardiovascular (CVD) risk using risk prediction chart. We then sought to demonstrate the performance of WHO and ACC/AHA risk score in Thai population which may result in excessive statin use. Local ASCVD risk score should be developed to accurately estimate the risk in Thai population.

**Conclusion:** This study showed overestimation in 10-year risk calculation from WHO and ACC/AHA risk score in Thai population which may result in excessive statin use. Local ASCVD risk score should be developed to accurately estimate the risk in Thai population.
associated with variables. External validation was performed on the population of the FAST-MI 2005 (1798 NSTEMI, 51% PCI) and FAST-MI 2010 registries (1928 NSTEMI, 66% PCI). Discrimination was assessed by the C-statistic and calibration by plotting predicted/observed probabilities by deciles of the population.

**Results:** Thirteen variables were predictors of Non-PCI and used to build the score; unstable angina (vs NSTEMI), female gender, age ≥ 80, no previous PCI, history of COPD, history of MI, no sinus rhythm, admission with Killip class ≥ 2, heart rate > 110 bpm, heart failure, anemia, troponin rise and creatinine level > 130 μmol/L. Discrimination was acceptable with a C-statistic = 0.69. External validation showed a C-statistic at 0.62 (FAST-MI 2010) and 0.67 (FAST-MI 2005). For an individual patient, according to the quartiles of Non-PCI score, the rates of non-PCI ranged from 78–72% (Q1), 70–59% (Q2), 68–49% (Q3) and 49–35% (Q4).

**Conclusion:** In patients with acute MI, a score easily available at admission can help to predict the probability of non-PCI during hospitalization and thus help tailor initial antithrombotic treatment.

**CLINICAL PARAMETERS TO IMPROVE RISK PREDICTION**

**P4630 | SPOTLIGHT**

Heritability of coronary calcium quantity and total plaque burden: a classical twin study


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Through the comparison of monozygotic (MZ) and dizygotic (DZ) twins phenotypic similarities can be quantified and the weight of genetic and environmental factors can be determined in an unique way. It has been reported that coronary atherosclerosis has a strong genetic determination. However, it is unclear if coronary calcium quantity and total plaque burden are inherited similarly. Our goal was to assess the magnitude of genetic and environmental impact on coronary calcium quantity and total plaque burden.

Coronary CT-angiography was performed in 208 twin subjects, of whom 62 were MZ pairs and 42 were DZ pairs (mean age: 58±8.7 vs. 55.8±9.8, p=0.218, respectively). Total Ca-score was calculated by Agatston-score measurement. Total plaque burden, which incorporates non-calcified, calcified and partially calcified plaques was assessed by the segment involvement score (SIS: total number of segments with plaque) and segment stenosis score (SSS: sum of all stenoses, minimal = 1, mild = 2, moderate = 3, severe = 4). SIS index (SISIS) was calculated by SSS/total segment number. Concordance between MZ and DZ pairs were assessed by non-parametric correlations. Rough heritability was calculated according to the Falconer-method.

The Agatston-score was <0 in 38.7% of the MZ twins (median:132.3 [IQR: 27.5–387.4]), and in 40.5% of the DZ twins (median: 107.8 [IQR: 39.5–230.3]), p=0.880. The SISI and SSSI were positive in 55.6% of MZ and in 59.5% of DZ twins. The median SISI of MZ versus DZ twins was 0.2 (IQR: 0.1–0.4) versus 0.1 (IQR: 0.0–0.2), respectively, p=0.972. The median SSSI of MZ versus DZ twins was 0.3 (IQR: 0.1–0.5) versus 0.3 (IQR: 0.1–0.7), respectively, p=0.940. Relatively strong heritability was found regarding Ca-score (h²=0.105), while the plaque burden showed a weaker genetic dependency (SISIS: h²=0.632 and SSSI: h²=0.446).

This classical twin study shows that coronary calcium quantity has a relatively strong heritability, whereas plaque burden, which incorporates non-calcified, calcified and partially calcified plaques, is more determined by environmental factors. The latter implies that non-calcified plaque development is predominantly affected by environmental factors, which underscores the importance of preventive measures in cardiovascular risk reduction.

**P4631 | BEDSIDE**

Cardiac function-specific risk factors for one-year mortality in patients admitted with acute coronary syndromes

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**Introduction:** Risk stratification in acute coronary syndromes (ACS) is based on clinical and laboratory values. LVEF is a strong predictor of mortality in coronary disease.

**Purpose:** To evaluate the prognostic implications of LVEF in patients admitted with ACS; to assess whether identification of cardiac function-specific risk factors can be used to improve risk stratification.

**Methods:** Demographic, clinical, laboratory and echocardiographic data of 8,974 patients enrolled in the Acute Coronary Syndrome Israel Surveys 2000-2010 were obtained. Multivariate cox proportional hazards regression modeling was used to identify cardiac function-specific risk factors for 1-year mortality in cardiac function groups defined as: severe LV dysfunction (LV dx <30%), moderate LV dx (30–49%), preserved LV (>50%).

**Results:** Through 2000 to 2010 more patients were admitted with preserved LV and less with LV dx. Patients with severe LV dx had high mortality rates at 1-year (36%) as compared with patients with mild/moderate LV dx and preserved LV (10% and 4%, respectively; Fig). Mortality according to EF at admission did not change over the years (p>NS). Multivariate analysis showed that among patients with preserved LV or mild/moderate LV dx the presence of co-morbidities such as hypertension, diabetes, hyperlipidemia and peripheral arterial disease were independently associated with 1-year mortality. In contrast among patients with severe LV dx, clinical features at admission such as syncope, anterior MI location, ST-segment elevation and Killip Class≥2 were independently associated with 1-year mortality.

**Conclusion:** Assessment of admission LVEF has important prognostic implications in patients with ACS and can be used to improve risk stratification through identification of cardiac function-specific risk factors.

**P4633 | BEDSIDE**

Relative performance of three different estimated glomerular filtration rates on clinical outcomes in patients with acute myocardial infarction undergoing percutaneous coronary intervention


**Background:** Chronic kidney disease has been associated with poor clinical outcomes in patients with acute myocardial infarction (AMI). Newer methods as the MDRD-4 formula and the new Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation were introduced to enhance estimation of glomerular filtration rate (eGFR) beyond the classical Cockcroft-Gault (C-G) formula.

**Purpose:** We aimed to compare the relative predictability for the clinical outcomes in patients with AMI among three different formulas.
Methods: We analyzed consecutive 11,454 AMI patients (66.9±12.5 years old, 8,412 males) undergoing percutaneous coronary intervention (PCI). The relative performance of each formula was assessed in the in-hospital and one-year clinical outcomes using continuous or categorical variables according to eGFR: ≥90, 89–60, 59–30, and <30 ml/min/1.73m². In-hospital outcome was defined as in-hospital mortality and complications. 1 year clinical outcome was defined as the composite of 1-year major adverse cardiac events (MACE) including death, recent MI, and target vessel revascularization (TVR) and CABG.

Results: The mean eGRFC-G was lower than those of eGFR MDRD-4 and eGFR CKD-EPI both from urban areas of Italy, Scotland, and China. For all subjects blood levels of traditional lipid markers were significantly lower in patients with hemodialysis or CrCl < 30 ml/min/m² compared to patients with CrCl ≥ 60 ml/min/m². Those were the highest in the group of patients with hemodialysis or CrCl < 30 ml/min/m² by all 3 formulas as a significant predictor for in-hospital outcomes as well as one-year mortality and MACEs. Predictability for in-hospital outcomes with eGRFC-G (area under the curve [AUC] 0.688, 95% confidence interval [CI] 0.67–0.71, p < 0.001) and eGRFR CKD-EPI (AUC 0.688, 95% CI 0.67–0.71, p < 0.001) was higher than that with eGFR MDRD-4 (AUC 0.684, 95% CI 0.66–0.70, p < 0.001). Predictability for one-year mortality and MACEs with eGFR CKD-EPI was higher than those with eGFR MDRD-4 and eGRFR CKD-EPI using categorical variables [AUC for mortality: 0.769 vs 0.728 vs 0.747, p < 0.001; AUC for MACES 0.619 vs 0.602 vs 0.615, p < 0.001]. Net reclassification index for improvement in risk prediction using PCE in different MRC populations eGRFC-G was 16.8%, 8.0%, respectively compared with eGFR MDRD-4, whereas 0.9%, 2.1% compared with eGRFR CKD-EPI.

Conclusions: Moderate renal dysfunction by any formula for eGFR was a significant predictor for one-year adverse clinical outcomes. The application of the eGRFC-G demonstrated better predictability for in-hospital and one-year adverse clinical outcomes compared with eGFR MDRD-4 and eGRFR CKD-EPI.

Conclusion: Patients with lower CrCl were highly associated with death and major bleeding.

Acknowledgement/Funding: Boehringer Ingelheim, Bayer Healthcare, Pfizer, Bristol-Myers Squibb, Astellas Pharma, AstraZeneca, Daiichi-Sankyo, Novartis Pharma, and MSD

P4634 | BEDSIDE
Predictive value of apoB/apoA1 ratio on the risk of myocardial infarction in different ethnic groups
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Background: Previous studies have shown that apoB/apoA1 ratio predicts the risk of acute myocardial infarction independently of risk factors profile and traditional lipid markers. Recently, the 2013 ACC/AHA guidelines on cardiovascular disease prevention introduced a new tool for risk assessment, the Pooled Cohort Equations (PCE).

Purpose: In a multicentric case-control study population, we evaluated whether the predictive value of apoB/apoA1 ratio is independent of the cardiovascular risk assessment provided by PCE in different ethnic populations.

Methods: The study population was composed by 1478 subjects enrolled in the FAMI study: 739 patients with documented ST-elevation myocardial infarction as their first manifestation of coronary artery disease and 739 matched control subjects free of heart disease from Italy, Scotland, and China. For all subjects blood serum samples were centrally analysed for total cholesterol (TC), LDL cholesterol, HDL cholesterol, apob and apoA1 and cardiovascular risk was estimated using the PCE.

Results: The mean values of traditional lipid markers were significantly lower in the Chinese population than in the European one (TC [mean±SD] 208±647.4 mg/dl vs. 230±950.2 mg/dl, p < 0.0001; LDL-C 137±43.7 mg/dl vs. 157±954.2 mg/dl, p < 0.0001; HDL-C 41±9.7 mg/dl vs. 45±8.9 mg/dl, p = 0.0001, respectively). In patients with STEMI, mean PCE cardiovascular risk score was similar between ethnic groups, but significantly higher than in matched controls (European STEMI 19.0±12.4 vs. European controls 14.7±12.7; p < 0.0001; Chinese STEMI 19.6±14.1 vs. Chinese controls 16.3±12.1; p = 0.0016). The accuracy of PCE risk score was comparable between ethnicities [AUC (95% CI), European 0.63 (0.59–0.66) vs. Chinese 0.57 (0.53–0.61), p < 0.0001]. In multivariate analysis, the incremental apoB/apoA1 ratio was significantly associated with a progressively increased risk of STEMI independently of the PCE risk score both in the European population [OR (95% CI) II vs I tertile: 1.5 (1.06–2.24), III vs I tertile: 2.63 (1.82–3.84) and in the Chinese one [OR (95% CI) II vs I tertile: 1.92 (1.27–2.91); III vs I tertile: 3.64 (2.33–5.74)].

Conclusions: In different ethnic groups, apoB/apoA1 ratio is associated with the risk of STEMI with an incremental predictive value independently of traditional lipid markers and the new PCE risk estimating model.

P4635 | BEDSIDE
Association of creatinine clearance with clinical outcomes in patients with atrial fibrillation: The Fushimi AF Registry
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Background: The adequate antithrombotic therapy including non-vitamin K antagonist oral anticoagulants was varied by the creatinine clearance (CrCl). However, the relationship between CrCl and clinical outcomes in patients with atrial fibrillation (AF) was not fully evaluated.

Methods: The Fushimi AF Registry is a community-based prospective survey of atrial fibrillation patients who visited the participating medical institutions in Japan. Follow-up data were collected in 3,390 patients enrolled between January 2013 and May 2014. The CrCl was calculated with the Cockcroft-Gault equation, and 2,872 patients with available CrCl data were examined.

Results: Significant differences in baseline characteristics and clinical outcomes were observed vs. 72.1±24.7 years old, and 72.9±22.4 years old, respectively)<; p < 0.001). Multivariable analysis showed that moderate renal dysfunction (eGFR < 60 ml/min/m²) by all 3 formulas was a significant predictor for in-hospital and one-year major adverse cardiac events (MACE) including death, recent MI, and target vessel revascularization (TVR) and CABG.

Conclusions: Moderate renal dysfunction by any formula for eGFR was a significant predictor for in-hospital and one-year adverse clinical outcomes compared with eGFR MDRD-4 and eGRFR CKD-EPI.

P4636 | SPOTLIGHT
The relation of ambulatory heart rate with all-cause mortality among middle-aged men: a prospective cohort study
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Background: Current evidence on the predictive role of ambulatory heart rate for mortality is conflicting. This may be due to lacking or insufficient adjustment for potential confounding factors like cardiorespiratory fitness and occupational and leisure time physical activity. Moreover, most of the existing studies are not based on objective measurements of heart rate throughout a day, but on relatively few measurements over short periods throughout the day.

Purpose: The aim of this study was to investigate the association between average 24-hours continuously measured ambulatory heart rate and all-cause mortality, while adjusting for resting clinical heart rate, cardiorespiratory fitness, occupational and leisure time physical activity as well as classical risk factors.

Methods: A group of 439 male workers free of baseline coronary heart disease and aged 40–55 years from the prospective Belgian Physical Fitness Study was included in the analysis. Data were collected by questionnaires and clinical measurements and examinations from 1976 to 1978. All-cause mortality was collected from the national mortality registration with a mean follow-up period of 16.5 years, with a total of 48 events.

Results: After adjustment for all before mentioned confounders in a Cox proportional hazards regression analysis, a significant increased risk for all-cause mortality was found among the tertile of workers with highest average ambulatory heart rate compared to the tertile with lowest ambulatory heart rate (Hazard ratio = 3.21, 95% confidence interval: 1.22–8.44). No significant independent association was found between resting heart rate and all-cause mortality.

Conclusions: In this study conducted within a group of male workers free of coronary heart disease at baseline, continuously ambulatory measured average heart rate was shown to be significantly associated with all-cause mortality while adjusting for resting clinical heart rate, cardiorespiratory fitness, occupational and leisure time physical activity as well as for classical risk factors. These findings support that average heart rate throughout the day, more than resting heart rate, is a strong independent predictor for all-cause mortality in healthy middle-aged working men.

Acknowledgement/Funding: Belgium Ministry of Public Health

Clinical parameters to improve risk prediction

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P4637 | BEDSIDE

Respiratory sinus arrhythmia: a surrogate of vagal tone independently predicts mortality after myocardial infarction

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Purpose: Respiratory sinus arrhythmia (RSA) is a non-invasive measure of cardiac vagal outflow that has been shown to predict adverse outcome in survivors of acute myocardial infarction (MI). We aimed at investigating whether the predictive potential for adverse outcome from other than MI-related risk factors of normal RSA persists in this population.

Methods: 941 survivors of acute MI were prospectively enrolled and followed up for 5-year all-cause mortality. Patients underwent 30-minute recordings of ECG, 12-lead ECG and 24-hour Holter monitoring within 7 days after the MI and were subsequently followed up at 1, 6, 12, 24 and 60 months; primary endpoint was SCD, secondary endpoint included all non-sudden deaths from cardiovascular diseases.

Results: During follow-up we registered 19 cases of SCD and 11 cases of non-sudden deaths from cardiovascular diseases (including 7 lethal MI and 3 lethal strokes). HRT2 significantly increased risk of all-cause mortality (odds ratio (OR) 2.3 (95% CI 1.1–5.1), p=0.04) with no significant increase in risk of all-cause mortality, whereas mTWA at 10.00 AM > 18 bpm in contrast, significantly increased risk of all-cause mortality (OR=2.3 (95% CI 1.5–3.3), p=0.001). However, at 60 months this predictive value for SCD decreased (OR=2.08 (95% CI 1.21–3.57), p=0.005) and completely disappeared for all-cause mortality, and maximum significance was observed for LVEF<40% in combination with ventricular tachycardia

Conclusion: In post-MI patients, abnormal HRT and mTWA can reliably predict increased risk of all-cause mortality and SCD. Patients with concomitant HRT2 and increased mTWA at heart rate 100 bpm are at the highest risk of SCD in the first year; but after the first year the group of highest risk include patients with low LVEF and VT+.

P4638 | BEDSIDE

Respiratory sinus arrhythmia (RSA): a non-invasive measure of cardiac vagal tone that is suitable as a mortality predictor in survivors of acute MI. RSA was independent from both well-established and recently-introduced non-invasive risk predictors.

P4639 | BEDSIDE

Relationship between cardiac autonomic dysfunction measured by heart rate recovery after exercise and coronary artery calcification

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Background: Patients with cardiac autonomic dysfunction have been shown to have increased cardiovascular events including sudden death and most of them are from coronary artery disease. Heart rate recovery (HRR) after exercise is one of the methods measuring cardiac autonomic function and impaired HRR has been suggested as a predictor of adverse cardiovascular events.

Purpose: We sought to investigate whether HRR is associated with the degree of coronary artery calcification as a marker of atherosclerotic coronary artery disease.

Methods: Patients without known coronary artery disease who underwent both exercise treadmill test and coronary computed tomography angiography as evaluations for chest pain or routine health examinations were analyzed retrospectively. HRR was defined as the difference between the heart rate at peak exercise and the heart rate 1 minute after exercise during a recovery phase. The degree of coronary artery calcification was represented as Agatston calcium score.

Results: Total 457 patients were identified. Median HRR value was 29 beat/min (bpm), and we compared clinical characteristics between the group with below median value and the other. The group with below HRR 29 bpm showed significantly older age, higher BMI, higher hypertension and diabetes prevalence. The severity of coronary artery calcification was also higher in the group with below HRR 29 bpm as compared with the other, but the difference was not statistically significant (112.7±308.8 vs 65.9±205.1, p=0.059). We calculated receiver operating characteristic curve according to the different calcium score level (≤ 10, >10–100, >100–400). The area under curve (AUC) of HRR showed its highest value at predicting calcium score of more than 100 (AUC=0.629, 95% CI 0.560–0.699), whereas the AUC of age was higher (AUC=0.744, CI 0.688–0.801). In the regression analysis using generalized linear model, age, hypertension, diabetes and low HRR was significant predictor for high calcium score, however, multivariate analysis showed age was the only significant parameter for high coronary calcium score (coefficient 5.55, standard error 1.25, p<0.0001).

Conclusion: We did not find significant correlation between cardiac autonomic dysfunction measured by HRR and the degree of coronary artery calcification. Age was more closely related to the severity of calcification than HRR.
P4642 | BEDSIDE
Exploration of risk factors for major bleeding in Japanese patients with atrial fibrillation: The Fushimi AF Registry
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Purpose: Atrial fibrillation (AF) is a common arrhythmic disorder among the elderly, and is increasing significantly as the population ages. Although oral anticoagulation is frequently recommended to prevent stroke and thromboembolism in AF patients, the major bleeding risk has not been fully elucidated in Japanese patients.

Methods: The Fushimi AF Registry, a community-based prospective survey, was conducted to investigate the major bleeding in Japanese patients with AF. The registry included 420 patients with AF who were registered between January 2007 and June 2008. The primary endpoint was major bleeding, and the follow-up period was 1 year. The procedure of the survey was approved by the ethics committee of each hospital.

Results: Of 420 patients, 121 (29.3%) had major bleeding during the year. Of 121 patients, 41 (34.0%) had major bleeding involving the gastrointestinal tract, 37 (30.6%) had hemorrhagic stroke, and 20 (16.6%) had intracranial hemorrhage. The incidence of major bleeding was significantly higher in patients with a history of major bleeding (p < 0.01) and in patients with a history of advanced adenoma or carcinoma (p < 0.01). The incidence of major bleeding was also higher in patients with a history of diabetes (p < 0.01) and in patients with a history of smoking (p < 0.01).

Conclusions: Major bleeding is a serious complication in Japanese patients with AF. The incidence of major bleeding is higher in patients with a history of major bleeding and in patients with a history of advanced adenoma or carcinoma. The incidence of major bleeding is also higher in patients with a history of diabetes and in patients with a history of smoking.
P4645 | BEDSIDE
What is the best genetic score to predict the risk coronary disease?
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Introduction: Several genetic polymorphisms have been associated with coronary artery disease (CAD) by genomic association studies. However, the individual predictive value of each polymorphism is limited and the approach for the incorporation of these in risk stratification has evolved in the form of “scores”. The method for performing a genetic risk score (GRS) which is more discriminative for CAD risk is still not clear.

 Aim: Evaluate the discriminative ability of various models of GRS as predictors for CAD.

 Methods: Case-control study which included 1321 consecutive coronary patients and 1148 controls selected to be similar to cases in terms of gender and age. Using specific primers, we evaluated 29 genetic polymorphisms: ACE I/D, AGT235 C/T, SMAD3 C/T, MIA3 C/A, MTHFD1L A/G, SLC30A8 C/T, TCF7L2 C/T, HNF4 C/G, FTO A/C, ADIPOQ C/G. Of all the analyzed polymorphisms, only 7 were associated with CAD risk. To calculate the additive GRS, a value of −1 was given for the homozygous wild-type genotype, 0 for heterozygous and 1 for the homozygous mutated genotype (risk). The multiplicative GRS was based on the risk multiplications of each of the 29 studied genes. The best GRS was selected by calculating the OR (case/control) of the highest tertile of each model versus the lower tertile, and the one showing an increased risk with statistical significance (P < 0.05) was selected (Table).

 Results: The discriminative capacity increased with the various evaluated models (1–4). The multiplicative model with all the studied genes was the more discriminative method for CAD risk, showing an OR=2.03 (CI: 1.67 to 2.48; P < 0.0001).

 Conclusions: In our population, the multiplicative GRS model was found to be preferably used to determine the coronary risk rather than using only a particular polymorphism.

P4646 | BEDSIDE
Genetic polymorphisms and cardiovascular disease - multivariate study including traditional risk factors

Several polymorphisms have been linked to coronary artery disease (CAD). However, many of these polymorphisms act in common pathophysiological axes and to have clinical significance as vascular risk markers, in one hand they must withstand the multivariate analysis and, in the other hand, they should have a predictive value independent of the well-known traditional risk factors (TRF).

 Aim: Analyze the genetic polymorphisms linked to CAD occurrence, in a multivariate study including the TRF.

 Methods: A case-control study was performed with 1321 consecutive coronary patients and 1148 controls selected to be similar to cases in terms of gender and age. The TRF (arterial hypertension, diabetes, dyslipidemia, smoking, obesity, sedentary lifestyle and family history) were defined according to the International criteria. A multiplicative genetic risk score (GRS) was calculated based on the risk multiplication (OR) of each genotype of the 29 variants: ACE I/D, AGT235 M/T, ATIR A/C, MTHFR C/T and 1298 A/G, PON1 QR and S5 LMA P/T C, APO E, Locus 9p21.3, CDKN2B, GJA4 C/T, PCSK9 A/G, TAS2R50 A/G, KIF6 C/T, IGF2BP2 G/T, ADAMTS7 A/G, MC4R T/C, PPARG Pro12 Ala, TCF7L2 C/T, HNF4 C/G, FTO A/C, ADIPOQ C/G. Subsequently, a logistic regression was done in order to test the predisposing factors of CAD, including the TRF and the GRS.

 Results: The factors that were significantly and independently associated with CAD were: the arterial hypertension, dyslipidemia, diabetes, smoking and the GRS (Table). Variable independently associated to CAD

<table>
<thead>
<tr>
<th>Variables</th>
<th>Odds ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial hypertension</td>
<td>1.86 (1.54–2.24)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>2.90 (2.20–3.82)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2.96 (2.38–3.67)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Smoking</td>
<td>3.08 (2.55–3.72)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Genetic risk score</td>
<td>2.05 (1.65–2.54)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

 Conclusions: This study clearly demonstrates that the genetic risk factors (OR=2.05, P < 0.0001) add risk to traditional risk factors relatively to the CAD development. Knowing the mechanisms involved, it may arise new approaches to prevent the coronary disease in healthy population, but with increased genetic risk.

P4647 | BEDSIDE
Can we characterize the risk of stroke and death in patients with non-valvular atrial fibrillation based on the parameter defining a CHA2DS2-VASc score equal to 1?
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Purpose: Stroke risk stratification is based on different clinical markers and therefore, using the available stroke risk stratification schemes the CHA2DS2-VASc score is the most widely used. However, non-valvular atrial fibrillation (NVAF) patients with a CHA2DS2-VASc score = 1 is a heterogeneous group. We sought to investigate whether patients with a CHA2DS2-VASc score = 1 have the same risk of developing stroke or death when considering each of the parameter.

Methods: Between 1998 and 2011, among 1,212 consecutive NVAF patients, hospitalised for AF, 246 had a CHA2DS2-VASc score = 1. All patients were followed-up at least 6 months and cardiovascular events recorded. The composite endpoint was defined as the first occurrence of stroke or death.

Results: Mean age was 55.5±10.8 years. At baseline, the distribution was the following: female (n=70), hypertension (n=60), diabetes (n=17), age 65–75 years (n=44), heart failure (n=37), VASc (n=18). At 1 year, stroke or death occurred in 2 (2.9%), 1 (1.7%), 0 (4.6%), 4 (10.8%) and 1 (5.6%) patients, respectively. A CHA2DS2-VASc score = 1 is associated with a stroke and deaths rate of 2.92 per 100 person-years (95% CI = 1.12–5.92) at one year.

Conclusion: These results suggest that a CHA2DS2-VASc score = 1, associated with a high risk of stroke and death, is not influenced by the presence of any parameter defining this score.

P4648 | BEDSIDE
Central obesity modifies the role of triglycerides in the risk of fatal and non-fatal cardiovascular event: 10-year follow-up (2002-12) of the ATTICA study
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Background: Elevated serum triglycerides have been treated as independent cardiovascular disease (CVD) risk factor, but, their net effect on 10-year CVD risk is still under research due to the multi-factorial basis of hypertriglyceridemia that combines hormonal, genetic, anthropometric and dietary characteristics. Moreover, central obesity has been linked with increased 10-year CVD risk that has been explained through glucose-metabolism paths, but rarely through triglycerides.

Aim: To investigate whether patients with a CHA2DS2-VASc score = 1 have the same risk of developing stroke or death when considering each of the parameter.

Methods: From May 2001 to December 2002, 1514 men and 1528 women (n=44), heart failure (n=37), VASc (n=18). At 1 year, stroke or death occurred in 2 (2.9%), 1 (1.7%), 0 (4.6%), 4 (10.8%) and 1 (5.6%) patients, respectively.

Results: The Kaplan-Meier curves (figure) show that there was no significant differences in the risk of stroke and death whatever the parameter defining the CHA2DS2-VASc score = 1.

Conclusion: These results suggest that a CHA2DS2-VASc score = 1, associated with a high risk of stroke and death, is not influenced by the presence of any parameter defining this score.

P4649 | BEDSIDE
Can we characterize the risk of stroke and death in patients with non-valvular atrial fibrillation based on the parameter defining a CHA2DS2-VASc score equal to 1?
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Purpose: Stroke risk stratification is based on different clinical markers and therefore, using the available stroke risk stratification schemes the CHA2DS2-VASc score is the most widely used. However, non-valvular atrial fibrillation (NVAF) patients with a CHA2DS2-VASc score = 1 is a heterogeneous group. We sought to investigate whether patients with a CHA2DS2-VASc score = 1 have the same risk of developing stroke or death when considering each of the parameter.

Methods: Between 1998 and 2011, among 1,212 consecutive NVAF patients, hospitalised for AF, 246 had a CHA2DS2-VASc score = 1. All patients were followed-up at least 6 months and cardiovascular events recorded. The composite endpoint was defined as the first occurrence of stroke or death.

Results: Mean age was 55.5±10.8 years. At baseline, the distribution was the following: female (n=70), hypertension (n=60), diabetes (n=17), age 65–75 years (n=44), heart failure (n=37), VASc (n=18). At 1 year, stroke or death occurred in 2 (2.9%), 1 (1.7%), 0 (4.6%), 4 (10.8%) and 1 (5.6%) patients, respectively. A CHA2DS2-VASc score = 1 is associated with a stroke and deaths rate of 2.92 per 100 person-years (95% CI = 1.12–5.92) at one year.

Conclusion: These results suggest that a CHA2DS2-VASc score = 1, associated with a high risk of stroke and death, is not influenced by the presence of any parameter defining this score.
P4649 | BEDSIDE
Lipoprotein-associated phospholipase A2 as independent predictor of atherosclerosis among patients with zero coronary artery calcium score
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Background: Despite patients with coronary artery calcium (CAC) score zero are considered as low risk of coronary events, however they may carry non-calcified vulnerable plaques. Lipoprotein-associated phospholipase A2 (Lp-PLA2) has been proposed as a highly specific biomarker of plaque vulnerability. It is unknown whether Lp-PLA2 is related to presence of non-calcified coronary artery plaques in patients with CAC score zero.

Material and methods: A total of 469 consecutive patients (61±2 years, 44.3% men) with intermediate pretest probability of coronary artery disease (CAD), referred for coronary computed tomography angiography (CCTA) between September 2010 and October 2012, were analysed. Coronary artery plaques were evaluated by CCTA in the whole study group. CAC score was calculated by Agatston method. Serum Lp-PLA2 mass was assessed by PLAC® test.

Results: CAC score zero was found in 215 (45.8%) of the patients. In this group coronary artery plaques were present in 153 (71.2%) subjects. Multivariable logistic regression analysis revealed that Lp-PLA2 concentration (OR 1.02, 95% CI 1.01–1.04, p=0.004) was an independent predictor of non-calcified coronary artery plaques in patients with zero CAC. In the ROC curve analysis Lp-PLA2 of 166 ng/ml presented as the optimal cut-off point for discriminating coronary artery plaque presence in patients with CAC score zero (sensitivity: 0.74, specificity: 0.73, AUC 0.734, p=0.0001).

Conclusions: The majority of patients with intermediate pretest probability of CAD and CAC score zero may carry coronary artery plaques, and Lp-PLA2 concentration is independently correlated to their presence.

P4650 | BEDSIDE
Sleep duration and risk of incident of ischaemic heart disease: a 7-year prospective study of 0.5 million Chinese adults
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Purpose: Sleep duration and risk of incident of ischaemic heart disease (IHD) have been repeatedly studied. However, few studies have been conducted in Chinese population to evaluate the association between sleep duration and IHD risk.

Methods: The CKB study is a prospective study of 512,891 adults aged 35–79 years who were recruited during 2004–8 from 10 diverse locations in China. Sleep duration was recorded by interviewer-administered questionnaires at baseline. During 7 years of follow-up, there were 3361 incident cases of new onset IHD. Cox regression was used to estimate risk ratios (RRs) for IHD incidence versus the referent group. Some common risk factors were adjusted for in the model.

Results: The Kaplan-Meier curves (figure) show that there was a significant difference in the risk of stroke/death when CRP level was considered.

Conclusion: Considering CRP levels at admission could refine the risk stratification in CHA2DS2-VASc score ≥ 1 NVAF patients and lead to a rationale to anticoagulate patients.

P4651 | BEDSIDE
Comparison of contemporary risk models for predicting mortality and major adverse events after combined aortic valve replacement and coronary artery bypass grafting
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Background: Aortic valve replacement (AVR) and/or coronary artery bypass grafting (CABG) make up the majority of cardiac surgeries with increasing demand as the population ages. Accuracy of risk stratification is important, especially as interventional aortic valve and coronary procedures continue to blossom, but have been rarely studied for the combined AVR+CABG operation.

Purpose: We compared the prognostic utility of EuroSCORE, EuroSCORE II and Society of Thoracic Surgeon’s (STS) Score for AVR+CABG.

Methods: All patients undergoing AVR+CABG at our City Hospital during 2005–2012 were included, with the three risk scores calculated and their discrimination and calibration for mortality and morbidities assessed.

Results: 450 patients undergoing AVR+CABG were included, with mean follow-up of 4.7 years. Operative mortality was 6.4% (29), and mean scores were EuroSCORE 12.5±11.1%, EuroSCORE II 6.6±1.6% and STS Score 5.5±4.4%. C-statistics were 0.587, 0.669 and 0.699 respectively for operative mortality. Hosmer-Lemeshow test P-values were 0.964, 0.718 and 0.567, and Brier Score 0.716, 0.585 and 0.588. Independent predictors of operative mortality were history of myocardial infarction and impaired renal function. STS score also was the best score at detecting late mortality (c=0.643), composite morbidity (c=0.827), stroke (c=0.842), prolonged ventilation–24 hours (c=0.842), and return to theatre (c=0.612).

Conclusion: The STS score has the best discrimination (albeit moderate) for mortality and most complications after AVR+CABG, while its calibration was similar to EuroSCORE II and better than EuroSCORE I. It should therefore be used in risk stratification and also consideration of surgical or percutaneous approach to patients with concurrent severe aortic valve and coronary artery disease.

P4652 | BENCH
Sleep duration and risk of incident of ischaemic heart disease: a 7-year prospective study of 0.5 million Chinese adults
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Purpose: Sleep duration and risk of incident of ischaemic heart disease (IHD) have been repeatedly studied. However, few studies have been conducted in Chinese population to evaluate the association between sleep duration and IHD risk.

Methods: The CKB study is a prospective study of 512,891 adults aged 35–79 years who were recruited during 2004–8 from 10 diverse locations in China. Sleep duration was recorded by interviewer-administered questionnaires at baseline. During 7 years of follow-up, there were 3361 incident cases of new onset IHD. Cox regression was used to estimate risk ratios (RRs) for IHD incidence versus the referent group. Some common risk factors were adjusted for in the model.

Results: The Kaplan-Meier curves (figure) show that there was a significant difference in the risk of stroke/death when CRP level was considered.

Conclusion: Considering CRP levels at admission could refine the risk stratification in CHA2DS2-VASc score ≥ 1 NVAF patients and lead to a rationale to anticoagulate patients.
Cairo University Hospitals, P4653 | BEDSIDE M. Benderly 1, B. Sapir 2, O. Kalter-Leibovici 1, R. Zimlichman 3.

Prediction
Lipoprotein associated phospholipase A2 does not improve mortality
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Background: Plasma brain natriuretic peptide (BNP) level is known to be elevated during normal pregnancy, as pregnancy is associated with volume expansion. In preeclampsia/eclampsia syndrome, the BNP level is shown to be even higher than non-pregnancy levels. Whether or not elevated BNP level is associated with increased maternal complications, is not clearly defined.

Purpose: To evaluate the role of elevated BNP as a marker of increased maternal complications in pregnant ladies suffering from preeclampsia/eclampsia syndrome.

Methods: Fifty pregnant ladies were included; all were diagnosed as having preeclampsia/eclampsia syndrome. Basic clinical characteristics and obstetric history and examination were evaluated. An echocardiography was performed, to ensure absence of any structural heart disease and a 24-hour urinary protein test was done. A venous sample was withdrawn from all pregnant ladies, on presentation, and tested for BNP plasma level using a point-of-care test. Ladies were followed up till delivery and maternal complications were reported.

Results: Twenty seven (54%) ladies had preeclampsia and 23 ladies (46%) had eclampsia syndrome. The mean systolic blood pressure was (177.5±21.3 mmHg) and the mean diastolic blood pressure was (110.4±11.2 mmHg). Thirty (60%) ladies developed complications during pregnancy, including HELLP syndrome (hemolysis, elevated liver enzymes, low platelet count), renal impairment, vaginal bleeding and cervical incompetence, and 2 ladies died before delivery. The median BNP plasma level, for all patients, was 92.6 ng/dl. The median BNP was significantly higher in patients who developed complications (130.2 Vs 52.5 ng/dl, p=0.002). The highest BNP level (1170 ng/dl) was found in a patient who died of pulmonary edema, shortly after presentation. Ladies who developed complications had significantly higher heart rate (mean 109.9 Vs 100.3 bpm; p<0.05), systolic blood pressure (mean 184.1 Vs 165.8 mmHg; p=0.001), diastolic blood pressure (mean 114.1 Vs 103.9 mmHg; p<0.001), 24-hours urinary protein excretion (mean 3.1 Vs 2.8 g; p=0.009) and delivered earlier than ladies without complications (mean pregnancy duration 34 Vs 36 weeks; p=0.04).

Conclusion: Higher BNP plasma level is helpful in defining preeclampsia/eclampsia patients with higher risk of maternal complications. Measuring BNP can help earlier detection and management of complications and it also prompts tighter blood pressure control.

P4654 | BEDSIDE Lipoprotein-associated phospholipase A2 does not improve mortality prediction
M. Benderly 1, B. Sapir 2, O. Kalter-Leibovici 3, R. Zimlichman 1, A. Donia 4.

Background: Lipoprotein-associated phospholipase A2 (Lp-PLA2) has been considered as a cardiovascular marker for inflammation and risk of cardiovascular events in observational studies. Nevertheless, its direct inhibitory effect on the formation and regression of atherosclerotic plaques and its positive influence to better lipid profile is controversial.

Purpose: To study the long-term association of Lp-PLA2 with mortality among coronary heart disease patients.

Methods: Among 3122 CHD patients included in the Bezafibrate Infarction Prevention (BIP) study, 2538 survived to the 5th follow-up year and had frozen serum sample tested for Lp-PLA2 activity. The 3rd Lp-PLA2 activity tertile (34.6%) vs. 5 (18.5%) vs. 2 (7.4%), (p<0.001) were observed across the three tertiles of increasing Lp-PLA2 activity.

Results: Among 3122 CHD patients, 1818 had untreated diabetes mellitus (T2DM) at presentation and 1304 (72%) were treated with intensive lipid-lowering therapy (BIP) study. The median BNP plasma level, for all patients, was 92.6 ng/dl. The median BNP was significantly higher in patients who had progressed to coronary disease (130.2 Vs 52.5 ng/dl, p<0.002). The highest BNP level (1170 ng/dl) was found in a patient who died of pulmonary edema, shortly after presentation. Ladies who had progressed to coronary disease had significantly higher heart rate (mean 109.9 Vs 100.3 bpm; p<0.05), systolic blood pressure (mean 184.1 Vs 165.8 mmHg; p=0.001), diastolic blood pressure (mean 114.1 Vs 103.9 mmHg; p<0.001), 28-hours urinary protein excretion (mean 3.1 Vs 2.8 g; p=0.009) and delivered earlier than ladies without complications (mean pregnancy duration 34 Vs 36 weeks; p=0.04).

Conclusion: Higher BNP plasma level is helpful in defining preeclampsia/eclampsia patients with higher risk of maternal complications. Measuring BNP can help earlier detection and management of complications and it also prompts tighter blood pressure control.

P4655 | BEDSIDE Relation between high-density lipoprotein efflux capacity and coronary plaque progression in type 2 diabetes patients with intensive lipid-lowering therapy
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Background: Despite intensive lipid-lowering therapy using statins, patients with type 2 diabetes mellitus (T2DM) still have a high "residual risk" of future cardiovascular events. High-density lipoprotein (HDL) may provide cardiovascular protection, but its relation to the residual risk is unknown.

Purpose: We assessed the association between HDL and coronary plaque progression by intravascular ultrasound (IVUS) in T2DM patients with intensive lipid-lowering therapy.

Methods: Thirty T2DM patients who received intensive statin treatment and percutaneous coronary intervention using IVUS were examined. IVUS analysis on non-culprit coronary lesions was performed at baseline and after follow-up for 8–9 months. Cholesterol efflux capacity of HDL, an index of HDL functionality, was measured with a validated in vitro system.

Results: During the follow-up period, intensive statin treatment reduced low-density lipoprotein cholesterol (LDL-C) level from 96±29 mg/dl to 83±21 in all of the patients. However, unexpectedly, a significant progression of coronary plaque was observed (a 3.4±8.8% increase in percent plaque volume, p=0.036). Patients who had progression of coronary plaque (Group P, n=20, male/female: 14/6) and regression of coronary plaque (Group R, n=10, male/female: 7/3) were similarly treated with LDL-C levels. But cholesterol efflux capacity of HDL and HDL cholesterol (HDL-C) level at follow-up were significantly lower in the group P than in the group R (16.9±1.6% vs. 18.7±1.4%, p=0.023 and 46±9µg/ml vs. 64±10µg/ml, p=0.001, respectively). Cholesterol efflux capacity and HDL-C were significantly inversely associated with the progression of coronary plaque (odds ratio [95% confidence interval]: 0.15 [0.02–0.65], p=0.019 and 0.09 [0.01–0.55], p=0.027, respectively) after adjusting for age by multiple logistic regression analysis.

Conclusions: Cholesterol efflux capacity of HDL, in addition to HDL-C level, may be a useful biomarker for predicting coronary plaque progression and a novel therapeutic target to reduce the residual risk in T2DM patients with intensive lipid-lowering therapy.

P4656 | BEDSIDE Cardioprotective role of fetuin-A in patients with end-stage renal disease on regular hemodialysis
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Background: Valvular calcification is an indicator of subclinical atherosclerosis and a risk factor for coronary artery disease specially in patients with end-stage renal disease (ESRD) on regular hemodialysis rather than only reflecting an end-stage disease. This study aims to evaluate the cardioprotective role of Fetuin-A in patients with ESRD on regular hemodialysis.

Patients and methods: This study included 80 patients (39 males and 41 females, with mean age 44.5±10.41 and hemodialysis duration was 5.5±4.3 years). Fifty patients with ESRD undergoing regular hemodialysis were assessed. Fetuin-A was measured by means of enzyme-linked immunosorbent assay (ELISA) kit. Serum levels of albumin, Calcium, phosphorus, triglyceride (TG), total cholesterol, high density lipoprotein cholesterol (HDL-c) and low density lipoprotein cholesterol (LDL-c) creatinine and urea were estimated using standard laboratory techniques. Correlations of fetuin-A with these parameters were studied. Comparison of means of were done using ANOVA test between more than two groups.

Results: Patients were stratified into 3 tertiles according to serum fetuin-A concentration [those with serum fetuin-A < 350 µg/ml (26 patients), serum fetuin-A 350 – < 430 µg/ml (27 patients), serum fetuin-A ≥ 430 µg/ml (27 patients)] respectively. Aortic valve calcification was seen in 23 (88.5%) vs. 16 (59.3%) vs. 6 (22.2%) (p<0.01) while mitral valve calcification was seen in 9 (34.6%) vs. 5 (18.5%) vs. 2 (7.4%) (p<0.05) in the 3 tertiles respectively. Statistically significant values of hsCRP (16.85±14.80 vs. 14.22±16.65 vs. 5.78±11.22 respectively in the 3rd compared to 1st and the 2nd tertiles) and serum albumin (0.17±0.02 vs. 0.24±0.44 vs. 3.86±2.28 respectively (p value <0.001) were observed across the three tertiles of increasing serum fetuin-A. No significant differences were seen in values of calcium phosphorus product and other laboratory across the 3 tertiles.

Conclusions: Fetuin-A levels is inversely correlated to valvular calcification and hs-CRP levels and hence may be cardioprotective in patients with ESRD on regular hemodialysis.
**P4657 | BEDSIDE**
Plasma hydroxyoxygenand acid and incident type 2 diabetes in patients with stable angina pectoris

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**Background:** The tryptophan metabolite hydroxyoxygenand acid (HAA) has been related to cardiovascular and atherosclerotic disease. Moreover, HAA was recently identified as a potent regulator of lipid metabolism and inflammation.

**Purpose:** We evaluated the associations of plasma HAA levels to incident type 2 diabetes (T2D) in patients with suspected stable angina pectoris (SAP).

**Methods:** A total of 4122 patients underwent elective coronary angiography at two Norwegian university hospitals in 2000–2004. Patients with self-reported diabetes mellitus and/or glycated haemoglobin ≥6.5% (n=1603) were excluded leaving 2519 patients eligible for the analyses. The participants were followed for incident T2D throughout 2009. Odds ratios (OR) and 95% confidence intervals (CI) for were calculated using logistic regression and were reported per standard deviation increment of plasma HAA (log-transformed). We assessed risk classification by calculating the continuous net reclassification improvement (NRI) = 0.

**Results:** Median age at inclusion was 62 years and 73% were males. During follow-up, a new diagnosis of T2D was recorded in 114 (4.5%) of the participants. Median plasma HAA values were substantially higher in those who subsequently developed T2D than in those who did not (40.0 vs. 33.8 nmol/L, P < 0.001). In age and gender adjusted analyses, HAA provided an OR (95% CI) for incident T2D of 1.57 (1.30–1.91), P < 0.001. Adding body mass index, study centre and fasting status to the multivariable model somewhat attenuated the association, which, however, remained statistically significant (OR [95% CI]: 1.34 [1.08–1.67], P = 0.009). Further adjustment including serum apolipoprotein A1, total cholesterol, triglycerides, C-reactive protein, glycated haemoglobin, and use of thiazides, statins and beta-blockers did not affect the risk estimate of HAA (OR [95% CI]: 1.34 [1.07–1.67], P = 0.01). Moreover, HAA significantly improved risk classification for T2D (NRI [95% CI]: 0.19 [0.07–0.38], P = 0.04).

**Conclusion:** In a large cohort of patients with SAP, we identified plasma HAA as a strong predictor of incident T2D. Underlying pathomechanisms should be further elucidated.

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**P4658 | BENCH**
The arachidonate 15-lipoxygenase product present in heart tissue from patients with ischaemic heart disease induces hypercoagulability

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**Background and introduction:** Platelet activation plays a significant role in haemostasis and thrombosis and also in the pathophysiology of cardiovascular disease. Recent studies suggest a link between atherothrombotic events and the enzyme arachidonate 15-lipoxygenase (ALOX15), which catalyses the formation of 15-hydroxy eicosatetraenoic acid (15-HETE) from arachidonic acid. Recent studies have shown that ALOX15 is highly expressed in human ischaemic heart tissue, and that 15-HETE increases platelet aggregation and thrombin generation. However, little is known about the effects of 15-HETE on clot formation. We hypothesised that increased production of 15-HETE may contribute to atherothrombotic events by increasing clot formation.

**Purpose:** To determine if the concentration of 15-HETE in heart tissue and serum is increased in patients with ischaemic heart disease and if 15-HETE induces hypercoagulability in human blood.

**Methods:** We used liquid chromatography - mass spectrometry (LC-MS) to analyse 15-HETE levels in heart tissue and in serum from 5 patients undergoing coronary artery bypass grafting (CABG; ischaemic tissue) and from 5 patients undergoing aortic valve replacement (AVR; non-ischaemic tissue). Whole blood clot formation was assessed with rotational thromboelastometry. Activation of clot formation was assessed using intrinsic (INTEM), extrinsic (EXTEM) and fibrin-based (FIBTEM) model in the presence or absence of 15-HETE. Clotting time, clot formation time, maximum clot firmness, and α-angle were measured.

**Results:** LC-MS analysis showed that 15-HETE concentrations were significantly higher in heart biopsy samples and serum from patients undergoing CABG compared with patients undergoing AVR. Clotting time of 15-HETE treated human blood reduced the clot formation time in the INTEM assay, increased the maximum clot firmness in the EXTEM assay, and shortened the tissue factor-activated clotting time and increased the α-angle in the FIBTEM assay.

**Conclusions:** The work identifies increased concentrations of the ALOX15 product 15-HETE in human ischaemic heart biopsies and our data demonstrate that the ALOX15 product secreted from ischaemic heart tissue accelerates clotting time and is thus prothrombotic. We suggest that patients with increased ALOX15 expression and increased 15-HETE levels have an increased risk of thrombotic events.

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**P4659 | BEDSIDE**
Relationship between serum beta-2-microglobulin and cardiovascular risk factors

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**Background and purpose:** Serum beta-2-microglobulin (B2M) level reflects cellular turnover (especially lymphocytes) and renal tubular function. We previously reported its association with cardiovascular and all-cause mortality. We sought to explain this association in terms of cardiometabolic risk factors.

**Methods:** Data on 6,474 participants (3114 men, 3360 women; age, mean±SD, 44.7±17.2 yrs) of the Third National Health and Nutrition Examination Survey were analyzed using ANCOVA. The relationship of B2M with age, BMI, blood pressure, glycemia, lipids, inflammation, liver and renal function were studied. Where appropriate, data were log-transformed.

**Results:** Serum B2M level (mean±SE) was 1.92±0.66 and 1.92±0.77 mg/L in men and women respectively (P = 0.05). It correlated with age (r = 0.57), BMI (r = 0.15), systolic blood pressure (r = 0.38), A1C (r = 0.21), triglycerides (r = 0.25), HDL (r = 0.14), AST (r = 0.18), ALP (r = 0.29), CRP (r = 0.28) and eGFR (r = 0.66) (all p-values ≤ 0.001). In the fully adjusted model, serum B2M remained positively associated with systolic blood pressure (p = 0.11, 95% CI: 0.04 to 0.18), AST (p = 0.14, 95% CI: 0.10 to 0.18), ALP (p = 0.10, 95% CI: 0.07 to 0.13) and CRP (p = 0.05, 95% CI: 0.04 to 0.07), and negatively associated with HDL (p = 0.11, 95% CI: − 0.07 to − 0.15) and eGFR (p = 0.85, 95% CI: − 0.60 to − 0.69) (all p-values ≤ 0.001).

**Conclusions:** The association of serum B2M level with Framingham risk factors as well as other risk factors of cardiovascular disease helps to explain why it is a good predictor of cardiovascular risk and mortality. This readily available blood test may be useful to identify high-risk patients and prompt the search for reversible causes.

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**P4660 | BEDSIDE**
Postoperative myocardial injury assessed by high-sensitivity cardiac troponin T and revised cardiac risk index in patients undergoing non-cardiac surgery

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**Introduction:** High-sensitivity cardiac troponin T (hs-cTnT) is useful for detecting myocardial injury and is expected to be a prognostic information marker in patients undergoing non-cardiac surgery. Revised cardiac risk index (RCRI) is also useful for risk stratification in patients undergoing non-cardiac surgery. The aim of this study was to evaluate perioperative myocardial injury assessed by hs-cTnT according to RCRI score.

**Methods and results:** This study was a prospective noninterventional trial, included 171 consecutive patients undergoing non-cardiac surgery. Serum levels of hs-cTnT were measured before and 24 and 72 hours after non-cardiac surgery. Myocardial injury was defined as postoperative hs-cTnT > 0.014 ng/mL and a relative hs-cTnT change of ≥20%. Two patients undergoing dialysis patients were excluded (n=169). Postoperative hs-cTnT levels were significantly increased before: 0.012±0.009 versus after 24 hours: 0.020±0.045 ng/mL, P < 0.001 and 43 patients (25.4%) were diagnosed as myocardial injury. The rates of myocardial injury for patients with RCRI score 0, 1 and ≥2 were 0 (n=0 of 30), 28.2 (n=22 of 78) and 34.4% (n=21 of 61), respectively. Multivariate logistic analysis revealed that heart failure was independently associated with myocardial injury (P = 0.001 OR 5.779).

**Figure 1.** Distribution of perioperative myocardial injury over RCRI score.

**Conclusions:** Postoperative myocardial injury was frequently observed in patients with high RCRI score, but it was not observed in patients with RCRI 0. Heart failure was an independent predictor for postoperative myocardial injury.
Conclusions: 4.67) and the adjusted model (HR: 5.67), absolute number of neutrophils was 1.69). Similarly, N/L was related with cardiovascular death in the unadjusted (HR: 1.05) and adjusted models (HR: 1.73, 95% CI 1.07–2.78, P = 0.02). The results of the present study confirm that the analysis of the N/L was a strong predictor of cardiovascular disease in a selected population sample at high cardiovascular risk. The present study supports the use of N/L as a simple, cost-effective, and readily available biomarker of cardiovascular risk.

Methods: Healthy adults aged 25–41 years were enrolled in a prospective population-based cohort study in the municipality of Liechtenstein. Main inclusion criteria were prevalent diabetes, overt cardiovascular disease or a body mass index <35 kg/m². Corrected QT (QTS) interval was automatically measured from a standard 12-lead electrocardiogram and validated by a trained physician. N-terminal prohormone brain natriuretic peptide (NT-proBNP) and high-sensitivity cardiac troponin I (hs-cTnI) were measured using an Immulite and a Roche analyzer, respectively. NT-proBNP and hs-cTnI were log transformed because of a non-normal distribution pattern. Multivariable regression models adjusting for potential confounders were constructed to assess the relationships of QTS interval with NT-proBNP and hs-cTnI.

Results: Our sample consisted of 2102 participants (53.6% females) with a median age of 36.7 years. The median hs-cTnI and NT-proBNP levels were 0.69 pg/ml and 34 pg/ml, respectively. The median (interquartile range) QTS interval was 0.40 (0.35–0.45) sec. Results of NT-proBNP and hs-cTnI across quartiles of QTS interval are shown in the Table. In multivariable analyses using NT-proBNP and hs-cTnI as log-transformed continuous parameters, the beta coefficients (95% confidence interval) were 2.48 (1.34, 3.62), p < 0.0001 per log(p) increase in NT-proBNP and −0.08 (−0.15; 1.00), p = 0.08 per log(p) increase in hs-cTnI.

Conclusion: There is a strong continuous relationship between NT-proBNP and QTS interval in young and healthy adults, an association that was not evident for hs-cTnI levels. These results may suggest that intravascular volume but not subclinical myocardial injury are related to QTS prolongation. Future studies should investigate whether these relationships are present in other populations and whether interventions aimed at correcting intravascular volume might be effective in reducing QTS interval.

Acknowledgement/Funding: Schweizerischer Nationalfonds, Schweizerische Herzstiftung, Singulex.
and the increase of PAPS correlated with neutrophil activation and with the increase (p<0.01) of the expression of intracellular and circulating PTX3 and ROS. In multivariate analysis the PAPS pre-ED and the circulating levels of PTX3 were independently associated with the values of FMD and CABLES.

Conclusions: The fluid overload can affect endothelial function and arterial stiffness, through an increase of PTX3.

RISK FACTORS IN CLINICAL PRACTICE

P4665 | BEDSIDE
Seasonal variation of the critical limb ischemic events in the whole Hungarian population
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Background: Seasonal manifestations of cardiovascular diseases (CVD) are described in case of acute myocardial infarction, sudden cardiac death, arterial fibrillation, aortic rupture/dissection, stroke, deep venous thrombosis and pulmonary embolism. Paucity of data is available concerning critical limb ischemia (CLI) on this regard.

Purpose: To assess the seasonal trend of critical limb ischemia events in the whole Hungarian population.

Methods: Based on the health care administrative data (disease classification and procedure codes) of the whole Hungarian population, in a nine years period (2004–2012), all the events were detected which meet the criteria of CLI. Case detection was based on finding the PAD related major limb amputation and lower limb revascularization (surgical/endo vascular) accompanied with pain/tissue necrosis. Seasonality was assessed in an Age-period model.

Results: In the whole Hungarian population, over a nine year period (2004–2012), in 44,200 subjects, 55,900 events were identified which met the definition of CLI. PAD related major amputations represented 70%, lower limb revascularization with pain/tissue necrosis was detected in 30% of the cases. The incidence rate of CLI events (taken together and separately also) showed significant decline in late summer and autumn. This was consistent over the whole observational time.

Conclusion: This analysis, as the most complete report so far showed consistent results with other smaller studies addressing seasonality of CLI. Biological plausibility is supported by other data showing that cardiovascular risk factors are also seasonal, characterized by a decline in summer. A meaningful temporal relationship, in this manner is also presumable.

P4666 | BEDSIDE
Atrial fibrillation and impaired renal function predict cardiovascular outcome in mostly hypertensive patients with symptomatic peripheral artery disease and preserved ejection fraction
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Purpose: The study investigated the prognostic role of atrial fibrillation (AF) and renal function in patients (pts) with symptomatic peripheral artery disease (PAD) and preserved left ventricular ejection fraction (LVEF).

Methods: The occurrence of major adverse cardiovascular events (MACE, composite endpoint of death, myocardial infarction, stroke, percutaneous coronary intervention and coronary bypass surgery) was prospectively assessed in 183 PAD pts, Fontaine stages IIB and III, LVEF > 50% (66% males, 86% hypertensive, mean age 69.7 years, mean ABI 0.59). The diagnosis of AF was based on history and electrocardiographic evidence of arrhythmia. Multivariate Cox regression analysis adjusted for age, gender, traditional cardiovascular risk factors, critical limb ischemia (CLI), estimated glomerular filtration rate (eGFR), AF, coronary and cerebrovascular disease and medications used was applied to assess the independent predictors of poor clinical outcome.

Results: The prevalence of AF was 15.3% among PAD pts. During the median follow-up of 24 months, 42 pts (23%) had an event. These pts were older (72 vs 69 years; p=0.03), more likely to have AF (29% vs 11%; p=0.013), CLI (50% vs 28%; p=0.015), history of coronary and cerebrovascular disease (52% vs 37%; p=0.07) and worse renal function (eGFR < 60 ml/min, 62% vs 41%; p=0.028). After multivariable adjustment, AF (HR=2.1, 95% CI: 1.07–4.10; p=0.03) and eGFR < 60 ml/min (HR=1.97, 95% CI: 1.05–3.68; p=0.03) remained the only independent predictors of unfavorable outcome (Figure). The model that incorporated AF and renal function to ABI tended to improve prediction of MACE (AUG increased from 0.60 to 0.68; p=0.07).

Conclusion: Impaired renal function and AF are strong and independent predictors of MACE in symptomatic PAD pts with preserved LVEF.
P4669 | BEDSIDE
Near-infrared spectroscopic hand imaging: a new tool to assess microcirculatory impairment in systemic sclerosis

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Background: Systemic sclerosis (SSc) causes functional and structural microcirculatory dysfunction, affecting also distal extremities. Optical Near-InfraRed Spectroscopy (NIRS) of blood HbO2 saturation (stO2) is able to evaluate O2 delivery/consumption balance in the explored tissue. The NIRS-sensitive camera non-invasively detects stO2 values in superficial tissues, automatically generating 2D imaging maps in real time.

Objectives: Whether NIRS hand imaging may evaluate peripheral microcirculatory dysfunction and its spatial heterogeneity in SSc pts compared to controls.

Methods: Fifty-four SSc pts (age 55±16 yrs) and twenty-one healthy controls (age 51±14 yrs, p=0.29) were studied by hand palm NIRS 2D imaging. A blood pressure cuff was applied to the forearm and 3-min ischaemia was induced. Images were acquired at basal conditions and each 10 secs during 3 mins of ischemia and 5 mins of reperfusion. Five regions of interest were positioned on each fingertip, from the second to the fifth finger and one on thenar eminence.

Results: A significant difference was found between controls and SSc in basal stO2 (84.3±7.5 vs 75.4±10.9%, p<0.001), minimum stO2 (65.2±8.0 vs 53.4±10.1%, p<0.001) and time to maximum stO2 during hyperaemia (63±38 vs 85±49 sec, p<0.05). Patients with Scd-70 antibodies had lower basal stO2 compared to pts without (69.3±12.7 vs 78.8±11.7, p<0.05), as well as pts with diabetes mellitus (69.3±12.7 vs 78.8±11.7, p<0.05).

Conclusions: NIRS hand imaging is a simple, automated tool to non-invasively detect regional microcirculatory defects in SSc, which seems to add significant functional information to current morphological picture of nailfold capillaroscopy.

P4670 | BEDSIDE
Ultrasound evaluation of the forearm arteries anomalies in patients undergoing percutaneous coronary intervention via radial artery access

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Background: A proven advantage of radial over femoral artery access has led A proven advantage of radial over femoral artery access has led to an increase in the number of interventions via radial artery access in patients with acute coronary syndromes. Transradial procedure failures can sometimes be due to variation in radial artery anatomy. An ultrasound examination of the forearm arteries provides important information about the anatomy of the forearm vasculature.

Objective: The aim of this ultrasonographic study was to assess the morphology and identify potential vascular abnormalities of arteries of the lower arm.

Methods: An ultrasound evaluation of forearm arteries was performed in 110 patients prior to intervention and then vascular anatomy was verified by angiography during the procedure.

Results: The mean age of participants was 59.2±7.9 years. 27% of the study population were females. The population mean for the right radial artery was 2.17±0.54 mm, and for the left radial artery was 2.25±0.43 mm. The measurements revealed sex-related differences in diameters of arteries forearm (p<0.003). Vascular abnormalities of the radial artery were identified in 11 patients (10%) on an ultrasound examination and confirmed in subsequent angiography. 8 patients had a high-bifurcating radial origin, 3 patients anomalous branching of radial artery. Procedural failure was more common in patients with anomalous anatomy than in patients with normal anatomy (18% vs 1%, p=0.001).

Conclusions: Ultrasound imaging is a reliable method of evaluation that enables to determine the size and enables reliable evaluation of abnormalities of the radial artery, especially in the distal forearm.

P4671 | BEDSIDE
Facies of hypertension and renal microcirculation

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Purpose: The present study sought to determine the relationship between renal resistive index (RI) and type of hypertension.

Methods: We studied 275 consecutive, newly diagnosed, never treated hypertensives (51±14 year, 55% male). Diabetic individuals and those with overt cardiovascular or renal disease were excluded. The evaluation of target organ damages (OD) was performed in accordance to the European Society of Hypertension guidelines. Moreover, all patients underwent renal Doppler ultrasound with RI measurement. The mean value of RI from both kidneys was used for the analysis. Based on office and ambulatory blood pressure (BP) levels, the population was split in four groups: masked (17%), isolated systolic (ISH, 15%), isolated diastolic (IDH, 13%) and mixed (systolic-diastolic, SDH, 55%) hypertension.

Results: Patients with SSc were older, predominantly male, with more severe OD, less fit and with the highest RI (Table). Patients with IDH were younger, predominantly female with excellent OD profile, physically active and with the lowest RI. Between these two extreme clinical profiles were patients with masked and SDH, who were middle-aged with intermediate OD profile, moderately active and intermediate RIs. Multinomial logistic regression analysis (reference category IDH) revealed that RI (ISH vs. IDH): OR 1.24 with 95% CI 1.08–1.40 - p<0.001, Masked vs. IDH: OR 1.13 with 95% CI 1.03–1.25 - p<0.008, SDH vs. IDH: OR 0.94 with 95% CI 0.84–1.04 - p=0.263), pulse pressure and heart rate were independent determinants of hypertension type after adjustment for age, gender, abdominal obesity and glomerular filtration rate.

Conclusions: Renal resistive index is closely associated with systolic and diastolic BP and is an independent determinant of hypertension phenotype.
P4672 | BEDSIDE
Correlation between arterial stiffness as measured by progression of carotid ankle vascular index and long term hypertension control status
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Background: Hypertension plays an important role in the development of arterial stiffness and is well known as a vascular risk factor associated with atherosclerosis. Arterial stiffness can be noninvasively measured by various methods including carotid-ankle vascular index (CAVI). This index can reflect the stiffness of the aorta and peripheral vessels eg., femoral artery and tibial artery. We sought to identify the correlation between arterial stiffness as measured by progression of CAVI and long-term hypertension control status.

Methods: Participants with complete CAVI data from Electricity Generating Authority of Thailand (EGAT study in 2007 and 2008) were longitudinally studied. CAVI measurement was performed in 2007–2008 survey with repeated measurement in 2012–2013 survey. Status of hypertension (HTN): awareness, treatment, and control; of participants in 2007, 2008, 2012 and 2013 was extensively reviewed. Correlation between status of hypertension during 5-year period and progression of CAVI were statistically analyzed.

Results: 2,596 participants were eligible for analysis (mean age was 57.7 ± 7.4 year, 23.4% was female). Baseline CAVI in 2007–2008 was 7.94, 8.23, 8.50 in normotensives, controlled, uncontrolled/ unaware HTN, respectively (p for difference <0.001). After adjusted for age, gender, BMI, smoking status, DM status and total cholesterol, participants whose HTN status was not controlled during the year of 2007–2008 and 2012–2013 (“Uncontrolled HTN” group) had the greatest progression in CAVI (CAVI change 0.54/year), followed by that of 0.52/year and 0.49/year in “No HTN to Uncontrolled HTN” group and “Previously-controlled to Uncontrolled HTN” group, respectively.

Conclusion: “Uncontrolled HTN” group has significantly higher percentage of CAVI progression than “Controlled HTN” group. These results imply that well control of blood pressure remains important to slow the progression of arterial stiffness which is reflected by CAVI change.

P4673 | BEDSIDE
Magnetic resonance angiographic follow-up of denervation-induced renal artery dissections
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Background: Renal denervation has been associated with acute vascular trauma, including the development of minor dissections in the treated vessels, identified by intravascular imaging. The long-term consequences and clinical significance of such dissections are unknown.

Purpose: To investigate by magnetic resonance angiography (MRA) the natural history of denervation-induced renal artery dissections detected by optical coherence tomography (OCT) within 6 months after the procedure.

Methods: Thirteen patients, that had undergone MRA of the renal arteries, underwent bilateral renal denervation with 4 different systems: Symplicity™ (n=3), Renal Symplicity® (n=2), AVE™ (n=2), and AVE™ (n=1). An example of minor dissections detected by MRA was further evaluated by OCT. OCT studies were reviewed for dissection. Dissection was defined as new luminal irregularities characterized by a signal void (100%) and was graded by the percentage of the stenosis with OCT compared to MRA.

Results: All patients were included in the study. Mean age was 60.6 ± 9.1 years, n=47). No patients were taking statins or other lipid-lowering therapies at baseline. Mean luminal area: 22.6±6.6 mm² vs. 21.1±6.0 mm², p=0.26; minimal lumen stenosis was 16.4±9.6%, and there was no binary restenosis. There was no statistically significant difference in lumen area (−2.4%, p=0.007) and plaque volume (−3.1%, p=0.007) after 8-month of follow-up in patients that had significantly decreased in the non-elderly patients but not in the elderly patients. A significant positive correlation was observed between age and percentage change in plaque volume (r=0.265, p=0.004). A multivariate regression analysis showed that age was a significant predictor of the percentage change in plaque volume during stent deployment (β=0.223, p=0.02).

Conclusions: Coronary atherosclerosis was more advanced and vascular responses to stent therapy were attenuated in the elderly patients compared to the non-elderly patients.

P4674 | BEDSIDE
Impacts of age on coronary atherosclerosis and vascular response to stent therapy
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Background: Age is a well-established risk factor for cardiovascular disease. In addition to the high likelihood of other cardiovascular risk factors being present in the elderly, aging process itself induces structural and functional changes in the vascular wall. Recent trials using intravascular ultrasound (IVUS) have shown that lipid-lowering therapy with statins halts the progression or induces the regression of coronary artery plaques. However, not all patients show regression of coronary atherosclerosis after stent therapy. We speculate that the residual risk for cardiovascular events after stent therapy can be explained in part by age.

Purpose: To examine the impacts of age on coronary atherosclerosis and vascular response to stent therapy.

Methods: The effects of 8-month stent therapy on coronary atherosclerosis were evaluated using virtual histology intravascular ultrasound from 119 patients who were divided into two groups according to age: elderly patients (≥65 years, n=72) and non-elderly patients (<65 years, n=47). No patients were taking statins or other lipid-lowering therapies at baseline.

Results: At baseline, external elastic membrane (EEM) volume (17.27 ± 14.95 mm³/mm, p=0.02) and plaque volume (9.49 ± 8.11 mm³/mm, p=0.03) in the elderly patients were significantly greater than in the non-elderly patients. The EEM volume (−2.4%, p=0.007) and plaque volume (−3.1%, p=0.007) after 8-month of stent therapy had significantly decreased in the non-elderly patients but not in the elderly patients. A significant positive correlation was observed between age and percentage change in plaque volume (r=0.265, p=0.004). A multivariate re-gression analysis showed that age was a significant predictor of the percentage change in plaque volume during stent therapy (β=0.223, p=0.02).

Conclusions: Impacts of age on coronary atherosclerosis and vascular response to stent therapy are attenuated in the elderly patients compared to the non-elderly patients.
P4676 | BEDSIDE
Is it necessary to use new antiplatelet agents in patients who are treated with a bioreosorbable vascular scaffold?

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Background: During the last months a few cases of late and very late bioreosorbable vascular scaffold thrombosis have been reported. Optimal duration and strategy of dual antiplatelet therapy after BVS implantation remains unclear.

Aim: To know the impact of different strategies of dual antiplatelet therapies (DAT) after BVS implantation at immediate and long term follow up.

Methods: Our study includes a group of 556 patients (p) with 680 coronary lesions treated with BVS. All patients were discharged free of symptoms under dual antiplatelet therapy (100 mg of aspirin, plus one P2Y12 inhibitor, establishing two distributions).

Results: In total 852 patients were included with a median age of 84 years (IQR 78–89%). The median SAME-TT2R2 score was 1 (IQR 0–2). Patients with a higher SAME-TT2R2 score were older and comorbidities were more often present. Mean follow-up was 1.2 years with no difference between groups. The median TTR was 0.95 (IQR 0.80–1.01).

Conclusions: The efficacy and safety of vitamin-K antagonists (VKA) depends on the quality of anticoagulation control which can be measured as the time in therapeutic range (TTR). Recently, the SAME-TT2R2 risk stratification scheme was developed as a tool to assess which patients are likely to have a high or a low TTR. However, this scheme was derived from a relatively young population.

Purpose: To study the association between the SAME-TT2R2 scheme and the risk for bleeding in very elderly.

Methods: In May 2011, patients with atrial fibrillation (AF) from the outpatient anticoagulation clinic aged 80 years or above were asked to participate in a clinical registry. Baseline characteristics of all included patients were derived from medical charts and INR measurements were collected from August 2012. In the Netherlands, the therapeutic INR range is set at 2.0–3.5. Using these boundaries, TTR was calculated using the Rosendaal method. Patients were categorized according to the SAME-TT2R2 score into low risk (0–1 points) or high risk (≥2 points) for stable INR control.

Results: In total 852 patients were included with a median age of 84 years (IQR 82–87). The median SAME-TT2R2 score was 1 (IQR 1–2). Patients with a higher SAME-TT2R2 score were older and comorbidities were more often present. Mean follow-up was 1.2 years with no difference between groups. The median TTR was 0.95 (IQR 0.80–1.01). In the current study, a decrease in same INR levels was associated with negative vessel remodeling and atheroma regression. Regression analysis showed that an increase in serum sRAGE level was an independent predictor of in-hospital death while the use of statins had been shown to increase sRAGE levels. Whether these differences will account for a reduction in case-fatality rate of anticoagulants-associated bleeding in favor of NOACs is still undefined.

P4677 | BEDSIDE
SAME-TT2R2 score and the time in therapeutic range in anticoagulated elderly with atrial fibrillation

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Background: The efficacy and safety of vitamin-K antagonists (VKA) depends on the quality of anticoagulation control which can be measured as the time in therapeutic range (TTR). Recently, the SAME-TT2R2 risk stratification scheme was developed as a tool to assess which patients are likely to have a high or a low TTR. However, this scheme was derived from a relatively young population.

Purpose: To study the association between the SAME-TT2R2 scheme and the time in therapeutic range in elderly AF patients.

Methods: In May 2011, patients with atrial fibrillation (AF) from the outpatient anticoagulation clinic aged 80 years or above were asked to participate in a clinical registry. Baseline characteristics of all included patients were derived from medical charts and INR measurements were collected from August 2012. In the Netherlands, the therapeutic INR range is set at 2.0–3.5. Using these boundaries, TTR was calculated using the Rosendaal method. Patients were categorized according to the SAME-TT2R2 score into low risk (0–1 points) or high risk (≥2 points) for stable INR control.

Results: In total 852 patients were included with a median age of 84 years (IQR 82–87). The median SAME-TT2R2 score was 1 (IQR 1–2). Patients with a higher SAME-TT2R2 score were older and comorbidities were more often present. Mean follow-up was 1.2 years with no difference between groups. The median TTR was 0.95 (IQR 0.80–1.01). In the current study, a decrease in same INR levels was associated with negative vessel remodeling and atheroma regression. Regression analysis showed that an increase in serum sRAGE level was an independent predictor of in-hospital death while the use of statins had been shown to increase sRAGE levels. Whether these differences will account for a reduction in case-fatality rate of anticoagulants-associated bleeding in favor of NOACs is still undefined.

P4678 | SPOTLIGHT
Antiplatelet drug resistance in Asian population

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Background: Stent thrombosis and consequent post PCI complication are being reported from many centres in India. There is very little data on Aspirin and Clopidogrel resistance in Indian population.

Aim: The study is to estimate the Prevalence of Aspirin and Clopidogrel resistance in Indian patients after Percutaneous Coronary Intervention. The study included 30 patients who underwent PCI from January 2013 to October 2013. All these patients were taking aspirin and clopidogrel as a part of dual antiplatelet therapy. We performed the diagnosis of anti platelet resistance using the genotype and phenotypic method. We used the OptiGen kit for genotyping and the VerifyNow assay for phenotyping. The results were as follows:

- Antiplatelet resistance to Aspirin was found in 19 (63.3%) patients using the genotype method and 20 (66.7%) patients using the phenotypic method.
- Antiplatelet resistance to Clopidogrel was found in 23 (76.7%) patients using the genotype method and 18 (60%) patients using the phenotypic method.

Conclusion: The results of this study suggest that antiplatelet resistance is common in Indian patients after PCI.

Abstract P4676 – Table 1. MACE and major bleeding

<table>
<thead>
<tr>
<th>Low risk (0–1 points)</th>
<th>High risk (≥2 points)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=465</td>
<td>N=397</td>
</tr>
<tr>
<td>TTR, median (IQR)</td>
<td>82.3 (72.7–90.0)</td>
</tr>
<tr>
<td>Labile INR (%)</td>
<td>24 (4.9)</td>
</tr>
<tr>
<td>Highly stable INR (%)</td>
<td>59 (12.0)</td>
</tr>
<tr>
<td>TTR, time in therapeutic range; IQR, interquartile range.</td>
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</table>

Conclusions: In this real-world registry of elderly AF patients, a low SAME-TT2R2 score had a statistically significant higher time in therapeutic range. Clinically, however, this score does not allow for discrimination between those with a labile or highly stable INR control, no difference was observed between groups.
Aims: In appropriately selected patients with isolated APW-TCC is a safe, effective & attractive alternative to surgery with encouraging outcomes.

P4682 | BEDSIDE
Comparison of hybrid endovascular and open surgical repair for thoracic aortic disease involving arch

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Objectives: To compare the outcomes of hybrid endovascular (Hybrid) and open surgical repair (OR) for thoracic aortic disease involving arch

Methods: A total 83 consecutive patients (men: 59 patients, mean age: 62±14.6 years) with thoracic aortic disease involving arch who underwent Hybrid (N=50) or OR (N=33) were analyzed.

Results: In the Hybrid, patients were older and more combined with COPD. While increased aneurysm and pseudoaneurysm were more common in the Hybrid, aortic dissection was more common in the OR. In all patients in the Hybrid, supra-aortic vessel transposition and stent-graft implantation were achieved. In the OR, total arch replacement was performed in 30 patients (91.9%), partial arch replacement in 3 patients (9.1%). Perioperative complications affected 15 patients (30.0%) in the Hybrid and 15 patients (45.5%) in the OR. In-hospital death was more common in the OR (27.3% vs. 6.0%, P=0.010). Primary success was achieved in 33 patients (66.0%) in the Hybrid. Five patients died after discharge during follow-up (mean: 73.8±76.7 months) in the Hybrid and three patient died in the OR. In 12 patients, reintervention was necessary in the Hybrid and 2 patient in the OR. Although the reintervention-free survival rate was lower in the Hybrid (p=0.012) the death-free survival rate during follow-up was not different between both groups (p=0.164).

Conclusions: Considering higher risk patients allocated and lower perioperative mortality in the Hybrid group, for thoracic aortic disease involving arch, hybrid endovascular repair may be an alternative option in frail patients in who open procedures is too risky. However, higher reintervention rate of hybrid endovascular repair should be considered for careful selection of treatment modality.

P4681 | BEDSIDE
Outcome of transcatheter closure using the amplatzer devices in largest series of patients with isolated aorto-pulmonary window (APW) defect

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Aims: To assess the outcome of transcatheter closure using the Amplatzer devices, Amplatzer duct occluder I (ADO I) and Amplatzer septal occluder (ASO) in patients with APW defect.

Methods and results: Seven patients, aged 07 months to 11 years (median 01 year) with isolated APW were selected for TCC. All patients were symptomatic for effort intolerance. On examination three patients had continuous to and fro murmur (mean 5.4 mm) at the aortic end as measured by angioigraphy. In all patients, the defect was closed from the venous side, using ADO devices 2–4 mm larger than the defect. The ADO sizes ranged from 8/6 to 10/8 mm (median 10/8 mm). An ASO device was put in one patient. The procedure was successful with no residual shunt in all patients except one who developed severe hemolysis requiring blood transfusion. One patient had significant aortic regurgitation (AR) immediate post procedure which was not related to device, postulated to be due to afterload mismatch & diminished to grade I on subsequently. All the patients were asymptomatic on follow up.
Methods: 45 renal arteries with mean RAS degree of 55.8±6.4% (50–69%) on angiography were evaluated for functional severity in 40 subjects, aged 65.4±8.4y., 26M. Criteria for functionally significant RAS were: MLA > 8.6mm², or either peak RDP > 20mmHg, or dopamine and papaverine HPG > 21mmHg, or RFR > 0.8. Patients with significant RAS were referred to PTA. The improvement of systolic and diastolic BP was assessed with a 24-hour ABPM and the number of blood lowering agents, as well as RF (eGFR) during 12 months following PTA. The improvement of BP was defined as SBP reduction of >15mmHg and/or DBP of >7mmHg, and/or a number of blood lowering agents reduction. RF improvement of smalld (RDP) 36±12.5% by 15% of the initial value.

Results: Mean MLA was 9.7±4.3mm² (range:2.4–20.9), mean reference area was 27.4±8.3mm² (range:15.5–45) and mean stenosis area was 70±12.5% (range:39.5–88.6) on IVUS, while mean dopamine RFRFR was 0.8±0.1 (range:0.66–1.1) on VUS. The symptom improvement during the follow-up (defined as reduction of NYHA Class ≥1 grade) was observed in 62% of cases.

Conclusions: Percutaneous repair of mitral and aortic paravalvular leak represents a viable option in selected patients at high surgical risk, with a reasonable rate of procedural success and a satisfactory clinical outcome.

P4684 | BEDSIDE
Deficiency of endothelial progenitor cells is associated with subacute thrombosis after angioplasty in hemodialysis patients
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Background: Subacute thrombosis after balloon angioplasty is much more frequent in patients than non-uremic patients. The pathophysiology of subacute thrombosis may be related to impaired vessel healing. Circulating endothelial progenitor cells (EPC) play a key role in vascular repair but are deficient in hemodialysis patients. We hypothesized that patients who develop subacute thrombosis may have reduced or dysfunctional EPCs.

Purpose: We aimed to investigate the relation between EPC level and function with the development of subacute thrombosis after angioplasty of venous stenosis in a prospective cohort.

Methods: Patients with venous stenosis of hemodialysis vascular access were prospectively enrolled, after excluding central vein stenoses, failed angioplasty, or recent acute illness. The proportion of peripheral mononuclear cells expressing CD34, KDR, and CD133 markers was evaluated by flow cytometry. Clinical, access, procedural and biochemical data were collected at baseline. Patients were followed prospectively at six month interval.

Results: From Jan 2010 to Jul 2011, 280 patients were prospectively enrolled. The follow-up was extended to Jan 2014 and the median follow-up duration was 36.7 months. Participants were stratified into tertiles according to baseline CD34+, KDR+ cell counts compared to the late thrombosis group (both p < 0.001). The occurrence of subacute thrombosis was significantly associated with tertile status (Low vs. Middle, p<0.001, OR 3.05 CI 1.6–5.8; Middle vs. High, p=0.03). Patients with subacute thrombosis had increased senescence EPCs (65.1±17.7% vs. 37.9±10.3, p<0.001) The incidence of subacute thrombosis after angioplasty was negatively correlated with the CD34+KDR+ cell tertiles. (Low, 29.3±15.6mmHg (range:8–60), dopamine HTG 47.7±29.2mmHg (range:6–105) and papaverine HTG 45.2±18.1mmHg (range:6–100). As a result of this assessment, 32 (71 %) out of 45 lesions in 28 subjects were referred to PTA. During 12 month F-U, clinical improvement was observed in 19 (67.9%) subjects, including RF improvement in 12 (42.8%), BP decrease, or agents reduction in 15 (53.5%). With respect to RF, none of the analyzed parameters occurred as predictor of the improvement. There was an insignificant trend for peak RPG (34 vs 22 mmHg, p=0.12), dopamine HPG (62 vs 30 mmHg, p=0.13), and papaverine HPG (57 vs 44, p=0.20) in the first month.

Conclusions: In 2/3 of subjects with borderline RAS, functional tests showed potentially significant stenosis, however, only half of them showed clinical improvement after PTA. The most promising predictor of BP improvement seems to be resting and hyperemic pressure gradient.

P4685 | BEDSIDE
Impact of age on the long-term clinical outcomes after carotid artery stenting: a single centre registry
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Background: Carotid artery stenting (CAS) is an accepted alternative strategy to carotid endarterectomy primarily in high risk patients (pts). Although the elderly are a growing population with significant comorbidities and surgical risk, CAS remains a controversial procedure due to scarce clinical data.

Purpose: To evaluate the impact of age on clinical outcomes of CAS in a single centre retrospective analysis.

Methods: From October 2006 to August 2014, 279 pts underwent CAS (285 procedures). Age groups (gp) were established based on the distribution of the population: gp 1 (<73 years, n=140, mean age 64.9±6.2) and gp 2 (>73 years, n=139, mean age 77.9±3.3). Embolic protection devices were used in 99.3% of cases. All patients had a 24 hour in-hospital surveillance post procedure. Mean follow-up was 33±20 months (gp 1: 31±19.5, gp 2: 33±20.5) in the first group. Primary endpoint was major adverse cardiovascular events (MACE) which included stroke, acute coronary syndrome (ACS) and cardiovascular death (CVD).

Results: Baseline characteristics were similar in both gps, except for the presence of hypertension (gp 1: 80 vs gp 2: 91%, p=0.02) and severe valvular disease (SVD) (gp 1: 4.3 vs 17.4%, p<0.001, OR 4.7 CI 1.8–11.9). Procedural success was achieved in 100% of the cases in both gps. In gp 2, proximal flow blockage was used in 12.3 vs 15.7% (p=NS), distal protection filter in 87.0 vs 83.6% (p=NS) and an embolic protection device in 99.2 vs 98.8% (p=NS). A greater carotid stenosis was more treated (gp 1: 59.7 vs 47.9%, p=0.04). Univariate analysis showed that ACS at 6 M (gp 2 vs gp 1: OR 3.2 CI 1.1–9.3) was more frequent in the older gp (gp 2). This significance, however, did not persist at 2 years FU. All-cause mortality was similar in both gps. Multivariate logistic regression analysis comprised several variables with prognostic value (prior neurologic symptoms, prior ACS, dyslipidaemia, diabetes, smoking, coronary artery disease, SVD) but the model only included age >73 (Exp(B)=3.25, p<0.028), thereby confirming its powerful independent value to predict the primary endpoint at 1 year FU. Notwithstanding the prognostic value of age in our population, all-cause mortality was similar in both gps.

Conclusions: Our data demonstrate that elderly pts are at higher risk for MACE in the first year post procedure, mostly driven by ACS. Therefore, CAS is safe and feasible in an older population with frequent SVD, as long as the pt selection is appropriate and performed by experienced operators.

P4679 | BEDSIDE
Balloon pulmonary angioplasty as treatment option for patients with unoperable chronic thromboembolic pulmonary hypertension
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Background: The natural course of chronic thromboembolic pulmonary hyper-
tension (CTEPH) is similar to a malignant disease. For operable patients pulmonary endarterectomy (PEA) provides a safe and often curative treatment option. Inoperable patients are usually treated with specific medication, often leading to an insufficient improvement. Dependent on the experience of the centre, the proportion of inoperable patients ranges from 10 to 37%. Balloon pulmonary angioplasty (BPA) is alternative treatment for these patients, but presently there are only limited data available that address the outcome of this procedure.

**Purpose:** This study was designed to determine the success rate of a select group of CTEPH patients undergoing BPA at our centre.

**Methods:** A total of 267 CTEPH patients were discussed regarding the treatment options in an interdisciplinary conference consisting of thoracic surgeons, cardiologists, pulmonary specialists, radiologists, and anaesthesiologists. All patients were characterized by technically operable findings according to several imaging modalities. Clinical history, physical examination, 12-lead ECG, laboratory tests, echocardiography, cardiopulmonary exercise test, 6-minute walk, coronary angiography, right heart catheterization, ventilation and perfusion scintigraphy, CT angiography, and pulmonary angiography were assessed for all patients. Seventy-eight (29.2%) patients were classified as being unsuitable for PEA. Out of these 40 patients were designated for BPA, which was planned as a staged procedure via femoral access.

**Results:** All patients undergoing BPA (mean age 64.7±13.5 years) were in WHO functional class III with depressed right ventricular function (TAPSE 16.4±8.9) and elevated systolic right ventricular pressure (68.2±14.7 mmHg). Almost half (46.2%) of the patients had been previously treated medically for pulmonary hypertension. After BPA the mean pulmonary artery pressure decreased significantly (40.5±12.3 mmHg vs. 29.6±9.2 mmHg, P<0.001). During BPA we observed 3 dissections of a segment artery, which was treated conservatively. Two patients developed reperfusion oedema with the need for non-invasive ventilation. After BPA 85% of the patients showed a better WHO functional class (P<0.01), increased 6-minute walk distance (P<0.01), and better right ventricular function (P<0.01).

**Conclusion:** BPA for well-selected high-risk CTEPH patients is a useful addition to the surgical and interventional procedure spectrum in high-volume centres performing both BPA and PEA. The long-term outcome following BPA needs to be evaluated in further clinical studies.

**Figure 1**

NT-proBNP levels and percent change

to baseline value was significant at 1, 2 and 4 hour after SAA (P value 0.040, 0.042, 0.038, respectively).

**Conclusions:** Our results show decreasing serum NT-proBNP levels after induction of myocardial infarction during septal alcohol ablation. These findings suggest that the observed changes in serum NT-proBNP levels may be related to the decrease of the left ventricular wall stress due to the procedure related reduction of the left ventricular outflow gradient.

**P4689 | BEDSIDE**

Stent implantation jailing deep femoral artery does not worsen clinical outcomes 6 months after endovascular treatment in patients with peripheral artery disease

**Purpose:** This prospective study included 143 patients who had undergone successful endovascular procedures for the superficial femoral artery (SFA) that involved the ostium of the SFA or the common femoral artery (CFA). They were classified in 2 groups whether the ostium of the DFA was jailed after stenting (n=79) or not (n=64). Critical limb ischemia (CLI) status, major adverse limb events (MALE) defined as major amputation, target lesion revascularization, and bypass surgery for the target limb was assessed. Amputation free survival in CLI patients and incidence of target lesion revascularization (TLR) in non-CLI patients at 6 month were also evaluated.

**Results:** There were 24 (30.4%) and 22 (34.4%) CLI patients in the jailed and non-jailed group, respectively (P=0.61). Patient and lesion characteristics were similar in both groups, except the higher incidence of chronic total occlusion of the ostium of the SFA (70.9% vs. 20.3%, p<0.001) in the jailed group. There were no significant differences in the incidence of CLI (7.6% vs. 6.3%, p=0.76) and MALE (11.4% vs. 7.8%, p=0.47) between the 2 groups. Amputation free survival in CLI patients (79.2% vs. 77.3%, p=0.88) and freedom from TLR in non-CLI patients (89.1% vs 90.5%, p=0.82) were similar in both groups.

**Conclusion:** Stent implantation jailing the DFA entry does not worsen clinical outcomes in patients with peripheral artery disease.

**P4690 | BEDSIDE**

Initial experience with the TightRail rotating mechanical dilator sheath for transvenous lead extraction: safety and efficacy

**Objective:** Herein, we aimed to present our initial experience in TLE by using a novel TightRail™ Rotating Mechanical Dilator Sheath.

**Methods:** Between October 2014 and February 2015, a total of 34 leads in 19 patients were removed at our tertiary referral centre. All of the extracted leads were >12 months old and indications for extraction were based on the recommenda-

**Background:** Owing to increasing implantation rates and patients’ longer life expectancy, the need for transvenous lead extraction (TLE) as a specialized procedure has exhibited a significant growth over years.

**Results:** Indications for lead removal included cardiac device infection in 9 (47.4%) cases, lead malfunction in the 9 (47.4%) cases and upgrade to CRT-D in the remaining 1 case (5.3%). The extracted devices were pacemaker in 8 (42.1%) cases, ICD in 6 (31.6%) cases and CRT in the remaining 5 (26.3%) subjects. Among 34 leads, 8 (23.5%) were right ventricular, 11 (32.4%) were atrial, 11 (32.4%) were defibrillator coil and 4 (11.8%) were coronary sinus electrodes. The median implantation time (insertion to extraction) was 72 (24–216) months. Complete procedural success with TightRail™ system alone was achieved in all 19 patients (34 leads, 100%). Clinical success was 100% and all of the patients discharged uneventfully without any complication.

**Conclusions:** Our preliminary data in a small series shows that the mechanical
P4691 | BEDSIDE
Endovascular treatment for subacute deep vein thrombosis
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Background: Deep vein thrombosis is a serious disease that causes complications such as pulmonary embolism and post-thrombotic syndrome (PTS). Generally, although thrombolytic therapy and anticoagulation therapy is performed, treatment for patients with drug is not effective has not been established. Here, we investigated the effect of endovascular treatment for anti-thrombotic therapy resistance of subacute deep vein thrombosis.

Methods: The target is 11 people who resisted the drug treatment have symptoms such as swelling and pain by the proximal portion deep vein thrombosis (4 male, mean 55.5 years). From onset until the endovascular treatment, an average of 16 days had passed. Until endovascular treatment is performed, unfractionated heparin, warfarin, Xa inhibitor, urokinase was administered. Before performing endovascular treatment, IVG filter was placed to prevent pulmonary embolism in all cases. The sheath (6–8 Fr) is inserted into the popliteal vein or contralateral femoral vein and passed through a wire in the blood vessel. We repeated the aspiration of thrombus using a guide catheter 6–8 Fr. After removal of the thrombus, urokinase was administered using a Fountain-infusion catheter, balloon dilation was performed for venous stenosis. After endovascular treatment, we examined the therapeutic effect in the image examination and clinical findings.

Results: Improved blood flow to the inferior vena cava is obtained in all cases, and needed to balloon dilation in 6 cases, stents were not used. Pulmonary embolism after endovascular treatment did not occur. Edema was improved in all patients, but the formation of thrombosis within one week was observed in two cases. Other cases did not develop PTS after more than 6 months.

Conclusions: Endovascular treatment for subacute deep vein thrombosis is an effective therapy for venous patent.

P4692 | SPOTLIGHT
Selective stent placement versus balloon angioplasty for renovascular hypertension caused by Takayasu arteritis: two-year results
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Objective: To investigate the long-term clinical outcomes of selective stenting versus percutaneous balloon angioplasty (PTA) in patients with renal artery stenosis caused by Takayasu arteritis (RASA).

Background: Long-term clinical outcomes of selective stenting in patients with RASTA need to be clarified.

Methods: We retrospectively analyzed the data of 152 consecutive patients with RASTA undergoing endovascular treatment in our hospital between 2005 and 2012.

Results: At two-year follow-up, the proportion of hypertension cure, improvement, and failure was 27.4%, 63.4% and 12.3% in PTA group (n=93), 22.4%, 62.1% and 15.5% in stent group (n=59), respectively, p=0.795. Primary patency rate was 90.1% in renal arteries (125 lesions) treated with PTA, 75.6% in renal arteries (64 lesions) treated with stent, p=0.008. Female, active disease in need of immunosuppressive agents, and medication for fibromuscular hyperplasia are predictors for stent patency. Most of those patients had hypertension and diabetes.

Conclusions: Though, PTA alone and selective stenting had no significant difference in terms of the effect on blood pressure, stenting resulted in inferior 2-year primary patency rate, higher occlusion rate and higher reintervention rate. It should be seriously considered before stenting was undergone in patients with RASTA, particularly in patients with high risk for restenosis.

P4693 | BEDSIDE
Endovascular treatment of aortic coarctation
Sousse, Tunisia

Background: Coarctation of the aorta (CAO) is a congenital cardiovascular malformation of high prevalence, characterized by a narrowing of the thoracic aorta usually just distal to the left subclavian artery. Untreated, it leads to early death predominantly because of hypertension and its cardiovascular sequelae. The traditional treatment is open surgical repair. More recently, endovascular techniques have been developed to avoid open surgical treatment with good results particularly in adults and older children.

Objective: The aim of this study is to report the results of our beginning experience on balloon angioplasty and stenting of native and recurrent CAO.

Methods: Since 2009, a total of 17 patients who underwent transcatheter intervention for COA in our faculty were assigned retrospectively. Procedural Success is defined as peak systolic pressure gradient after balloon therapy or stent implantation <20 mm Hg.

Results: There were 11 males and 6 females. The mean age was 11.47 years (3 months to 39 years old). There were 12 native COA. 9 patients underwent stent implantation and balloon angioplasty was the treatment in 7 cases. Procedural success was achieved in 14 cases (82%). 1 case was complicated with stent migration to the left iliac artery. The peak systolic pressure gradient decreased from 58±20 mmHg to 12±11 mmHg immediately after the procedure. There were no deaths related to the procedure. On follow-up, 3 patients (17%) aged 17, 18 and 24 years old, treated with initial stent implantation underwent balloon angioplasty for recoarctation. The mean time course to restenosis was 7 months. Aneurysm of the left subclavian artery was found in one patient and was treated with the implantation of a covered stent.

Conclusion: Our small and beginning experience in endovascular management of CAO reinforce the impression of an effective and safe therapeutic option, with low rate of complications and less invasive particularly in adults and older children.

P4694 | BEDSIDE
Prognosis and its predictors after endovascular therapy in hemodialysis patients with critical limb ischemia in contemporary practice
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Background: Little is known about the prognosis of hemodialysis (HD) patients with critical limb ischemia (CLI) undergoing endovascular therapy (EVT). The purpose of the present study was to evaluate the prognosis and its predictors after EVT in this high-risk subset.

Methods and results: Mortality and major amputation free survival of 131 consecutive HD patients with CLI undergoing EVT were examined. The mean age was 67±14.9 years old, 77% of them were male, 75% had diabetes, 56% were comorbid with coronary artery disease, 32% had history of coronary intervention and 29% had prior stroke. The results are shown below.

Conclusions: Seventy seven of survival rate and 89% of major amputation free survival rate at 1-year in this high-risk subset was quite acceptable and diabetes was an only independent predictor of all-cause death.

TECHNICAL ASPECTS OF PCI

P4695 | BEDSIDE
Acute coronary syndromes in women undergoing percutaneous coronary intervention with drug-eluting stents: a patient-level pooled analysis of randomized controlled trials
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Background: The safety and efficacy of new-generation drug-eluting stents (DES) versus bare metal stents (BMS) in women presenting with acute coronary syndrome (ACS) is uncertain. Previous trials were not powered to detect differences in women, particularly among those with acute presentations.

Objectives: We evaluated: (i) the prognostic impact of ACS presentation in
women undergoing percutaneous coronary intervention (PCI) with DES, and (ii) the effect of new-generation DES on the risk of major adverse cardiac events (MACE) in women with or without ACS.

Methods: We pooled patient-level data for women enrolled in 26 randomized trials. Study population was categorized according to the clinical presentation: stable angina (SA), unstable angina (UA) or NSTEMI and STEMI. MACE was defined as the composite of death, myocardial infarction, definite or probable stent thrombosis or target lesion revascularization. Outcomes were reported at 3 years of follow-up. Women who received BMS were excluded from this study.

Results: Out of 11,090 women included in the pooled database, 10,133 received a DES. A new-generation DES was used in 6,190 (61.1%). Overall, 5760 (57%) women had a SA, 3594 (35%) had a UA/NSTEMI and 779 (8%) had a STEMI as clinical presentation. Women presenting with STEMI were younger, more commonly had diabetes, and were less likely to smoke or have hyperlipidemia. For pre-specified covariates, adjustment was performed and the results remained significant. Compared to women with a STEMI, women with a SA had a higher risk of MACE (HR: 1.17, 95% CI: 1.00–1.37, p = 0.05) at 5 years, and no differences were observed for STEMI vs. NSTEMI. Women with a UA/NSTEMI had a lower risk of MACE compared to women with STEMI (HR: 0.61, 95% CI: 0.41–0.91, p = 0.02), and this remained significant after adjustment for pre-specified covariates (HR: 0.60, 95% CI: 0.40–0.89, p = 0.01). In post-hoc analysis, the risk of MACE was significantly lower in women with a UA/NSTEMI compared to women with a STEMI at 5 years (HR: 0.58, 95% CI: 0.40–0.85, p = 0.005), but not at 3 years (HR: 0.71, 95% CI: 0.50–1.01, p = 0.055). The risk of MACE was not significantly different between women with a SA and those with a UA/NSTEMI at 5 years (HR: 1.03, 95% CI: 0.85–1.25, p = 0.74). Women with a UA/NSTEMI had a lower risk of MACE compared to women with a STEMI at both 3 years (HR: 0.70, 95% CI: 0.50–0.98, p = 0.04) and 5 years (HR: 0.78, 95% CI: 0.57–1.09, p = 0.10).

Conclusion: Women presenting with UA/NSTEMI had a lower risk of MACE compared to women with STEMI, and this difference remained significant after adjustment for pre-specified covariates. Future studies are needed to confirm these findings in larger and more diverse populations.

Gender differences on short-term outcomes after contemporary percutaneous coronary intervention

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Purpose: We investigated the relationship between sex and the risks of short-term clinical outcomes after PCI in current practice, using data on 13259 acute coronary syndromes (ACS) consecutive patients from January 2010 to January 2015. Patients treated in a conservative manner or with CABG were excluded, leaving a final study population of 7792 patients who underwent PCI (28.7% were women). Cox proportional hazards regression model was adjusted to covariates significantly different between groups in univariate analysis. The primary endpoint was 30-days mortality; the secondary endpoint was the composite of cardiovascular mortality, stent thrombosis, stroke or major bleeding; the tertiary endpoint was left ventricular dysfunction (LVD) defined as an LV ejection fraction <40% at 6 months.

Results: Patients were older (mean age: 65.5 vs. 59.7 years, p < 0.001), had higher rates of diabetes (30.9% vs. 22.0%, p < 0.001), hypertension (77.8% vs. 65.6%, p < 0.001), cerebrovascular disease (4.7% vs. 3.3%, p = 0.003) and higher rates of Killip class ≥ 2 (25.1% vs. 19.6%, p < 0.001), but lower rates of smoking (30.3% vs. 45.3%, p < 0.001) than male patients. Unadjusted mortality was significantly higher in women than men (7.1% vs. 4.4%, p < 0.001), as well as the overall rates of the secondary outcome (10.5% vs. 7.1%, p < 0.001). No differences were observed in the unadjusted rates of the tertiary endpoint (19.1% vs. 21.2%, p = 0.16). After multivariable adjustment, female sex was no longer associated with a higher risk of death (HR: 1.13, 95% CI: 0.87–1.48) and higher risk of secondary endpoint (HR: 1.18, 95% CI: 0.97–1.45). On the contrary female sex was associated with a lower risk of LVD (adjusted HR: 0.73, 95% CI: 0.60–0.89). These sex-specific findings for outcomes were consistent across patient subgroups using bare metal stents (HR: 1.25, 95% CI: 0.88–1.77) or drug-eluting stents (HR: 1.13, 95% CI: 0.78–1.62).

Conclusions: In our cohort, among patients undergoing contemporary PCI, no gender differences were observed in short-term outcomes after drug-eluting stent implantation between women and men. Women undergoing PCI has a lower risk of LVD than men. There was no association between sex and stent type on short-term outcomes.
Objectives: To compare outcomes between old- and new-generation DES in women with underlying chronic kidney disease (CKD), however, remains unclear.

Methods: We pooled patient-level data for women enrolled in 26 randomized trials (n=11,557). Study population was categorized according to the presence or absence of CKD, defined as a creatinine clearance (CrCl) ≤60 ml/min. The primary endpoint was the incidence of major adverse cardiac events (MACE; defined as the composite of death, myocardial infarction (MI), definite or probable stent thrombosis (ST) and target lesion revascularization). Outcomes were reported at 3 years of follow-up.

Results: Out of 4,217 women included in the pooled database for whom estimation of CrCl was possible, 1,414 (33.5%) had CKD. Women with CKD were older, had lower body mass index and a higher prevalence of cardiac and non-cardiac comorbidities. Moreover a higher prevalence of multisessel coronary artery disease and moderate or severe calcifications were present in women with CKD. Following multivariable adjustment for baseline confounders new-generation DES were associated with a significantly lower risk of MACE (adjHR: 0.57; 95% CI: 0.36–0.92; p=0.02), MI (adjHR: 0.50; 95% CI: 0.26–0.95; p=0.03) and death (adjHR: 0.50; 95% CI: 0.27–0.91; p=0.02) in women with CKD. Moreover a trend toward lower risk of ST (adjHR: 0.29; 95% CI: 0.08–1.13; p=0.07) was observed in women with impaired renal function using new-generation DES. The magnitude of benefit was consistent between CKD and non-CKD women, without evidence of interaction (p-int > 0.05).

Conclusion: In women with CKD undergoing PCI, use of newer as compared to older generation DES yields significant and uniform clinical benefits over 3-year period.

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P4700 | BEDSIDE
Impact of successful recanalization of chronic total occlusions using combination stents on long-term clinical outcomes: a meta-analysis

Background: Although coronary stent implantation dramatically reduced the occurrences of restenosis and the needs for repeat revascularization, there is still uncertainty as to the prognostic impact of successful recanalization of chronic total occlusion (CTO) lesions.

Methods: Databases were searched for clinical studies that compared outcomes after successful recanalization of CTO lesions using coronary stent deployment with those of unsuccessful recanalization from January 2003 to October 2014. The end points of this study were mortality; myocardial infarction (MI); major adverse cardiac events (MACE); and the need for coronary artery bypass graft surgery (CABG) at the longest follow-up.

Results: We identified 18 studies encompassing 11,425 patients with a median follow-up period of 12–60 months after successful versus unsuccessful CTO recanalization using coronary stent. There were 396 (4.9%) deaths of 9,037 patients after successful recanalization compared to 329 (10.6%) among 3,111 patients after unsuccessful recanalization (odds ratio [OR] 0.46, 95% confidence interval [CI] 0.37 to 0.58). Successful CTO recanalization significantly reduced the incidence of MI (OR 0.67, 95% CI 0.45 to 0.99) and MACE (OR 0.58, 95% CI 0.43 to 0.77).

The need for subsequent CABG was significantly lower after successful recanalization (OR 0.16, 95% CI 0.12 to 0.21). There was no evidence of publication bias, as evidenced by a symmetrical funnel plot (Figure).

Conclusions: Successful recanalization of CTO lesions using coronary stent deployment appears to be associated with improvement in mortality and reduced needs for CABG as compared with unsuccessful PCI.

P4701 | BEDSIDE
The hybrid toolkit for chronic total occlusions: materials used in the RECHARGE Registry (REGistry of Crossboss and Hybrid procedures in FrAnce, the NetherLands, BelGium and UniteD Kingdom)
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Background and introduction: The hybrid algorithm is designed to improve both procedural success rates and efficiency in revascularizing chronic total occlusions (CTO). Data on 1000 hybrid CTO procedures are collected.

Purpose: To provide the first report on the equipment and various strategies, used within the framework of the hybrid algorithm for CTO recanalization.

Methods: Patients treated for a coronary CTO were prospectively enrolled in 18 centers. CTOs were classified according to the Japanese score. Data were captured on various materials and techniques applied during the procedures.

Results: 482 patients have been included from Jan 2014 to Feb 2015 of which 48, 109, 150 and 175 were classified as easy (0), intermediate (1), difficult (2) and very difficult (3) respectively (Table). An average of 1.38±0.64 strategies were used per CTO. Frequently used dual injection resulted in an average of 1.99±1.00 guiding catheters. As CTO complexity rises, the average number of guidewires, balloons, stents and microcatheters increases. Likewise, the use of the CrossBoss and Stingray systems (for antegrade dissection & re-entry) and additional devices also rises.

Table 1. Average number of materials used

<table>
<thead>
<tr>
<th>J-CTO score</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td># of patients</td>
<td>48 (100%)</td>
<td>109 (96%)</td>
<td>150 (87%)</td>
<td>175 (78%)</td>
<td>482 (87%)</td>
</tr>
<tr>
<td># of techniques</td>
<td>1.08±0.28</td>
<td>1.22±0.53</td>
<td>1.31±0.59</td>
<td>1.62±0.74</td>
<td>1.38±0.64</td>
</tr>
<tr>
<td>Guiding catheter</td>
<td>1.68±0.74</td>
<td>1.89±1.00</td>
<td>1.97±1.00</td>
<td>2.20±1.04</td>
<td>1.99±1.00</td>
</tr>
<tr>
<td>Guidewires</td>
<td>2.83±2.25</td>
<td>3.58±3.29</td>
<td>5.04±4.22</td>
<td>6.62±4.10</td>
<td>5.01±4.04</td>
</tr>
<tr>
<td>Balloons</td>
<td>2.33±1.40</td>
<td>2.77±2.12</td>
<td>3.02±2.56</td>
<td>3.83±3.26</td>
<td>3.19±2.71</td>
</tr>
<tr>
<td>Stents</td>
<td>1.60±0.71</td>
<td>1.93±0.90</td>
<td>2.33±1.12</td>
<td>2.73±1.62</td>
<td>2.25±1.01</td>
</tr>
<tr>
<td>Microcatheters</td>
<td>0.85±0.62</td>
<td>0.91±0.57</td>
<td>1.16±0.60</td>
<td>1.25±0.58</td>
<td>1.10±0.61</td>
</tr>
<tr>
<td>CrossBoss catheter</td>
<td>1.16</td>
<td>22</td>
<td>45</td>
<td>84</td>
<td>89</td>
</tr>
<tr>
<td>Stingray system*</td>
<td>1</td>
<td>14</td>
<td>24</td>
<td>94</td>
<td>99</td>
</tr>
<tr>
<td>Additional devices1</td>
<td>0.10±0.31</td>
<td>0.19±0.52</td>
<td>0.21±0.44</td>
<td>0.38±0.58</td>
<td>0.26±0.50</td>
</tr>
</tbody>
</table>

Values are given as n, n (% success) or mean ± SD. *Stingray system consists of Stingray balloon and Stingray needle. Additional devices are the Rotablator, Guideliner and/or Torus system.

Conclusions: Treatment of complex (J-CTO 2) and very complex CTO (J-CTO ≥3) lesions, results in an average use of more than 5 wires, 3 balloons, 2 stents and need of additional materials. This requires specific reimbursement policies.

P4702 | BEDSIDE
Adjunctive balloon post-dilatation in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention
P.S. Song1, J.Y. Hahn2, E.K. Kim1, Y.B. Song2, S.H. Choi3, J.H. Choi2, H.C. Gwon3 on behalf of the Effects of Postconditioning on Myocardial Reperfusion in Patients with ST-segment Elevation Myocardial Infarction (POST) trial.
1 Haeundae Paik Hospital, Inje University College of Medicine, Busan, Republic of Korea; 2 Samsung Medical Center, Cardiovascular Center, Seoul, Korea, Republic of Korea

Background: Adjunctive balloon post-dilatation has been shown to improve both post-procedural stent dimensions and stent apposition, but the relation to outcomes is not clarified. Furthermore, there have been some concerns regarding the risks of this practice, particularly in the setting of acute myocardial infarction (AMI).

Purpose: Our aim was to evaluate how adjunctive balloon post-dilatation influences procedural and 1-year clinical outcomes following primary percutaneous coronary intervention (PCI) in patients with ST-segment elevation myocardial infarction (STEMI).

Methods: Outcomes were assessed in 679 patients undergoing stent implantation for STEMI in the Effects of Postconditioning on Myocardial Reperfusion in Percutaneous Coronary Intervention with ST-segment Elevation Myocardial Infarction (POST) trial. We used multivariate logistic regression and Cox proportional hazard modeling to estimate risk of outcomes with vs. without adjunctive balloon post-dilatation. The procedural outcomes included the rate of no-reflow after adjunctive balloon post-
dilatation. Thrombolysis in Myocardial Infarction (TIMI) flow after PCI, myocardial blush grade (MBG), the rate of complete ST-segment resolution on ECG obtained 30 minutes after the procedure. Clinical outcomes were major adverse cardiac events (MACEs: a composite of death, MI, and target vessel revascularity) at 1-year.

Results: Adjunctive balloon post-dilatation was associated with a higher no-reflow (adjusted risk ratios of 3.66, 95% confidential interval [CI] 1.36–9.81, p=0.01), but TIMI 3 flow, MBG 0 or 1, and complete ST-segment resolution after PCI did not differ between procedures with or without adjunctive balloon post-dilatation. A treatment effect analysis revealed no significant differences were observed in the incidence of MACEs between groups (22/197 patients [6.5%] in the adjunctive balloon post-dilatation group and 19/482 patients [5.6%] in the control group, adjusted hazard ratio 1.15; 95% CI 0.49–2.71; p=0.78). The rates of occurrences for individual components of MACEs, stent thrombosis, and heart failure were also similar between groups.

Conclusions: In this post hoc analysis, the risk of no-reflow appeared to be higher with adjunctive balloon post-dilatation. Contrary to our expectation, adjunctive balloon post-dilatation did not improve procedural and clinical outcomes in patients with STEMI undergoing primary PCI with current standard practice. Based on our findings, it is better operators to use this adjunct in primary PCIs of confined lesions in the contemporary era of AMI.

P4705 | BEDSIDE
Multivessel disease diagnosed at the time of primary PCI for STEMI: complete revascularization versus conservative strategy
O. Hilnomaz1, L. Groch2, L. Polokova1, F. Lehar1, T. Vekov2, M. Griva3, J. Sitar1, M. Rezek1, B. Gersh4, P. Widimsky5 on behalf of Prague-13 investigators.

Methods: 590 patients presenting for PPIC from Jan 2012 to Dec 2013 were identified from the prospective database of our high-volume tertiary centre. Of these, 168 were excluded from analysis because they had presented >12 hours after the onset of major pain, required intubation or cardiopulmonary resuscitation before arrival at the hospital, had had previous CABG or did not actually receive PPCI. Logistic regression was used to examine the relationship between bSS, rSS and the primary end-point of 12-month mortality.

Results: Of the 422 patients (mean age 59) analysed, 81% were male and 18% had known diabetes. At 12 months, the mortality rate was 5.45% (23/422). Logistic regression analysis showed an odds ratio (OR) for mortality of 1.05 (95% CI: 1.02–1.10; P=0.007) for bSS and 1.06 (95% CI: 1.02–1.11; P=0.009) for rSS.

Conclusion: Both baseline SS and residual SS at primary PCI can predict mortality at 12 months. The higher the bSS or rSS, the worse the prognosis. After PCI, unperformed and the use is examined as a simple practical additional factor to help decide whether and when more intervention on the non-IRA is desirable.

P4707 | BEDSIDE
Beneficial effects of an old drug - intracoronary verapamil improves left ventricular function in acute anterior STEMI
L. Pascualau, V. Turi, M. Badalica-Petrescu, M. Valcovici, R. Christodorescu, S.R. Dragan. University of Medicine Victor Babes, Cardiology, Timisoara, Romania

Objective: Coronary microvascular dysfunction is frequently observed in patients presenting STEMI, leading to failure of the collateral circulation. Intracor- onary adenosine is recommended by guidelines for improvement of myocardial repufersion. However, side effects including bradycardia and hypotension are fre- quent, limiting its use. We evaluated the effects of intracoronary administration of verapamil on left ventricular function in patients with acute anterior STEMI after PCI. Logistic regression with stepwise method was used to examine the relationship between baseline and follow up LV function and all-cause mortality.

Methods: This prospective study included 98 consecutive patients diagnosed with acute anterior STEMI, randomized into two groups: CON-control (n=47) and VER-verapamil (n=51). In the VER group, 250–500 mcg verapamil di- luted to 1 ml improves 0.2 mEq NaCl solution were injected into the infarct-related artery immediately after stenting, while 2 ml NaCl were injected in the CON group. Left ventricular function was assessed by echocardiographic parameters (EDV, ESV, EDD, EF) at admission, at 6 weeks and after 1 year. Wall motion of the LV was assessed in segments 7, 8, 13, 14, 15, 16 and 17, according to the AHA Con- sensus. Statistical analysis was performed using Mann-Whitney and X2 tests for nominal variables.

Results: The groups were homogeneous regarding age, gender, heart rate, SBP, DBP, left ventricular volumes, and the rate of acute complications (p>0.05 for all). The most significant between-group differences were in the decreases in peak and mean EF and slope of ESPVR (all p<0.05).

Conclusions: This study demonstrated the beneficial effects of intracoronary verapamil can improve left ventricular function in patients with acute anterior STEMI after PCI.
P4707 | BEDSIDE
Natural history of stent malapposition in patients treated by primary percutaneous coronary intervention: Subanalysis of ROBUST trial
M. Jašká1, P. Červinka2, P. Kanovský3, A. Kupčík2, J. Vaněk4, K. Tanaka5, S. Nishino5, A. Schnell5, H.G. Bezerra1, 1University of Defense, Faculty of Military Health Sciences, Hradec Králové, Czech Republic; 2Masaryk Hospital, Department of Cardiology, Usti nad Labem, Czech Republic; 3University Hospital Brno, Cardio-Vascular Department, Brno, Czech Republic; 4Faculty of Informatics and Management of the University of Hradec Králové, Department of Informatics and Quantitative Methods, Hradec Králové, Czech Republic; 5University Hospital Case Medical Center, Cardiology, The Harrington Heart and Vascular Institute, Cleveland, United States of America

Background: Stent malapposition is anticipated to be unfavorable for long-term outcomes, but data from patients treated by primary percutaneous coronary intervention (PCI) are rare.

Purpose: To evaluate association of baseline stent malapposition to minimal lumen area, area stenosis, and percent of uncovered struts in 9-months follow-up.

Methods: 105 patients with acute STEMI treated with primary PCI and coronary intervention underwent OCT. Stent diameter was determined by two operators on short-term, probably by reducing microvascular dysfunction and consequently increasing myocardial blood flow in patients with acute anterior STEMI. Also, we emphasize that intracoronary administration of verapamil prevents left ventricular remodeling, which could explain the better long-term outcomes in these patients.

Conclusions: Intracoronary administration of verapamil after primary PCI improves left ventricular function on short-term, probably by reducing microvascular dysfunction and consequently increasing myocardial blood flow in patients with acute anterior STEMI. Also, we emphasize that intracoronary administration of verapamil prevents left ventricular remodeling, which could explain the better long-term outcomes in these patients.

Abstract P4707 – Result table

<table>
<thead>
<tr>
<th>Percent of malapposed struts in baseline</th>
<th>Area stenosis; %</th>
<th>Uncovered struts; %</th>
<th>Minimum lumen area; %</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–1%</td>
<td>5.4 (11.9–17.4)</td>
<td>6.9 (4.1–13.3)</td>
<td>6.5 (5.3–8.5)</td>
</tr>
<tr>
<td>1–2%</td>
<td>3.9 (2.7–15.6)</td>
<td>8.2 (5.7–8.7)</td>
<td>6.5 (6.2–7.3)</td>
</tr>
<tr>
<td>2–3%</td>
<td>9.4 (8.8–29.9)</td>
<td>16.4 (14.5–37.5)</td>
<td>6.7 (5.7–7.1)</td>
</tr>
<tr>
<td>≥3%</td>
<td>28.7 (22.5–43.5)</td>
<td>20.0 (5.8–30.2)</td>
<td>5.4 (3.6–6.2)</td>
</tr>
</tbody>
</table>

P4709 | BEDSIDE
Effect of guidewire passage and mechanical thrombus aspiration on ST segment displacement in primary percutaneous coronary intervention for STEMI
P. Russhard1, F. Al-Janabi1, M. Parker2, G.J. Clesham1, 1Basildon and Thurrock University Hospitals NHS Foundation Trust, Essex Cardiothoracic Centre, Basildon, United Kingdom; 2Anglia Ruskin University, Postgraduate Medical Institute, Chelmsford, United Kingdom

Background and purpose: We studied the effect of guidewire passage and thrombus aspiration on ST segment resolution in patients treated by primary percutaneous coronary intervention (PCI) for acute STEMI. 417 patients presenting to a large cardiothoracic centre were studied.

Methods: A Witt biomedical ECG system was used for all ECGs. A 12 lead trace was recorded in the angiography laboratory at the start of the case and further ECGs were recorded after a guidewire had been passed down the occluded coronary artery, after mechanical thrombus aspiration and at the end of the case whilst the patient was still on the cath lab table. ST segment deviation was evaluated in each lead with maximum elevation, measured 75 msec after the J point. ECGs with left bundle branch block were excluded. A proportion of the ECGs were independently assessed by a second individual to evaluate reproducibility and good concordance was found. A repeated analysis of variance was used to compare the absolute ST segment elevation means at different stages.

Results: The mean ST segment elevation at the beginning of the case was 5.1mm and this fell to 4.2mm after guidewire passage (p<0.001). When thrombus aspiration was performed the mean ST segment elevation was 4.1mm (not significantly different from guidewire passage). Mean ST segment elevation at the end of the case was 3.4mm.

The proportion of patient who achieved more than 50% resolution of the original ST segment elevation was 15.7% cases after guidewire passage, 23.6% after thrombus aspiration and 43.0% at the end of the case. Adverse ST segment changes (decreased ≥3% after the device time) to assess PPCI services. Thrombus aspiration appears to exert a mixed effect on ST resolution in STEMI in that more patients achieve more than 50% resolution compared to guidewire passage alone, however, more patients exhibit a worsening of ST segment displacement with thrombus aspiration. These data are consistent with the uncertain role of routine thrombus aspiration in PPCI for STEMI.
P4710 | BEDSIDE Safety and effectiveness of deferring definitive treatment of the culprit lesion in STElevation myocardial infarction

C. Granda Nistal1, B. Rubio Alonso1, A. Jurado Roman2, J. Garcia Tejada3, S. Mayordomo Gomez1, A. Miguel Gutierrez3, E.P. Garcia Martin3, M.T. Velazquez Martin3, F. Hernandez Hernandez2, A. Albaranz Gonzalez-Trueba1,2,3,4,5.

Background: In selected patients (p) with ST segment elevation myocardial infarction (STEMI), deferring definitive treatment of the culprit lesion after achieving reperfusion might be a better option. There is lack of strong evidence about the safety and the effectiveness of this strategy.

Methods: Retrospective study was performed comparing STEMI p with deferred definitive treatment after reperfusion (Group,Gr A) versus STEMI p with immediate stenting (Gr B) during primary percutaneous coronary intervention (PPCI). We compare baseline characteristics, peak CK, and incidence of ischemic (MACE, death, MI, new target vessel revascularization) and major bleeding (BARC=3 criteria).

Results: Patients of Gr A were younger than Gr B, with no other difference in baseline characteristics. A high residual thrombus burden was associated to the decision of deferring definitive treatment of the culprit lesion in 74%. Severe coronary calcification was the reason in 17%. Intensive pharmacologic anti-thrombotic treatment was administered during 8±3 days. The delayed coronary angiogram showed TIMI flow grade in 95% of the p. There was a significant reduction in thrombus burden between the baseline angiography and the delayed one (TIMI thrombus grade change=0.90±0.47, p<0.01). 52% of p in Gr A did not show significant residual lesion. A delayed stent implantation was needed in 48% of Gr A and 16.5% in Gr B (p=0.05).

Conclusions: In selected STEMI patients who underwent a PPCI, the deferred treatment of the culprit lesion showed similar results in effectiveness (ischemic MACE and safety and bleeding) comparing with immediate stenting, with a trend of reduction in infarct size measured by CK.

P4711 | BEDSIDE In-hospital, thirty-day and six-month result of biodegradable polymer coated sirolimus-eluting stent in coronary artery lesions (i-TRIAL study)

R.S. Polavarapu1, J. Prajapati2, A. Raheem3, K. Thakkar4, V. Pamidimukkala1, M.T. Velazquez Martin1, F. Hernandez Hernandez1, A. Albarran Gonzalez-Jaume10 on behalf of ESTROFA group.

Background and introduction: The i-TRIAL study was a multi-centre, retrospective, non-randomized, single-arm study, which enrolled 1008 consecutive patients treated with Indolimus, between April 2012 and June 2014. The only exclusion criteria was patients with high-risk characteristics and complex lesions.

Methods: The i-TRIAL study was a multi-centre, retrospective, non-randomized, single-arm study, which enrolled 1008 consecutive patients treated with Indolimus, between April 2012 and June 2014. The only exclusion criteria was patients with high-risk characteristics and complex lesions.

Results: All patients had completed one year follow-up. Outcomes at 12 months were: composite of cardiac death, myocardial infarction, target-lesion revascularization and stent thrombosis 16.5% with aspiration vs. 10.1% without aspiration (p<0.01), TLR 3.9% vs. 1.8% (p<0.01) and definite or probable stent thrombosis 3.6% vs. 1.1% (p<0.01).

Conclusions: In this registry half of patients over 75 years underwent thrombus aspiration during primary angioplasty. A propensity score matching analysis of the use of thrombus aspiration was associated to a significant improvement in clinical outcomes at 12 months.

P4712 | BEDSIDE Real-world experience with ultra-thin biodegradable polymer coated sirolimus-eluting coronary stent: Six-month clinical outcomes of FLEX-Registry

A. Abhyankar1, P. Chandwani2, S. Saxena3, P. Kumar4, P. Verma5, M.S. Sandhu6, N. Park7, A. Bhupal8, S. Jain9, J. Prapapati10, Shree B.D. Mehta Mahavir Heart Institute, Department of Cardiology, Surat, Gujarat, India; 2Heart & General Hospital, Department of Cardiology, Jaipur, Rajasthan, India; 3Max Superspeciality Hospital, Department of Cardiology, Mohali, Punjab, India; 4Kasturba Medical College & Hospital, Department of Cardiology, Manipal, Karnataka, India; 5Prime Heart & Vascular Institute, Department of Cardiology, Mohali, Punjab, India; 6Artemis Hospital, Department of Cardiology, Gurgaon, Haryana, India; 7S. K. Soni Hospital, Department of Cardiology, Jaipur, Rajasthan, India; 8Apple Hospitals and Research Institute, Department of Cardiology, Kolkata, West Bengal, India; 9Hospital General de Ciudad Real, Ciudad Real, Spain; 10University Hospital Gregorio Maranon, Madrid, Spain.

Background and introduction: FLEX-Registry is a prospective multicenter registry, sought to examine safety and efficacy of ultra-thin biodegradable polymer coated sirolimus-eluting Supraflex (Sahajanand Medical Technologies Pvt. Ltd, India) coronary stent for the treatment of coronary artery disease across a wide range of unselected patients treated in routine clinical practice, including those with high-risk characteristics and complex lesions.

Methods: FLEX-Registry is a retrospective, non-randomized, single-arm and multicentre registry. A total of 995 consecutive patients who received 1,399 Supraflex stents for the treatment of 1,184 lesions between periods of July 2013 to May 2014 at 9 different tertiary care centres were enrolled. The patients were followed-up at 6 months after the index procedure by telephone contact or clinical visit. The primary end-point of the study was major adverse cardiac event, a composite of cardiac death, myocardial infarction, target-lesion revascularization and target-vessel revascularization at 6-month clinical follow-up.

Results: FLEX-Registry included high risk patients, among whom 441 (44.3%) were hypertensive and 231 (23.2%) were diabetics. Average number of stents cumulative incidence of cardiac death, MI and TLR at 6-month was 75 patients. There were 2 (0.20%) cases of MI at 6-month follow-up.

Conclusions: The use of Indolimus is associated with lower incidence of TLR, ST and consequent MACE. Thus, the i-TRIAL study gives an idea about favor-
P4714 | BEDSIDE
Safety and efficacy of angio-seal vs exo-seal in patients undergoing primary percutaneous coronary intervention for ST-elevation myocardial infarction

N. Pinilla Echeverri1, I. Sanchez Perez2, A. Jurado Roman3, M.T. Lopez Lluna4, J. Benitez Peyrat5, M. Marina Breyss6, J. Piqueras Flores7, A. Moreno Acosta8, E. Guevara Sanchis9, F. Lozano Poveda10, 1McMaster University Department of Medicine, Cardiology Division, Interventional Cardiology Service, Hamilton, Canada; 2Hospital General de Ciudad Real, Ciudad Real, Spain; 3University Hospital Infanta Leonor, Madrid, Spain

Background: Patients undergoing primary percutaneous coronary intervention (PCI) for ST-elevation myocardial infarction (STEMI) are at high risk of femoral vascular complications (VC). In spite of the growing use of the radial approach, femoral remains the most common in primary PCI. The use of femoral vascular closure devices (VCDs) has expanded in recent years despite the controversial in previous trials. The objective is to evaluate safety and efficacy, and to compare these VCDs in primary PCI.

Methods: A total of 827 consecutive patients undergoing primary PCI for STEMI via femoral were studied for in-hospital and 6 months out-patient outcomes through a registry from January 2010 to October 2013. The primary end point was the presence of VC defined as a composited of hematoma≥6 cm, recurrent bleeding, pseudoaneurysm, arteriovenous fistula, arterial thrombosis or retroperitoneal bleeding.

Results: 404 (48.8%) patients received Angio-Seal® and 423 (51.2%) Exo-Seal®. 39 (4.7%) patients had a VC, with a similar incidence of events between the 2 VCDs: 40.5% in Angio-Seal® and 21% in Exo-Seal® (p=0.7). The risk of VC was significantly associated with body mass index (BMI) OR 2.1 (95% CI 0.77–0.86, p=0.01), sheath size OR 1.2 (95% CI 0.12–0.84, p=0.04), presence of chronic kidney disease (CKD) OR 1.5 (95% CI 1.1–1.7, p=0.005) and peripheral arterial disease (PAD) OR 3.2 (95% CI 1.78–3.1, p=0.03). There was just a trend to present hematoma (6.6% vs. 3.5%; p=0.4) and arteriovenous fistula (3.3% vs. 1.7%; p=0.5) in Exo-Seal®; pseudoaneurysm (5.2% vs. 1.1%; p=0.3) and recurrent bleeding (2.2% vs 0%; p=0.5) in Angio-Seal®.

Risk factors associated with vascular complications

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI &gt; 30 kg/m²</td>
<td>2.1</td>
<td>0.77–0.86</td>
<td>0.01</td>
</tr>
<tr>
<td>Sheath size &gt; 18F</td>
<td>1.2</td>
<td>0.12–0.84</td>
<td>0.04</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>1.5</td>
<td>1.1–1.7</td>
<td>0.005</td>
</tr>
<tr>
<td>Peripheral arterial disease</td>
<td>3.2</td>
<td>1.78–3.1</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Conclusions: VC after femoral approach in patients undergoing primary PCI for STEMI rises in a high incidence despite the routine use of VCDs in our hospital. These VC were significantly associated with individual characteristics (BMI, CKD, PAD) and procedure-related (sheath size). The safety and efficacy of both VCDs is similar after primary PCI in patients with STEMI.

P4715 | BEDSIDE
ST-elevation myocardial infarction and multivessel disease: predictors of non-culprit lesion revascularization


Introduction: In patients with multivessel disease (MVD) undergoing primary percutaneous intervention (PCI), revascularization of the non-culprit lesions within the first month is associated with a significant improvement in clinical outcome. Yet, it is not clear how to select non-culprit lesions and what is the right timing of revascularization.

Purpose: We investigated in our daily clinical practice the predictors of non-culprit lesion revascularization (percutaneous or surgical [CABG]) within 30 days from the primary PCI.

Methods: All consecutive patients undergoing primary PCI (pPCI) from 2012 to 2014 at our cath lab were included. Multivessel disease was defined as the presence of >50% stenosis in at least one non-culprit vessel. Study endpoint was any revascularization performed in the non-culprit lesion within 30 days from pPCI. Patients receiving a stent between clinical, angiographic and procedural factors with the study endpoint were explored with logistic regression analysis. Relationship between the study endpoint and clinical outcome was analyzed by Cox-regression analysis.

Results: We enrolled 299 patients of whom 192 (64%) presenting with MVD. Revascularization of the non-culprit lesion was performed within 30 days in 71 patients (68 with PCI, 3 with CABG) and 97 lesions: 1 LM (1%), 30 (30%) LAD, 35 LCX (36%), 31 RCA (32%) (p<0.01). Most of the non-culprit lesion revascularizations (79%) occurred within the first 3 days from the pPCI. Dyslipidemia (p=0.01), % diameter stenosis of non-culprit vessels (p=0.01), MVD (p<0.01), and rate of 2-vessel disease with LAD involved (p<0.01) or 3-vessel disease (p<0.01) were significantly associated to the study endpoint at the univariate analysis. No association was found with left ventricular ejection fraction or diastolic volume. At the multivariate analysis, a significant association was observed only with the % diameter stenosis of the non-culprit lesion (OR 1.05, 95% CI 1.03–1.07). A mean follow-up of 16 months was obtained in 108 (36%) patients. At the Cox-regression, revascularization of the non-culprit lesion within 30 days was not associated with the composite endpoint of death and MI (HR 0.9, 95% CI 0.21–3.75; p=0.88).

Conclusion: Revascularization of non-culprit lesion occurred within 30 days from pPCI and it was mostly guided by the angiographic stenosis severity. Furthermore, patients undergoing revascularization of non-culprit lesions within 30 days from the acute event did not show higher risk of death and MI.

P4716 | BEDSIDE
The impact of operator fatigue and sleep deprivation on primary percutaneous intervention procedure technique and outcomes

A. Arabi1, J. Alsuwaidi1, A. Gehani1, A. Alqahani1, S. Arafa1, A. Alnabi2, I. Rafie1, O. Alameemi 1, M. Yacoub2, 1Hamad Medical Corporation Heart Hospital, Doha, Qatar; 2Qatar Cardiovascular Research Center, Doha, Qatar

Background: Studies have demonstrated that operator fatigue and sleep deprivation may impact the procedural performance and outcomes, but little information is available about this subject in Primary Percutaneous Intervention (PCI).

Methods: We compared the PCI procedural strategy and clinical outcomes between patients who present during night time (11:00 PM to 7:00 AM) vs. those who present during day time (7:00 AM to 11:00 PM) in high volume center using the PCI data registry.

Results: 721 patients underwent PCI at our Heart Hospital between October 1, 2013 and September 15 2014. Among those 216 (29%) cases were performed during night time and 505 (71%) during day time. There was no significant difference in age, gender, type of STEMI and TIMI flow prior to the procedure. We did not observe significant difference in the PCI procedure technique (use of aspiration thrombectomy, pre dilatation, post dilatation or use of IVUS) or procedure outcomes (success rate, referral to CABG or mortality rate) between cases performed during day time vs. night time.

Comparison of PCI procedure technique or outcomes

Conclusion: Operator fatigue and sleep deprivation does not seem to have significant impact on the PCI procedure technique or outcomes.

P4717 | BEDSIDE
Clinical outcomes of successful percutaneous coronary intervention for chronic total occlusion treated with sirolimus-eluting stent: results from the multicenter CTO registry

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Background and introduction: Survival benefits have been reported after successful percutaneous coronary intervention (PCI) in patients with chronic total occlusion (CTO). The development of bioabsorbable polymer on drug-eluting stents (DES) geared up interest in CTO-PCI. We aim to analyze the immediate, short and mid-term clinical outcomes of patients, with CTO treated with the Indolimus bioabsorbable polymer coated sirolimus-eluting stent (SES), from day-to-day clinical practice.

Methods: We analyzed immediate (in-hospital), short (30-day) and mid-term (6-month) clinical outcomes in 170 patients, who underwent successful recanalization of CTO (defined as >3 months’ duration) and received Indolimus SES, at four tertiary care centres in India between April-2012 and June-2014. During 6-month, main clinical outcome parameter was target lesion failure (TLF), a composite of cardiac death, myocardial infarction (MI), or target lesion revascularization (TLR). We also analyzed stent thrombosis (ST) as a safety endpoint during 6-month of follow-up.

Results: The mean age was 50.7±10.2 years and 142 (83.5%) of patients were men, 29.4% (n=50) and 25.9% (n=44) of patients had arterial hypertension and diabetes, respectively. Of the lesions treated (n=170), 166 (97.6%) were classified as American College of Cardiology/American Heart Association type C. The left anterior descending artery was the target vessel in 76 (44.7%) cases. The target stent length and diameter were 30.8±2.4 mm and 3.1±0.4 mm, respectively. The mean number of stents implanted per patient was 1.1±0.4. The in-hospital and 30-day, TLF rate were 0.6% (1/170) and 0.6% (1/170), respectively. A total of 169 (99.4%) patients followed at the end of 6-month, 1 patient...
suffered a cardiac death (0.6%), 2 had MI (1.2%), and 1 underwent TLR (0.6%) and overall TLF rate was 2.4% (4/168). No stent thrombosis occurred during 6-month of follow-up.

Conclusions: In day-to-day clinical practice, treatment of CTO with Indolimus SES showed favourable immediate, short and mid-term clinical outcomes.

P4718 | BEDSIDE Clinical outcomes of first and second generation drug-eluting stent implantation for unprotected left main coronary artery bifurcation M. Tsutsumi, T. Muramatsu, Y. Ito, K. Hirao, M. Yamawaki, M. Araki, N. Kobayashi, H. Takimura, S. Mori, Y. Sakamoto, Saiiseikai Yokohama City Eastern Hospital, Department of Cardiology, Yokohama, Japan

Aims: To investigate the outcomes of first and second generation drug-eluting stent (DES) implantation for unprotected left main coronary artery (ULMCA) bifurcation lesions.

Methods and results: This is a single center, retrospective study. Between April 2007 and March 2013, a total of 1075 percutaneous coronary intervention were performed in our hospital. Among these, we performed elective DES implantation for 241 stable angina patients with ULMCA bifurcation lesions. 86 Sirolimus-eluting stents and 32 Paclitaxel-eluting stents were implanted. (118 patients in first generation group) 4 Zotarolimus-eluting stents, 82 Everolimus-eluting stents and 37 Biolimus A9-eluting stents were implanted. (123 patients in second generation group) We evaluated their backgrounds and clinical outcomes. The end points were the occurrence of major adverse cardiac events (MACE) and target lesion revascularization (TLR). First and second generation groups were followed up for 1389±532 days and 583±381 days. Backgrounds are similar in both groups. Kaplan-Meier survival curves showed that freedom from MACE at 1 and 3 years was 97% and 96% in second generation group compared with 95% and 91% in first generation group (p=0.24). Freedom from TLR at 1 and 3 years was 95% and 92% in second generation group compared with 93% and 88% in first generation group (p=0.54).

Conclusion: Second generation DES offers no statistically significant advantage over first generation DES in long-term outcome after ULMCA bifurcation stenting.


Background: Quantitative coronary angiography (QCA) is not used in routine clinical practice and stent size is chosen by visual reference. New radiological equipments of percutaneous coronary intervention (PCI) allow to create a customizable screen design in different sizes.

Purpose: To determine the influence of screen size in the number, diameter and length of implanted stents, the need of post-dilatation and the presence of intimal dissection.

Methods: 334 consecutive patients who underwent coronary intervention (449 lesions) were randomized into two groups. 162 patients group S (small) with 180 lesions and 172 patients group L (large) with 273 lesions. Those lesions not measurable with QCA, like chronic total occlusions or ostial lesions, were not included. In-stent restenosis and patients with clinical or hemodynamical lesions not measurable with QCA, like chronic total occlusions or ostial lesions, were randomized into two groups. 162 patients group S (small) with 180 lesions and 172 patients group L (large) with 273 lesions were included.

Results: Baseline characteristics and procedural variables were comparable in the two groups. S (n=220) and L (n=229): mean age (66.6±12.6 vs. 67.2±11.2; p=ns), gender (male 71.6% vs. 75.0%; p=ns), diabetes (29.0% vs. 20.3%; p=ns), number of stents (>1 stent implanted 8.2% vs. 7.0%; p=ns), gender (male 71.6% vs. 75.0%; p=ns), diabetes (29.0% vs. 20.3%; p=ns), number of lesions treated (>1 lesion 28.4% vs. 27.3%; p=ns), pre-dilatation (40.4% vs. 41.9%; p=ns), reference diameter by QCA (2.88±0.56 vs. 2.89±0.53; p=ns), length by QCA (16.60±9.78 vs. 17.27±9.46; p=ns). No significant differences were found in any of the studied variables between both groups: stent length (18.21±8.19 vs. 18.78±8.41 mm; p=ns), stent diameter (3.06±0.47 vs. 3.06±0.46; p=ns), number of stents (>1 stent implanted 8.2% vs. 7.0%; p=ns), need of post-dilatation (24.5% vs. 27.1%; p=ns), and presence of intimal dissection (5.0% vs. 3.5%; p=ns). Likewise, there were no differences in contrast dye used (186.83±79.1 vs. 181.93±66.8 ml; p=ns) neither fluoroscopy time (1.39±1.70 vs. 1.07±1.72 min; p=ns).

Conclusions: Display screen size does not influence the choice of stent size by interventional cardiologists, neither the immediate results of the implant.

P4720 | BENCH Catheter substrate mapping to guide left ventricular aneurysm exclusion in patients post myocardial infarction P. Neuzil, J. Petru, J. Skoda, L. Sediva, M. Janotka, M. Chovanec, S. Kralovec, I. Skalsky, S. Cerny, P. Pavel, Na Homolce Hospital, Prague, Czech Republic

Background: Substrate of ventricular tachyarrhythmias (VTA) is caused by post infarction (MI) scar. The purpose of this single center study was to evaluate the efficacy of the electroanatomical mapping (EAM) prior aneurysmectomy to identify the arrhythmogenic areas and of the myocardium in order to guide the surgeons to navigate resection and cryodestruction of the most critical areas of the myocardium.

Patients and methods: 69 pts (♂ age 64 years, 56 m/13 w, with documented post MI aneurysms (Echo, MRI, LV angiography) were included into the study. In all pts VTA induction was tested prior to surgery and electroanatomical mapping (EAM) with identification of specific late and fractionated potentials was performed. Surgeon used the predefined EAM to navigate the surgery to eliminate most of the arrhythmogenic zones by resection of the aneurysm plus cryoablation. EAM with programmed stimulatory stimulation was repeated 2–3 months after aneurysmectomy to evaluate the effect of the surgical procedure.

Results: In all 69 pts we created EAM as a guide for surgical LVAR plus cryoablation of the most important areas. Prior surgery VT was inducible in 34 pts (49%), after surgery VT was induced in only 3 pts (4.3%). EAM was performed in 57 pts after LVAR procedure and in all we demonstrated significant change of the substrate including reduction of late and fractionated potentials. Average of follow-up is 31.8 months (3–47) with only 2 deaths due to noncardiac reasons.

Conclusions: EAM reconstruction prior LVAR could play important role: 1. arrhythmogenic surgery by cryo-ablation of very specific substrate leads to dramatic reduction of VTA induction; 2. guide accurate LV reconstruction.

P4721 | BENCH A randomized comparison of subcutaneous “Z” stitch versus manual compression to achieve hemostasis after large caliber femoral venous access R. Pracon, J. Henzel, I. Cendrowska-Dernkow, B. Pregowska-Chwala, A. Tarnowska, M. Dernkow, National Institute of Cardiology, Warsaw, Poland

Background: With the growing number of interventions requiring large caliber venous access, there is need for a safe and effective method of achieving hemostasis post procedurally. Subcutaneous stitches have been introduced for this purpose but systematic data on their performance are lacking.

Purpose: The study sought to: 1. compare “Z” stitch to manual compression in attaining hemostasis after femoral venous access with large bore sheaths, and 2. assess vein patency with the stitch in place and after its removal.

Methods: In this single center, randomized study, 86 consecutive patients with 90 femoral venous access sites requiring >10F sheaths were randomly assigned to “Z” stitch or compression group for hemostasis in a 2:1 fashion. “Z” stitch is a modified figure-of-eight suture introduced at our centre that allows for performance of deep stitches longitudinally to the vein’s long axis for improved safety and efficacy. Participants underwent structured assessment at baseline, peri-procedurally, at discharge, and at target 30 days follow-up. Duplex ultrasonography of groins was performed at discharge, and also in a subgroup of 28 unselected participants with the stitch in place.

Results: Mean age of study participants was 61.7±19.1yrs. 33.3% were males. The mean sheath size was 13.8±2.6F, (range 10 to 22F). Baseline patients characteristics were distributed equally between the groups. In the stitch vs. the compression group hemostasis was achieved quicker (<1 min vs. 12.1±5.2 min resp.), patients were sooner able to ambulate (9.3±7.4 vs. 16.2±5.7 hours after the procedure resp.), there were less minor access site bleedings (10% vs. 33% resp., p=0.05 for all). At visual inspection, 20% of patients in each group presented groin bruises greater than 1cm up to the target 30 days follow-up. Discharge ultrasound showed groin hematoma in 3.3% of patients in the stitch group vs. 10% in the compression group (p=0.18). All veins were patent at discharge with similar lumen diameters between the groups (9.3mm for the stitch vs. 10.4mm for compression group, p=0.11). Ultrasound study before stitch removal showed vein patency with no significant difference in veins’ diameter when compared to the contralateral side (8.6±2.6 vs. 9.7±3.4mm, p=0.14 resp.)

Conclusions: The “Z” stitch is a safe, effective, and cheap method of achieving hemostasis after large bore venous femoral sheaths removal. The stitch saves cath lab teams’ time and allows for earlier patients’ ambulation when compared
to manual compression. It does not compromise vessel's patency. It appears like the method of choice in the studied settings.

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BASIC MECHANISMS, VENTRICULAR FUNCTION, PROGNOSIS III

P4724 | BEDSIDE
Cytotoxic serum activity is independent mortality predictor of patients with chronic heart failure
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Introduction: Elevated serum level of neurohormones, cytokines and other agents is a major determinant of prognosis in chronic heart failure (CHF). This circulating cytotoxic load damages endothelial cells and increases the risk of cardiovascular events.

Purpose: We aimed to determine whether the damaging activity of serum may predict prognosis of patients with CHF.

Methods: Fifty seven patients with CHF and left ventricular systolic dysfunction (ejection fraction <40%) participated in this study (mean age 52±8 years, 81% male). Ten sex- and age-matched healthy subjects served as a control group. According to NYHA criteria 40 (70%) patients were in stable class II and 17 (30%) in class III. Ischemic etiology of CHF was confirmed by coronary angiography in 34 (60%) patients and ruled out in 23 (40%). Mean left ventricular ejection fraction was 25±8%. Endothelium-dependent flow-mediated dilation (FMD) of the brachial artery was assessed by high resolution ultrasound. Human umbilical vein endothelial cells (HUVEC) were incubated for 72 hours with 20% of serum of patients. Cell viability was detected using the fluorescein-annexin V/propidium iodide double-staining and analysis with a flow cytometer. Patients were monitored over a minimum follow-up of 30 months (median 35,5 months). All-cause mortality was a single endpoint.

Results: Serum from patients with CHF increased the level of dead endothelial cells when compared with healthy subjects (18% vs 7%, p<0.0001) and decreased the level of viable cells (respectively 82% vs 93%, p<0.0001). Rate of dead HUVEC cells was similar for serum from patients with ischemic and non-ischemic CHF (respectively 17% and 19%, p=ns). There was a significant inverse correlation between percentage of dead endothelial cells in vitro and endothelium-dependent vasodilation in vivo (r=−0.28, p=0.001). Cox regression analysis revealed that high cytotoxic serum activity [Exp:B 0.631, SE 0.039, p<0.001] was the independent predictors of death.

Conclusions: Circulating blood of patients with CHF damages endothelial cells. This action is irrespective of etiology of CHF and related to impaired FMD. Cytotoxic activity of serum is independently associated with a worse prognosis in patients with CHF. Assessment of serum-induced cellular injury could provide important, integrative estimate.

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P4725 | BEDSIDE
Right ventricular function is a powerful independent predictor of adverse heart failure outcomes
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Background: There is significant heterogeneity in advanced heart failure disease trajectory related in part to the ability of the right ventricle to respond to the failing left heart.

Aim: To investigate the predictive value of clinical, biochemical, haemodynamic and echocardiographic indices in this setting.

Methods: 405 patients referred for cardiac transplantation at our institution between 2006–2013 were included. Univariate and multivariate analyses were performed to identify indices associated with poor prognosis.

Results: 182 consecutive patients listed for cardiac transplantation were studied. During follow-up, 20 patients died, 62 patients received a cardiac transplant and 60 patients required ventilator assist device (VAD) insertion. Median freedom from death, VAD or cardiac transplant was 236 days. Univariate factors associated with death/ VAD/ transplantation included body mass index, left ventricular ejection fraction, right ventricular function, cardiac index, right ventricular stroke work index, pulmonary vascular resistance, pulmonary arterial wedge pressure (PAWP), glomerular filtration rate (GFR), bilirubin, albumin and sodium (P<0.05 for all). Excluding serum markers in multivariate analysis, the functional indices of cardiovascular risk was calculated by mathematical summation of all ranks of independent predictors, which occurred in the patients included in the study. The findings showed that the average value of the index of cardiovascular risk in patients with CHF was 3.17 points (95% CI = 1.65 - 5.10 points.). Kaplan-Meier analysis showed that patients with CHF and the magnitude of the risk of less than 4 units have an advantage in survival when compared with patients for whom obtained higher values of cardiovascular risk score ranks.

Conclusion: Biomarker risk score for cumulative cardiovascular events, constructed by measurement of circulating NT-pro-BNP, galectin-3, hs-CRP, osteoprotegerin, CD31+annexin V+, EMPs and CD31+/annexin V+ EMPs to CD14+CD309+ MRC Paris, allowing reliably predict the probability survival of patients with CHF, regardless of age, gender, state of the contractile function of the left ventricle and the number of comorbidities.

P4724 | BEDSIDE
Prognostic value of cystatin C-derived estimated glomerular filtration rate in the patients with acute decompensated heart failure

Background: Glomerular filtration rate (GFR) is one of the potent prognostic markers in patients with heart failure. Recently, cystatin C-derived GFR has been proposed for more precise estimation for GFR. We aimed to test the prognostic value of cystatin C-derived GFR in patients with heart failure of acute decompensation and compare with conventional methods.

Methods: This retrospective study included 262 patients with acute decompensated heart failure. Prognostic value of the estimated GFRs, derived from the Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) equation for cystatin C (CKD-EPI-Cystatin C equation) and CKD-EPI-creatinine (CKD-EPI-creatinine equation), were compared with estimated GFR derived from the classic equations containing only serum creatinine levels (Modification of Diet in Renal Disease (MDRD) equation and CKD-EPI-creatinine equation). Prognosis was evaluated with the composite of all-cause mortality and readmission for decompen- sated heart failure within one year.

Results: Mean age was 65.8±14.9 and 126 (48.1%) were men. Among the patients, 106 (40.5%) were with ischemic etiology. During the follow-up (mean follow-up 264.0±136.1 days), 67 (25.6%) events occurred. Mean estimated GFRs were 67.7±32.2, 64.8±27.4, 54.2±26.2 and 57.2±24.1 (ml min−1·1.73m−2) for MDRD, CKD-EPI-creatinine, CKD-EPI-cystatin C, and CKD-EPI-cystatin C-creatinine, respectively. Estimated GFR using CKD-EPI-cystatin C was the best for predicting 1-year outcome in receiver operating characteristic curve (AUC of 0.585, 0.607, 0.669, and 0.652 for GFRs estimated by MDRD, CKD-EPI-creatinine, CKD-EPI-cystatin C, and CKD-EPI-cystatin C-creatinine equation, respectively). AUC of GFR by CKD-EPI-cystatin C equation was significantly greater than that of GFR by MDRD and CKD-EPI-creatinine equation (p<0.001 and p=0.016) AUC of GFR by CKD-EPI-creatinine equation was also significantly greater than that of GFR by MDRD and CKD-EPI-creatinine equation (p=0.001 and p=0.004) Kaplan –Meier survival curve analysis according to the subgroups of estimated GFR showed that only the two estimated GFRs derived from the equations containing serum cystatin C significantly differentiated 1-year outcome in patients with acute decompensated heart failure (log rank p of <0.001 and 0.002 for the CKD-EPI-cystatin C, and CKD-EPI-cystatin C-creatinine equations).

Conclusion: Estimated GFRs, which were derived from cystatin C, predicted the prognosis more accurately in patients with acute decompensated heart failure, compared to those from creatinine-only equations.
which remained significant included haemodynamic variables derived from right heart catheterisation including PAWP, pulmonary vascular resistance, right ventricular stroke work index, as well as right ventricular function on echocardiography (P < 0.01 for all). Right ventricular indices were closely associated with bilirubin, GFR, albumin (P < 0.03 for all), PAWP was associated with sodium (P < 0.02).

Conclusion: Echocardiographic and haemodynamic measures of left ventricular function do not have as strong an impact on prognosis as those of right ventricular function. The strong correlations between bilirubin, albumin and GFR with prognosis, as well as their close association with haemodynamic and echocardiographic markers of right ventricular function, suggest that right ventricular adaptation is important in determining outcomes in patients with heart failure.

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P4726 | BEDSIDE
Heart rate / systolic blood pressure ratio at discharge as a simple prognostic factor for adverse clinical outcomes in patients with acute heart failure
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Background: Increased heart rate (HR) and low systolic blood pressure (SBP) are the most important clinical outcomes in patients with acute heart failure (AHF). However, the clinical significance of pre-discharge HR/SBP ratio was not evaluated in patients with AHF. Therefore, the aim of this study was to investigate the impacts of pre-discharge HR/SBP ratio on early clinical outcomes in patients AHF following discharge.

Methods: A total of 5,660 patients (68.5±14.5 years, 3,019 males) with AHF were consecutively enrolled in Korean AHF registry (KorAHF) who had BP and HR measurement at discharge, and 279 patients who died during hospitalization were excluded. Receiver operating characteristics (ROC) curve analysis to predict mortality was performed to identify the optimal cut-off value of HR/SBP ratio before dividing groups. They were divided into two groups according to HR/SBP ratio; high HR/SBP ratio group (≥0.66, n=2,751, 66.9±14.9 years, 1465 males) and low HR/SBP ratio group (<0.66, n=2,630, 69.9±13.9 years, 1388 males). Composite endpoints including all-cause mortality, and rehospitalization at 3 months of follow-up were compared between the groups.

Results: Baseline clinical characteristics were not different between the groups except for the higher prevalence of hypertension (49.6% vs. 32.4%, p<0.0001), diabetes (66.7% vs. 62.3%, p<0.0001), and ischemic heart disease (76.6% vs. 67.8%, p<0.0001) in high HR/SBP ratio group. ROC curve analysis identified HR/SBP ratio >0.66 as the optimal cut-off value for prediction of mortality in patients with AHF (AUC=0.584; 95% CI 0.551–0.617, p<0.0001). Moreover in patients who could not be prescribed BB at discharge, the incidence of endpoint was significantly higher in high HR/SBP ratio group than in low HR/SBP ratio group (26.4% vs. 21.8%, p=0.008). In patients with BB use, however, there were no significant differences between the groups (17.9% vs. 16.5%, p=0.333). This phenomenon was also shown for ACEI or angiotensin II receptor blocker. In multivariate analysis using Cox proportional hazard model, high HR/SBP ratio (HR: 1.290, 95% CI: 1.031–1.605, p=0.021) was an independent predictor of composite endpoint (HR 1.35, 95% CI 1.20–1.53, p<0.0001).

Conclusions: Pre-discharge HR/SBP ratio was a significant prognostic factor of early adverse clinical outcomes in patients with AHF after discharge. AHF patients who have high HR/SBP ratio might have to be subscribed BB before discharge for better long-term clinical outcomes. Pre-discharge HR/SBP ratio would be useful in the risk stratification or predicting future clinical events after discharge in patients with AHF.

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P4727 | BEDSIDE
The presence of metabolic syndrome predicts long-term outcome in heart failure patients
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Background and aim: It has been shown that the Metabolic Syndrome (MS) is independently associated with increased incidence of heart failure (HF) and coronary artery disease. We investigated the prognostic value of MetS in addition to other well-known Doppler echocardiographic parameters on the clinical outcomes in HF patients.

Methods: This study included 188 consecutive patients (62±10 years) with congestive HF. The primary outcomes were cardiac events (CE = mortality or need for hospitalization) due to acute HF signs and/or symptoms. LV end-diastolic and end-systolic dimensions, ejection fraction (EF), mitral and tricuspid annulus peak systolic excursion (MAPSE and TAPSE), myocardial velocities (s', e' and a'), left atrial (LA) dimensions, LA volume and LA emptying fraction were all measured. Based on the on the NCEP-ATP III criteria, patients were divided into MetS (n=83) and non-MetS (n=105) groups.

Results: During the follow-up (18±6 months) period, 87 patients (47%) had CE. The creatinin level was higher (P<0.01), LV mass index was higher (P<0.01), LA was larger (P<0.001), LV EDD (P<0.001) and LV ESD (P<0.001) were greater, E/e' lower (P<0.001), septal MAPSE lower (P<0.01), diabetes and MetS more prevalent (P=0.03 and P=0.01, respectively), NYHA-2 more frequent (P<0.001), in patients with cardiac events compared to those without. Patients with HF and MetS were older (p=0.008), had larger LA (p=0.04), lower systolic and diastolic e' (p=0.006, respectively), and reduced LA emptying fraction (p=0.01) compared to those with HF non-MetS. Multivariate analysis identified E/e' (OR=0.1.121, 95% CI 1.03–1.26, p=0.02) and MetS (OR=3.967, 95% CI 1.673–9.409, p=0.002) as independent predictors of CE.

Conclusions: In medically treated patients with chronic HF, the presence of MetS, in addition to increased LV filling pressure, was associated with increased risk of cardiac events. This finding highlights the need for better optimization of medical therapy in HF patients with MetS.

P4728 | BEDSIDE
Outcome of cardiac sarcoidosis patients treated with cardiac resynchronization therapy- comparison with other non-ischemic cardiomyopathy patients
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Background: Cardiac sarcoidosis (CS) is a progressive myocardial inflammatory disease. In a subset of patients with CS, cardiac resynchronization therapy (CRT) is often indicated due to severe left ventricular dysfunction. However, there has been no report examined the significance of CRT in CS patients compared with other non-ischemic cardiomyopathy (NICM) patients.

Methods and results: We retrospectively investigated 96 patients with NICM, including 6 patients with CS, treated with CRT. We compared several parameters and prognosis of CS patients with those of non-CS patients. Fourteen patients with CS received steroid therapy. Prednisolone was administered in all CS patients with positive inflammation confirmed with galium-68 citrate scintigraphy. CS patients had a similar frequency of positive CRT response, compared to non-CS patients (p=NS). During follow-up, cardiac death occurred in 1 patient with CS and 21 patients with non-CS (p=NS). Appropriate ICD therapies occurred in 7 patients with CS and 27 patients without CS (p=NS). In multivariate Cox proportional hazards analysis, the prognosis of CS patients was relatively better, but not significant compared with non-CS patients (HR: 0.214, 95% CI: 0.028 to 1.161, p=0.135).

Conclusions: Although CS commonly progresses, CS patients, in whom steroid therapy was administered if inflammation is positive, showed similar frequency of positive CRT response, appropriate ICD therapy and cardiac death compared to non-CS patients with NICM.

P4729 | BEDSIDE
Transient systolic hypotension worsens the 2-year prognosis of chronic heart failure with preserved left ventricular ejection fraction
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Introduction: Although more than half of all patients with chronic heart failure (CHF) are patients with preserved ejection fraction, factors influencing the prognosis of CHF in such patients are not clear now.

Purpose: The aim of this study was to determine the prognostic value of episodes of arterial hypotension in patients with chronic heart failure (NYHA Class II-III) with preserved left ventricular ejection fraction (LVEF). Methods: 169 patients with CHF (95 females and 74 males, mean age was 56.3±10.9 years) and preserved ejection fraction (LVEF>50%) were studied. Left ventricular ejection fraction was 60.6±5.4%. 105 patients had functional class II

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of CHF, 64 - Class III according to NYHA classification. Causes of CHF were: arterial hypertension in 16 patients, coronary artery disease (CAD) - 9 patients, CAD and arterial hypertension - 144 patients. The follow up period was 2 years. Combined endpoint included nonfatal myocardial infarction (MI) and cardiovascular death (CVD death). Patients were treated according to the European Society of Cardiology guidelines. The 24-hour ABPM was performed using MnSDP-2 and MnSDP-3 BPLab devices. During ABPM arterial hypotension was diagnosed according to criteria P.E. Owens and T.E. O’Brien (1996).

Results: Episodes of systolic arterial hypotension during the 24-hour were revealed in 7 of 36 patients with arterial systolic arterial hypotension - in 45 (29.6%), of systolic-diastolic hypotension - in 54 (32.0%), absence of arterial hypotension episodes – in 65 (38.4%) patients. There were 8 MI or CVD deaths: 2 – in the group of patients with episodes of diastolic arterial hypotension 6 and - in the group of patients with episodes of systolic-diastolic hypotension. Instead of these there were no combined endpoints were found in the group of patients with CHF without episodes of arterial hypotension (χ²=0.98, p=0.3 and χ²=5.46, p=0.019, respectively). Relative risk of nonfatal MI or CVD death in patients with CHF with episodes of systolic arterial hypotension was 9.5 (95% CI, 2.5 to 12.2).

Conclusions: Episodes of arterial hypotension are diagnosed in 61.6% of patients with chronic heart failure (NYHA Class II-III) with preserved left ventricular ejection fraction. The presence of episodes of systolic or diastolic hypotension in patients with chronic heart failure increased the 2-year risk for nonfatal myocardial infarction and total cardiovascular death.

P4730 | BEDSIDE

KIM-1 and NAG: new renal biomarkers for prognosis in acutely decompensated heart failure

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Background: Patients with acutely decompensated heart failure suffer often from cardiorenal syndrome (CRS). The aim of the present study was to assess whether novel kidney injury markers are relevant for prognostication in acute heart failure. Methods: The new renal biomarkers Kidney injury molecule-1 (KIM-1), N-acetylated β-D-glucosaminidase (NAG), Neutrophil Gelatinase-Associated Lipocidin (NGAL) and IL-18 (Interleukin 18) were assessed from urine samples of 58 patients with acutely decompensated heart failure at admission and at discharge, beside NT-proBNP and serum creatinine. Results: Patients were followed for a median duration of 644 days (IQR 316, 837 days). Upon survival analysis, a total of 22 deaths and 34 events regarding the combination of death or rehospitalisation for congestive heart failure occurred. Admission and discharge NT-proBNP as well as admission serum creatinine and discharge KIM-1 and NAG were significant predictors for all-cause mortality and the combination of all-cause mortality and rehospitalisation for heart failure (all p<0.05). On a Cox regression analysis including EF, occurrence of acute kidney injury, NYHA stage >2, BMI, age, serum creatinine and respectively one of the markers, KIM-1 and NAG at discharge performed as independent predictors for both endpoints beside NT-proBNP at begin and end of therapy (each p<0.05). Upon ROC analysis, especially discharge KIM-1 showed satisfying predictive values (AUC 0.68 for both endpoints).

Conclusions: High KIM-1 and NAG offer important prognostic information in patients with acutely decompensated heart failure, opposite to admission values. Therefore, these findings allow new insights in kidney injury in patients with heart failure and the potential role of new tubular markers in prognostication of acute heart failure.

Acknowledgement/Funding: none

BASIC MECHANISMS

P4731 | BEDSIDE

Octadecatrienal and phosphatidylcholine as a potential new biomarkers in heart failure - novel insights from the analysis of serum metabolome in chronic heart failure patients

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Introduction: Incomplete knowledge of the pathophysiological basis of the heart failure (HF) enforces further exploration of new analytical methods, as well as predictive and prognostic markers that would allow to trace molecular stages of the HF development and its progression. Aim: The new metabolomics to identify changes in the blood metabolome profile, occurring as a result of heart failure development. Methods and results: We prospectively studied 36 optimally treated patients with stable chronic HF (61±13.9 years, 58% ischemic etiology, left ventricular ejection fraction - LVEF 45±9.2%, NYHA II-IV 52%); 20 patients with chronic heart failure, occurred as a result of heart failure development.

Background: Phospholipids may play a significant role in exercise tolerance in HF patients with chronic heart failure increased the 2-year risk for nonfatal myocardial infarction and total cardiovascular death.

Conclusions: HF patients’ serum metabolome profile differs from controls especially in terms of lipids (fatty aldehyde, sphingolipids, phospholipids, polyunsaturated essential fatty acids - PUFA) and its derivatives. PUFA metabolisms appears to be altered especially in terms of changed desaturation and elongation processes. Phospholipids may play a significant role in exercise tolerance in HF patients with chronic heart failure and its progression.

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P4732 | BENCH

Angiotensin II activates MCP-1 through the infiltration of monocytes and macrophages into the heart and induces cardiac hypertrophy and dysfunction via Toll-like receptor 4

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Background: Angiotensin II (AngII) produces reactive oxygen species (ROS), contributes to the development of cardiac hypertrophy and subsequent heart failure, and stimulates the expression of monocyte chemoattractant protein-1 (MCP-1). It is reported that Toll-like receptor 4 (TLR4) is involved in the upregulation of MCP-1, but it has not been known whether TLR4 modulates AngII signal transduction or whether it is involved in the proinflammatory process of AngII and the subsequent cardiac dysfunction. Purpose: To clarify whether TLR4 is involved in the cardiac dysfunction caused by AngII stimulation, we investigated the effects of TLR4 on oxidative stress, AngII-induced inflammation, and its effects on cardiac hypertrophy and function in AngII-induced hypertensin. Methods: TLR4-deficient (TLR4deficient) and wild-type (WT) mice were randomized into groups treated with AngII, nor epinephrine (NE) or a sub-depressor dose of the AngII receptor blocker Irbesartan (IRB) with AngII for 2 wks. The mice from each group were subjected to echocardiography for our evaluation of the standard basic echocardiography measurements and calculations for the estimation of left ventricle (LV) morphology and function. We used immunohistochrometry to determine the expressions of p-nF-κB, MCP-1 and the infiltration of monocytes/macrophages in the heart tissues. We evaluated the O2- content using fluorescent dihydroethidium for the in situ imaging of ROS generation in the myocardium. NADPH oxidase activities were determined by a luminescence assay. Immunoblotting was performed by the ELISA method. Results: AngII and NE resulted in similarly significant increases in systolic blood pressure in all drug-treated groups compared to the control group in both the WT and TLR4deficient mice (P<0.05). In the WT mice, AngII induced cardiac hypertrophy, vascular remodeling, perivascular fibrosis of the intramyocardial arteries, and monocyte/macrophage infiltration into the heart (P<0.05). AngII also decreased the LV diastolic function and induced a greater LV end-systolic dimension (P<0.05), and it produced a fivefold increase in NADPH oxidase activity, ROS content, and p-nF-κB and MCP-1 expression (P<0.05). The TLR4deficient mice showed little effects of AngII on these indices. In the WT mice, IRB treatment reversed these changes compared to the mice treated with AngII alone. NE produced little effect on any index in either the WT or TLR4deficient mice. Conclusions: TLR4 may be involved in the increased oxidative stress, selectively and the inflammatory effects of AngII-1 and cardiac hypertrophy and dysfunction seen in AngII-induced hypertension.

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P4735 | BEDSIDE
IL-6 signaling in patients with chronic heart failure treated with cardiac resynchronization therapy
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Increased IL-6 concentration has been described in ventricular dysfunction and chronic heart failure (CHF). Apart from the direct effect on membrane bound receptors, IL-6 activity (trans-signaling) is mediated by the soluble IL-6 receptor (sIL-6R) and soluble gp130 (sgp130). Cardiac resynchronization therapy (CRT) is a unique treatment method dedicated for CHF patients, that may reverse the course of the disease.

We evaluated IL-6 signaling, including sIL-6R and sgp130 concentrations, in patients with CHF taking into account the effect of CRT treatment.

Methods: The study enrolled 88 CHF patients (age–64±11, 10 females, BMI–29±4 kg/m²), with stable CHF, NYHA class II or III, EF–35%, confirmed by echocardiography and 35 healthy controls matched for age, sex and body weight (age–63±10, 8 females, BMI–28±4 kg/m²). 45 CHF patients underwent CRT device implantation and were controlled after 6 months. All patients underwent transthoracic echocardiography, cardiopulmonary exercise test (CPET) and venous blood tests. Concentrations of IL-6, sIL-6R and sgp130 were determined using ELISA kits.

Results: The CHF patients were characterized by significantly higher IL-6 (median 2.6 IQR: 1.6–3.8 vs 2.1 IQR: 1.4–3.1 pg/ml, p=0.03) and lower sIL-6R serum concentrations comparing to control subjects (median IQR: 37–64 vs 53 IQR: 45–76 pg/ml, p=0.008). There was no significant difference between sgp130 concentrations.

At the baseline in CHF group IL-6 level correlated positively with BNP (r=0.4, p<0.05) and CRP concentration (r=0.32, p<0.05), while concentration of sgp130 correlated only with BNP (r=0.39, p<0.001). Among CPET parameters death space/tidal volume ratio (VD/VT) and VE/VC02 slope correlated with sIL-6R level (r=0.25, p<0.05; r=0.3, p<0.05, respectively).

After 6 months of CRT significant improvement in NYHA class (2.8±0.4 vs 2.3±0.4, p<0.001) was observed, as well as echocardiographic parameters, e.g. EF (23±6% vs 32±10%, p<0.001) and LVESV (193±68 vs 143±68 ml, p<0.001), was observed. Based on clinical and echocardiographical parameters 31 patients were qualified as responders. In this group a more pronounced decrease from baseline of sIL-6R concentrations was observed when comparing to nonresponders (sIL-6R: GR–0.18±0.076 vs 6.97±14.02 pg/ml; p=0.029), while IL-6 and sgp130 concentrations did not significantly change.

Conclusions: Patients with CHF present higher serum IL-6 and lower sIL-6R serum concentrations compared to control subjects. The positive response to CRT is associated with IL-6 trans-signaling decrease due to lowered sIL-6R concentration. The exact role of IL-6 pathway in the CRT response remains to be established.

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between their expression and the LVEF (r=0.68; -0.64) and LVEDV (r=0.61; 0.76) in TAC-mice. Microarray analysis identified additional 11 genes associated with Wnt-signaling as differentially expressed (TAC vs. Sham, fold change ≥ 1.5) over time. First results of in-vitro studies using the activator of canonical Wnt pathway Wnt3a revealed a concentration-dependent induction of hypertrophic HL-1 cell growth (1% for 0.5 nM; 22% for 1 nM and 29% for 2 nM versus control). This regulatory process was comparable to Endothelin-1 (19% for 100 nM ET-1 versus control), which is a stimulus known to be involved in pathological cardiac remodelling. While ET-1 led to a robust increase in HF gene expression (1.86- and 1.84-fold for Normal and ET-1 treated, respectively), Wnt3a expression changes were unchanged or even slightly downregulated. Expression of all those genes after Wnt3a incubation was not regulated.

Conclusion: Gene expression analysis in mice suffering from cardiac hypertrophy and HF suggest an important participation of Wnt-signaling in disease progression. Sufficient expression of Wnt3a gene and the expression of its FZD receptor Strp2 and Wisp2 support this hypothesis. Further, induction of cardiac cell enlargement and HF gene expression by Endothelin-1 demonstrate similar regulation in an in-vitro model, but hypertrophic growth induced by Wnt-activating protein Wnt3a seems to be regulated by different mechanisms.

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P4737 | BENCH
Klotho and FGF receptor are concomitantly expressed in human individuals with heart failure
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Introduction: In clinical studies elevated levels of FGFR23 have been linked with the advent and progression of heart failure. Klotho acts as an essential coreceptor for FGFR23 whereby tissue-specific expression of Klotho determines target organs of FGFR23. Moreover, Klotho is an antilaging protein and actively involved in the prevention of arteriosclerosis. Previous data in mice suggest that FGFR23 exerts its effects on LV hypertrophy independently of Klotho due to not detectable expression of the Klotho receptor. Since no information is available on Klotho expression in human individuals with heart failure we aimed to investigate the cardiac expression of Klotho and FGF receptor in patients with heart failure.

Methods: Endomyocardial biopsies from patients with non-ischemic cardiomyopathy (n=6) and patients 3-4 weeks after successful heart transplantation (n=6) were analyzed for the expression of Klotho and FGF receptor. The latter were correlated with heart function tests and the emergence of hypertrophic cell growth.

Results: Klotho mRNA and FGFR2 were detectable in non-ischemic cardiomyopathy and in healthy hearts by RT-PCR and immunohistochemistry. Expression of both Klotho mRNA and FGFR1 mRNA was significantly upregulated in cardiac biopsies derived from individuals suffering from non-ischemic cardiomyopathy as compared to healthy controls by quantitative RT-PCR (2.65±0.70 vs. 1.32±0.43; p<0.002, and 1.65±0.43 vs. 1.08±0.21; p=0.01, respectively). Immunohistochemically, double staining revealed colocalization of Klotho and FGF receptor in diseasedcardiomyocytes.

Summary and conclusion: We show that Klotho and FGFR2 are concomitantly and highly expressed in non-ischemic cardiomyopathy. Whether adverse cardiac effects of FGFR2 are mediated by its coreceptor Klotho and/or cardiac expressed Klotho and its soluble ligand exerts independent effects in heart failure has to be addressed in future studies.

P4738 | BENCH
Hepcidin and its regulator molecule hemojuvelin in systolic heart failure
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Introduction: Hepcidin (HPC) is a key regulator of iron metabolism. Hemojuvelin (HJV) is believed to stimulate hepcidin production. Derangement of iron homeostasis is well described in chronic heart failure (CHF) and confers a poor prognosis in this group of patients. HJV serum concentration was never determined in CHF patients.

Aim of the study: The aim of the study was to assess HPC and HJV serum levels in patients with systolic CHF and in control group and evaluate its potential prognostic value.

Material and methods: The study group consisted of 130 consecutive patients admitted to the hospital with systolic heart failure and LVEF <45%. In 65 patients primary reason for admission was CHF exacerbation. The control group consisted of 32 healthy adults matched for age and sex. Fasting blood samples were taken from all study participants for HPC and HJV determination. Routine laboratory tests, including natriuretic peptide, were performed in all CHF patients. Telephone follow-up visits were performed every three months for one year. Endpoints of the study were: death from all causes, and hospitalisation with heart failure exacerbation.

Results: Significantly higher median level of hepcidin was observed in CHF patients than in controls (28.35 vs 13.47 ng/ml p<0.0001). Unexpectedly, decreased HPC concentration was found in exacerbated patients comparing to stable ones (19.57 vs 37.71 ng/ml; p=0.002). No significant difference between CHF patients and control group was found regarding hemojuvelin serum level. HPC and HJV serum levels were not correlated with each other neither in CHF patients nor in the control group. From among iron metabolism markers HPC was only correlated negatively with soluble transferrin receptor. No correlation was found with these parameters and HJV. None of the studied parameters turned out to be a valuable predictor of survival nor of hospitalization with CHF exacerbation.

Conclusion: There is no direct association between hepcidin and hemojuvelin serum levels. 2. CHF has no clinically evident impact on HJV serum level. 3. HPC may not be strongly related to iron status in heart failure but tissue ischamia may induce hepcidin expression and exacerbation may lead to inhibition of HPC production.

Acknowledgement/Funding: Scientific Grant of Collegium Medicum Nicolaus Copernicus University, Bydgoszcz Poland

P4739 | BEDSIDE
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Acknowledgement/Funding: Scientific Grant of Collegium Medicum Nicolaus Copernicus University, Bydgoszcz Poland

P4740 | BENCH
Fish oils may promote lipotysis by reducing phospholamban expression in human heart
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Introduction: Fish oils (omega-3 fatty acids, n-3 PUFA) supplementation has been reported to improve outcome in heart failure (GISSI-HF trial) but the mechan-ism of such benefit is unclear. Myocardial contractility is intricately linked to calcium dynamics.

Purpose: To evaluate the effect of n-3 PUFA supplementation on calcium han-dling in human heart.

Methods: Patients undergoing coronary artery bypass graft (CABG) surgery re-cieved supplements of fish oils (Omacor, 2g/day) or a matched placebo (as part of a clinical trial) prior to surgery and right atrial tissue obtained during CABG. Tissue samples divided into 4 parts and used for quantitative polymerase chain reaction, immunohistochemistry and Western blot for calcium handling proteins and esti-mation of tissue n-3 PUFA using gas chromatography. Rats fed with diet rich in n3-PUFA were used to obtain ventricular myocytes and functional studies evalu-ating calcium transient amplitudes by field stimulation experiments were carried out on these myocytes.
Results: Supplementation of n-3 PUFA reliably increased tissue levels in human heart. Expression of phospholamban was reduced in the n-3 PUFA group. Ryanodine receptor expression, at mRNA level, appeared to be increased. Other calcium handling proteins were not significantly altered. A positive lusitropic effect (faster rate of decay of systolic calcium transient) was demonstrated in rat ventricular myocytes. Fish oil incorporation in human cardiomyocyte membrane reduces expression of phospholamban. A more rapid relaxation, the positive lusitropic effect was seen in rat ventricular myocytes. This could be the mechanism by which fish oils improve clinical outcome in patients with heart failure.

BASIC MECHANISMS / VENTRICULAR FUNCTION

P4741 | BEDSIDE
Left ventricular deformation accurately predicts the extent of myocardial fibrosis in patients with advanced heart failure requiring transplantation

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Purpose: To evaluate potential relationships between left ventricular (LV) longitudinal deformation function and histopathological evidence for myocardial fibrosis in patients undergoing heart transplantation.

Methods: The study population included patients with advanced heart failure, referred for an echocardiographic examination before heart transplantation. Traditional LV function measurements and global longitudinal strain (GLS) by speckle tracking echocardiography, averaging all LV segments in 4-, 2-, and 3-chamber views were obtained in all subjects, LV tissue samples were obtained from all patients undergone heart transplantation. Myocardial fibrosis was assessed using Masson’s staining.

Results: Of 106 patients referred for cardiac transplantation, 47 underwent cardiac transplantation and were enrolled in the study. LV myocardial fibrosis and its grade strongly correlated with GLS (r=0.75, p<0.0001), modestly with global circumferential strain and LV torsion (r=0.61, p=0.001 and r=0.52, p=0.01, respectively) and weakly with mitral S wave (r=−0.41, p<0.01) and MAPSE (r=−0.035, p=0.05) but did not correlate with LV ejection fraction (r=−0.12, p=NS). GLS had the strongest accuracy for detecting LV fibrosis (AUC=0.92). None of the echo parameters correlated with patient’s exercise capacity.

LV strain and LV fibrosis

Conclusion: LV GLS is the most accurate LV global function measure that correlates with the extent of myocardial fibrosis in patients with advanced systolic HF requiring heart transplantation.

P4742 | BEDSIDE
Ventricular-vascular coupling is altered in marfan syndrome but preserved in TAAD

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Background: Marfan syndrome (MFS) and familial non-syndromal thoracic aortic aneurysm (TAAD) are associated with aortic dilatation and increased aortic stiffness. Impairments of abnormal left ventricular function in Marfan syndrome may reflect increased afterload.

Purpose: This study examined load-independent measures of left ventricular function in MFS and TAAD, in order to determine whether ventricular-vascular coupling was altered.

Methods: Patients with MFS (n=67, 34F, 34±15 yrs Ghent criteria, mutation) and TAAD (n=70, 33 F, 47±15 yrs family history, mutation) were studied by echocardiography and compared with matched controls (n=89, 45F, 37±18 yrs).

Results: There were no differences in age, gender, smoking habits, diabetes, hypertension, beta-blockers or time since transplantation. Left ventricular filling pressures, and therefore ventricular-vascular coupling, were preserved in TAAD (r=0.92, p<0.0001). None of the echo parameters correlated with NYHA functional class and microCFR (r=0.61, p<0.0001). There was a significant correlation between LV mass and microCFR (r=−0.6, p<0.0001), with a stronger correlation after adjustment of CAV (r=0.61, p<0.0001) and right ventricular filling pressure (mean pulmonary capillary wedge pressure; r=0.43, p=0.01) and right ventricular filling pressure (mean right atrium pressure; r=0.42, p=0.01), whereas only the correlation to RAP remained significant at peak exercise (r=0.46, p=0.01). Interestingly, we found microCFR significantly correlated to peak exercise cardiac output (r=0.44, p=0.01) and pulmonary arterial compliance both at rest (r=0.42, p=0.01), and at peak exercise (r=0.48, p=0.01).

Conclusion: The presence and degree of macrovascular CAV strongly correlates with microvascular function. Additionally, microCFR significantly correlated to exercise capacity, NYHA functional class and maximal cardiac output. Finally, a significant correlation between microCFR and pulmonary arterial compliance was seen, indicating remodeling of pulmonary arteries in HTx patients with microvascular dysfunction.
P4745 | BEDSIDE
Advanced heart failure with reduced ejection fraction and severe mitral insufficiency is associated with a reduced cardiac output vs oxygen uptake response to maximal exercise
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Background: In heart failure (HF) the mitral regurgitation (MR) is clinical and prognostic relevant. Cardiopulmonary exercise testing (CPET) allows evaluating functional capacity and provides indexes for HF risk stratification such as peak oxygen consumption (VO2). Since MR determines a severity-related backward flow to left atrium, it may result in an unfavorable central blood flow exercise redistribution that is physiological relevant to VO2 increase. Aim: To evaluate the cardiac output (CO) and VO2 exercise-response in HF reduced ejection fraction (HFpEF) patients according to MR severity to dissect what mechanism may be predominant in the VO2 increase.

Methods: 104 HFpEF patients (mean age 64±11 y, male 72%, ischemic etiology 68%, mean LVEF 34±9%) underwent a maximal CPET (incremental ramp protocol) combined with exercise-echo. CO was non-invasive estimated by echo.

Results: Population was divided into 2 groups according to the rest MR: group A (n=80) non-severe MR and B (n=24) severe MR. Despite the groups did not differ in rest CO (A vs B 3.8±1 vs 3.4±1.8 L/min, p=ns) and VO2 (0.27±0.06 vs 0.28±0.09 L/min, p=ns) group B showed higher peripheral extraction (C(a-v)O2 8±2 vs 9±1 mL/100 mL, p=0.036) already at rest (Figure). At peak exercise group B had an impaired increase both in CO (7.0±2.0 vs 5.2±3.3 L/min) and VO2 (1.0±0.3 vs 0.8±0.3 L/min, p=0.001) partially compensated by a greater C(a-v)O2 contribution (15±5 vs 18±5 for A vs B, p=0.047).

Conclusions: Severe MR and consequent partial abnormal CO redistribution to the pulmonary circulation seems a relevant physiological mechanisms that limits overall exercise performance in HFrEF. In this high risk subset of patients peripheral extraction compensates for the reduced CO and makes the basis for novel perspectives in these patients.

P4745 | BEDSIDE
Multipoint pacing acutely induces better hemodynamics and QRS narrowing compared to conventional biventricular pacing
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Background: In comparison with conventional biventricular pacing (BiV) and multipoint pacing (MPP) respectively.

in contractility was associated with significantly greater narrowing of the QRS complex than conventional BiV pacing.

P4746 | BEDSIDE
Strain pressure product- an afterload corrected myocardial strain measure and its association with features of preclinical heart failure and outcomes
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Background: Left ventricular global longitudinal strain (GLS) is a marker for subclinical myocardial dysfunction, particularly afterload. We propose a new GLS measure with blood pressure and heart rate correction, named Strain Pressure Product (SPP) and assess its association with HF risks, exercise capacity, quality of life and outcome in a non-ischemic Stage A Heart Failure (SAHF) population.

Methods: Asymptomatic subjects ≥65 yo with SAHF ≥1 HF were recruited from the community. All subjects underwent standard Patient report outcome measures, a 6-minute walk test (6MW) and a comprehensive echocardiogram including GLS. SPP was calculated as the product of GLS and SBP divided by heart rate (HR). New HF symptoms including shortness of breath on exertion or at rest, orthopnea and leg edema were assessed at 1 year follow-up.

Results: Total 521 subjects (age 71±5 y; 49% men) were recruited. 19% had one; 40% had two and 41% had ≥ three risk factors. At baseline, mean LVEF and GLS were 63±5% and −18±3%. Mean SPP was 0.39±0.09. SPP was significantly associated with HF risks, diastolic parameters and PROMs measures independent of age and gender (Table). After an average follow-up time of 10±3 months, 308 subjects underwent assessment of early HF symptoms. 63 developed early HF symptoms. SPP was associated with new HF symptoms (p<0.05) and composite cardiovascular outcome (p=0.043) table.

Conclusion: Strain pressure product, which is a blood pressure and heart rate corrected GLS measure, showed significant association with HF risk, exercise capacity, PROMs measure and diastolic function. It is also associated with early HF symptoms. SPP may be an effective means of addressing the load-dependence of strain.

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A novel and practical method to quantify mitral annulus motion and tricuspid annulus motion from cardiac magnetic resonance

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Background: We have developed a new tracking method to track the mitral annulus motion (MAM) and tricuspid annulus motion (TAM) from cardiac magnetic resonance (CMR). In this study, we compared myocardial velocities (Sm, Em and Am) - calculated at systolic and early and late diastolic filling periods, respectively - with myocardial velocities from tissue Doppler imaging (TDI). We also examined the correlations of MAM and TAM with left ventricular mass and EF.

Methods: We prospectively performed CMR and echo TDI scans on the same day in 20 normal healthy volunteers (age range: 23 to 70 years) and consecutive 104 patients. MAM and TAM velocities were tracked automatically using in-house customized algorithm. Velocities (Sm, Em and Am) of the MAM and TAM were calculated as first time-derivatives of the displacement. For MAM assessment, 4-chamber, 3-chamber and 2-chamber views were used and the derived myocardial velocities were averaged. For TAM assessment, only 4-chamber right ventricular lateral site was used. TDI was performed following by the standard protocol based on ASE recommendations.

Results: There were significant good correlations in myocardial velocities between CMR and TDI methods for both MAM and TAM (all p < 0.001). However, significant but relative weak correlations were found between TAM and MAM velocities (Sm: r=0.39; Em: r=0.65; Am: r=0.40, all p<0.001) from CMR. This may indicate the anatomical and physiological differences between the left and right ventricles.

Table 1. Correlations of myocardial velocities from MAM and TAM between CMR and TDI methods

<table>
<thead>
<tr>
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<th>MAM</th>
<th>TAM</th>
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<tr>
<td>r</td>
<td>p</td>
<td>r</td>
</tr>
<tr>
<td>Sm</td>
<td>0.74</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Em</td>
<td>0.84</td>
<td>&lt;0.001</td>
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<tr>
<td>Am</td>
<td>0.70</td>
<td>&lt;0.001</td>
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Conclusions: Myocardial velocities of MAM and TAM calculated from CMR images correlated well with TDI method. CMR method is independent of angle position and imaging reference frames, and thereby computationally light-weight. They can be derived by post-processing of routine CMR images without additional image acquisition. This shall potentially extend routine CMR’s capability for LV and RV systolic and diastolic function assessment.

P4748 | BEDSIDE
Rapid improvement of symptoms, filling pressures and pulmonary congestion estimated by combined echo and lung ultrasound protocol during early course of AHF treatment

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Introduction: Rapid decline in left side filling pressures (LSFP) during early course of acute heart failure (AHF) treatment could result in rapid improvement of symptoms and pulmonary congestion.

Objectives: To examine the time course of response to treatment in pulmonary congestive AHF patients using a thoracic FAST ultrasound protocol including echo derived left side filling pressures (medial E/e’) combined with lung ultrasound (LUS), and simultaneous symptom assessment.

Methods: We included 70 adult dyspneic patients with a positive thoracic FAST protocol for AHF who were followed up with FAST and VAS scores simultaneously. The FAST protocol was positive if E/e’ was >15 and LUS presented bilateral B lines (BL) or pleural fluid (PF) right sided or bilaterally. Patients were classified as “responders” if they became asymptomatic at rest and capable of walking > 20 meters. LUS was considered normalized when absent of PF and bilateral BL.

Results: 39/70 (56%) of the FAST - positive patients were responders. Responders had a bigger mean change of E/e’ (4.44 vs. 1.10 Ul, p<0.004) and VAS scores (6.28 vs. 4.19 Ul, p<0.002) than non-responders during the whole treatment course. The fastest change among responders occurred during the first 12 hours of treatment (mean Δ E/e’ 2.34 (SD 3.31) and mean Δ VAS 3.74 (SD 3.13)) compared with a mean Δ E/e’ of 1.77 (SD 2.90) and a mean Δ VAS of 2.47 (SD 2.58) during the rest of total hospital stay (p<0.001 for mean Δ Ul hour). The mean time until normalization of LUS was 47.3 hours. Among non-responders, VAS score changed slowly and linearly, and E/e’ very little at all during hospital stay.

Conclusions: Both symptoms and echo derived LSFP improve rapidly among AHF patients. These changes foresee decongestion as measured by normalization of LUS.

P4749 | BEDSIDE
Microvascular function as a link to left ventricular longitudinal deformation capacity in heart transplanted patients

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Background: Microvascular dysfunction and reduced left ventricular (LV) longitudinal myocardial function is common in heart transplanted (HTx) patients and associated with coronary allograft vasculopathy and high rejection burden.

Methods: The aim of the study was to evaluate the influence of microvascular function on LV longitudinal deformation capacity during exercise in stable HTx patients.

Results: Fifty-four HTx patients underwent coronary angiography. We excluded 14 patients due to significant CAV. The remaining 40 HTx patients were randomly assigned to perform age-matched controls underwent comprehensive assessment of microvascular function during rest and symptom-limited semi-supine exercise test with measure of LV longitudinal deformation by 2D speckle tracking echocardiography. We assessed microvascular function by non-invasive Doppler coronary flow velocity reserve (CFVR) and divided patients into two groups: Group A: reduced CFVR < median CFVR and group B: preserved CFVR > median CFVR.

Results: CFVR was significantly lower in the HTX-group compared to controls (2.8±0.6 versus 3.8±0.8, p<0.001), and the HTX-group had significantly reduced exercise capacity compared to healthy controls (102±39 watt versus 179±43 watt, p<0.001). At peak exercise, HTX patients showed significantly lower LV longitudinal myocardial deformation compared to controls, with global longitudinal strain (GLS) of −20±4% versus −25±2%, p<0.001. Diastolic parameters revealed sign of restrictive LV filling in HTX patients with higher E/e’ ratio (p<0.10), a shorter E-deceleration time (p=0.03) compared to controls. The HTX patients with reduced CFVR were in significantly higher NYHA functional class compared to the group with preserved CFVR (p=0.02). During exercise, the HTX-group had significantly reduced exercise capacity compared to healthy controls (102±39 watt versus 179±43 watt, p<0.001). We found a strong correlation between CFVR and peak exercise GLS in HTX patients (r= −0.42 and −0.45, p = 0.031 and 0.034). An higher S:D also correlated with peak exercise capacity compared to healthy controls (102±39 watt versus 179±43 watt, p<0.001) and shorter E-deceleration time (p=0.03) compared to controls.

Conclusion: HTX patients without severe macrovascular CAV had significantly reduced CFVR and reduced LV longitudinal deformation capacity measured by non-invasive Doppler QLS compared to healthy controls. LV longitudinal deformation capacity in addition to NYHA functional class is highly dependent on preserved microvascular function in HTX patients.

P4750 | BEDSIDE
Right to left ventricular interdependence evaluated by the ratio between pulmonary systolic to diastolic time at rest and during exercise in heart failure reduced ejection fraction: clinical insights

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Background: The ratio between the duration of right ventricular (RV) systole and diastole (S:D ratio) has been proposed as an index of RV performance in a pediatric population with pulmonary arterial hypertension in whom it may predict prognosis and functional capacity. In heart failure (HF) S:D may provide relevant insights in the exercise response.

Aim: To analyze the correlation between rest and peak exercise S:D and functional and cardiac parameters in HF/EF.

Methods: 94 HF/EF patients (mean age 66±11 y, male 70%, ischemic etiology 71%, mean LVEF 34±9%) underwent a symptom-limited cardiopulmonary exercise testing (incremental ramp protocol) combined with exercise-echo. RV S:D was assessed by echo at rest and peak exercise.

Results: A good correlation was found between rest and peak S:D and CPET indexes of exercise capacity, such as peak oxygen consumption (VO2) (Spearman’s rho −0.40 and 0.38 respectively, p=0.02 and 0.023) and maximal workload (r=−0.42 and −0.45, p=0.03 and 0.034). An higher S:D also correlated with more impaired ventilatory efficiency or higher VE/VCO2 slope (r=0.49 and 0.32,

Correlation of E/e’ and VAS score.
p<0.019 and 0.024). Looking at echo phenotype, interestingly S-D is associated with parameters of mitral regurgitation (MR) severity, such as effective regurgitant orifice (rho rest 0.63, peak 0.35, p<0.01) and pulmonary artery systolic pressure (PASP, rho rest 0.53, peak 0.35, p<0.01) particularly at rest. S-D also correlated with right RV fractional area change at rest and peak exercise (<0.39 and <0.39, p<0.035 and 0.04).

Conclusions: In HFpEF population the assessment of S-D at rest and peak exercise predicts functional status and is related to more advanced hemodynamic impairment (increased PASP and MR) as expression of more unfavorable ventricular interdependence.

P4751 | BEDSIDE
Impact of persistent pulmonary hypertension on patients with severe aortic valve stenosis following TAVI
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Background: Severe aortic stenosis leads to augmented afterload, changes in cardiac function and often increased systolic pulmonary arterial pressure. The persistence of these changes after surgical aortic valve replacement has been linked to unfavorable outcome. There is a controversy regarding the impact of persistent pulmonary hypertension (PHT) on prognosis of patients undergoing transcatheter aortic valve implantation (TAVI).

Purpose: We sought to investigate the impact of persistent PHT on 3-year all-cause mortality of patients with severe aortic stenosis following TAVI.

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 our institution were prospectively enrolled. Prospectively collected echocardiographic data before and after TAVI were retrospectively analyzed in all patients. Systolic pulmonary arterial pressure was estimated as the sum of the right ventricular to the right atrial gradient during systole and the right atrial pressure. PHT on prognostic of patients undergoing transcatheter aortic valve implantation (TAVI).

Results: Among the 133 patients (mean age: 80±7 years) who were included in the study, the primary clinical endpoint occurred in 22 patients (17%) during a median follow-up period of 3 years. Mean systolic pulmonary arterial pressure was reduced in all patients following TAVI (43±11 versus 40±8mmHg, p<0.001). Mortality rate was higher in patients with persistent PHT compared to patients with normal systolic pulmonary arterial pressure following TAVI (32% versus 10%, p<0.002). Patients that reached the primary clinical endpoint had a higher post-procedural mean systolic pulmonary pressure (44±8 versus 40±8mmHg, p<0.02).

In multivariate regression analysis, persistence of PHT (OR: 3.310, 95% CI: 1.182–9.224, p=0.02) and logEuroSCORE (OR: 1.051, 95% CI: 1.006–1.098, p=0.026) were independent predictors of mortality.

Conclusions: The persistence of pulmonary hypertension post TAVI is associated independently with long term mortality. Further investigation is warranted for the early identification of this population with severe aortic stenosis.

P4752 | BEDSIDE
Statin effects on clinical outcomes in patients with acute myocardial infarction with acute severe systolic heart failure
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Background: The CORONA and the GISSI-HF trials failed to elucidate a beneficial effect of statin treatment in chronic systolic heart failure (HF). But there are lacking data demonstrating statin effects on acute myocardial infarction (AMI) patient with acute severe systolic HF.

Methods: Between 2008 and 2011, 12,557 patients were enrolled in a registry, and patients who had severe left ventricular dysfunction (EF<40%) with AMI were analyzed. They were divided into 2 groups; treated with statin group (n=337) and treated without statin group (n=158). To overcome the differences of baseline characteristics and discharge medication between 2 groups, we performed propensity score matched analysis. And 1-year incidence of major adverse cardiovascular event (MACE) and all-cause mortality were analyzed.

Results: In original cohorts, 1-year composites of MACE (all-cause mortality, myocardial infarction and any revascularization) was similar between 2 groups (1-year MACE-free survival rate [SR] of treated with statin group: 87.1%, 1-year MACE-free SR of treated without statin group: 86.2%, p=0.78). Likewise, 1-year all-cause mortality was not statically different between 2 groups (1-year SR of treated with statin group: 93.8%; 1-year SR of treated without statin group: 90.8%, p=0.42). Propensity-score matching yielded 158 pairs, and in that cohorts, we could obtained comparable results in terms of MACE (1-year MACE-free SR of treated with statin group: 87.2%, 1-year MACE-free survival rate of treated without statin group: 86.2%, p=0.85) and mortality (1-year SR of treated with statin group: 94.0%; 1-year SR of treated without statin group: 90.8%, p=0.51). Cox-regression analysis showed that statin therapy was not an independent predictor for MACE (Hazard ratio [HR] 1.06, 95% CI 0.56–2.03, p=0.85) or all-cause mortality (HR 1.34, 95% CI 0.56–3.17, p=0.42).

Conclusions: Statin did not reduce the MACE or deaths from any cause in AMI patients with acute severe systolic HF.

BASIC MECHANISMS, VENTRICULAR FUNCTION, PROGNOSIS I

P4753 | BEDSIDE
Preserved ventricular-arterial coupling but more myocardial oxygen consumption and less mechanical efficiency in haemodialysis patients
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Purpose: Ejection fraction is limited to assess contractility in haemodialysis (HD) patients due to its slow dependency. This study aimed to elucidate whether there are any differences in load independent cardiovascular parameters among the HD patients and others.

Methods: Echocardiography was performed in patients receiving maintenance HD (HD group, n=210, age 65 yrs, 147 males), hypertension controls (HT group, n=162, age 69 yrs, 114 males) and normotensive controls (NT group, n=126, age 61 yrs, 85 males). End-systolic elastance (Ees) and arterial elastance (Ea) were measured using a noninvasive single beat technique. Ventricular-arterial coupling was calculated as Ea/Ees. Stroke work (SW) and pressure-volume area (PVA) were estimated, and LV mechanical efficiency was expressed as SW/PVA x 100.

Results: A HD group had significantly larger EDV index and LV mass index than either HT or NHT group. Ea tended to be higher, but Ees was significantly higher, in HD than NT controls. These abnormalities led to significantly greater PVA in HD patients, suggesting elevated myocardial oxygen consumption. Although ventricular-arterial coupling did not differ among groups, LV efficiency was significantly reduced in the HD patients among groups. In HD patients, age, diabetic nephropathy, EDV index, Ea, and Ees were independent determinants of worsening LV efficiency after adjusting for confounders (sex, BMI, HD duration, inter-diabetic weight gain, and Kt/V).
Purpose: To determine how LBBB and CRT modifies RV work.

Methods: In 8 anaesthetised dogs, LBBB was induced by radiofrequency ablation, and CRT was applied by pacing the septum and the LV lateral wall. Pressures were measured by micromanometers. LV and RV short-axis diameters and septal and free wall longitudinal segment lengths were measured by sonomicrometry enabling estimation of work as the area of pressure-dimension loops.

Results: LBBB caused marked septal preejection shortening with subsequent rebound stretch (Arrow, Fig.A). Therefore, septal longitudinal work was reduced from 97±49 to 7±60 mmHg*mm (p < 0.01). This was accompanied by an increase of work in the LV lateral wall from 126±97 to 198±113 mmHg*mm, p < 0.001, but LV short-axis work decreased (Fig.B). In the RV, LBBB caused opposite changes with preejection lengthening of the RV short-axis diameter, and an increase in RV short-axis work. However, in the RV free wall LBBB caused a decrease in longitudinal work from 34±16 to 25±16 mmHg*mm, (p < 0.05). CRT essentially normalized the abnormal septal contraction patterns and restored work in both ventricles (Fig.B). LV and RV dP/dtmax were increased by CRT (p < 0.05).

Conclusions: Induction of LBBB caused opposite effects on RV and LV short-axis work due to altered septal motion. There were compensatory changes in work in the free wall of both ventricles. CRT restored LV work, but reduced RV short-axis work. It should be explored if the marked changes in RV work have impact on the effect of CRT in patients with RV failure.

P4757 | BEDSIDE

Kinetic energy patterns: towards quantitative non-invasive measurement of heart failure using magnetic resonance 4-dimensional flow

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Background: Diagnosis of heart failure remains a challenge. Measurements of kinetic energy (KE) of intracardiac blood have the potential to improve the assessment and understanding of heart failure.

Purpose: To compare the left ventricular (LV) KE throughout the cardiac cycle in patients with LV systolic heart failure with healthy controls using cardiac magnetic resonance imaging (CMR).

Methods: Twenty-six patients with systolic heart failure (NYHA class I-IV) and 12 healthy controls underwent CMR including acquisition of four-dimensional phase contrast flow images (4D flow). The LV was manually delineated using Segment v1.9 and ventricular KE calculated as KE=1/2mv^2, summed over all voxels inside the LV.

Results: Patients showed three distinctive KE patterns (Figure 1B-D) unrelated to NYHA classification. 6-minute walk test, echocardiographic measures of diastolic dysfunction. The KE patterns in patients were markedly different from the controls (panel A). Mean KE was slightly higher in the patient group (2.7±1.8 mJ vs 1.8±0.7 mJ, p=0.06), while there was no difference in neither absolute systolic (p=0.54) nor diastolic (p=0.18) KE. However, KE/SV was higher in patients both during systole and diastole (systolic KE/SV: 29.0±19.2 μJ/ml vs 13.4±4.5 μJ/ml, p<0.0001; diastolic KE/SV: 42.5±31.0 μJ/ml vs 16.1±4.7 μJ/ml, p=0.0001). In patients with myocardial infarction, mean KE correlated with percentage scarred myocardium (R^2=0.23, p<0.05), but not when indexed to LV EDV (p=0.67).

Conclusions: Our system could be a powerful clinical tool in managing patients with decompensated HF.

P4756 | BENCH

Computer-controlled infusion system of cardiovascular drugs to automatically optimize hemodynamics in decompensated heart failure

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Purpose: In the management of patients with decompensated heart failure (HF), vasodilators and diuretics are used to relieve congestion. To maintain cardiac output (CO), inotropes are sometimes indicated. These require strict hemodynamic monitoring and frequent adjustments of drug infusion rates, which is difficult and time-consuming, especially in seriously ill patients. To overcome this difficulty, we have developed a computer-controlled drug infusion system for simultaneous control of arterial pressure (AP), CO and pulmonary capillary wedge pressure (PCWP).

Methods: Our system estimates CO (COest) using transthoracic Doppler aortic velocity and peripheral AP contour, and PCWP (PCWPest) from jugular venous pressure corrected by tissue Doppler tricuspid/mitral annulus velocities. Using AP, COest and PCWPest, our system computes arterial resistance (R), stressed blood volume (V) and Frank-Starling slope of left ventricle (S). Our system controls R with nitroprusside (NP), V with furosemide (Fur)/dextran (DEX), and S with dobutamine (DOB), thereby controlling the three variables. In 9 dogs, we created HF by chronic right ventricular tachycardia pacing. We then connected the system to HF dogs, and activated it.

Results: Our system immediately started NP and Fur, and if necessary started DEX/DOB, and optimized R, V and S in 30 minutes. Normalization of R, V and S resulted in restoring normal AP, COest and PCWPest with small deviations from targets values (Figure). Pulmonary artery catheterization confirmed optimization of CO and PCWP from respective baseline values (CO, from 1.3±0.5 to 2.8±0.4 L/min/m2; PCWP, from 28±7 to 14±2 mmHg).

Conclusions: Our system could be a powerful clinical tool in managing patients with decompensated HF.
LVESVi, increase in TAPSE and lowest RAp) (Table 1), and clinical outcomes were most favourable in these patients (Fig. 1).

Conclusion: LBBB and reversal of activation vector post-Biv (evidenced by RV1) are associated with changes in left and right heart function. The latter is associated with better clinical outcomes.

P4758 | BEDSIDE
Acute hemodynamic comparison of biventricular, LV only and multipoint pacing in CRT patients
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Background: In CRT, the comparison of the benefits derived from conventional biventricular vs LV only pacing is still under investigation.

Purpose: Aim of the study was to evaluate the acute effects of different pacing configurations, with and without the adjunctive contribution of Multipoint pacing (MPP), on LV dP/dtmax and QRS narrowing.

Methods: In 31 patients (22 male, 20 LBBB, 18 ICM) 98 measurements (3.2±0.8 pacing sites per patients) were analyzed. The hemodynamic effects of pacing at different sites were evaluated by invasive measurement of LV dP/dtmax at baseline and during different pacing protocol. “LV only MPP” pacing protocol refers to dual bipolar LV pacing. One-way analysis of variance (ANOVA) with repeated measures and with Bonferroni post-hoc testing was applied to evaluate differences in pacing protocols.

Results: Baseline LVdP/dtmax was 985±189 mmHg/s. During the various pacing protocols (LV only, Biventricular, MPP LV only, and MPP BiV) LVdP/dtmax steadily increased, values during LV-MPP being higher than LV-only and values during BiV-MPP being higher than during BiV (panel A). While QRS duration was considerably higher during LV than during BiV pacing, MPP reduced QRS duration during both LV and BiV pacing (panel B).

Conclusions: MPP increased the hemodynamic benefit during both LV only and BiV pacing. This improvement is associated with a reduction in QRS duration.

P4759 | BEDSIDE
Increased galectin-3 was closely associated with arterial wave reflections and provided incremental prognostic value upon natriuretic peptide in patients with acute heart failure
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Background: Galectin-3, a marker of cardiac fibrosis, is an emergent prognostic biomarker in heart failure. However, its associations with hemodynamic parameters and whether it has an incremental prognostic value upon natriuretic peptide in acute heart failure syndrome (AHFS) remains unclear.

Methods and results: Galectin-3 and N-terminal pro-brain natriuretic peptide (NT-proBNP) levels were measured in 125 participants hospitalized due to AHFS (mean age 70.4 years; 82% women). We assessed determinants of increased Galectin-3 using logistic regression model and the relation of Galectin-3 to adverse cardiovascular (CV) outcomes by proportional hazards regression. Measures of hemodynamic parameters by tonometry and thoracic fluid content (TFC) by impedance cardiography were obtained within 24 hours of admission. During a median follow-up of 601 days, 66 adverse events developed. In multivariate model, increased Galectin-3 (>25.9ng/ml) was significantly associated with estimated creatinine clearance with odd ratio (OR) 0.194 (95% confidence interval [CI] 0.101–0.373; p<0.0001) and backward arterial wave reflections (Pb; OR 2.59; 95% CI 1.20–5.05; p=0.002). Elevated Galectin-3 was associated with risk for adverse outcomes after adjustment for clinical variables and NT-proBNP (HR: 3.49; 95% CI: 1.04 to 11.72; p=0.04). Moreover, the addition of Galectin-3 resulted in significant net incremental improvement in risk assessment (net reclassification index 0.514, 95% CI 0.078–0.949, p=0.021).

Conclusion: The association of Galectin-3 with Pb linked increased Galectin-3 with small arteriolar pathology in AHFS. The independent and incremental prognostic value of Galectin-3 upon NT-proBNP lend support to the clinical application of Galectin-3 in the management of AHFS.

P4760 | BEDSIDE
Model of end-stage liver Disease excluding INR (MELD-XI) scoring system provides the additional prognostic information to hyponatremia in patients admitted with acute decompensated heart failure
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Background: Liver dysfunction has a prognostic impact on the outcome of patients (pts) with advanced heart failure. A model of end-stage liver disease excluding INR (MELD-XI), a robust scoring system of liver dysfunction, has been shown to provide prognostic information in heart failure pts. Hyponatremia is also a prognostic marker in heart failure pts. However, there is no information available on the long-term prognostic significance of MELD-XI score in pts admitted with acute decompensated heart failure (ADHF), relating to hyponatremia.

Methods and results: We studied 32 consecutive ADHF pts discharged with survival. MELD-XI score was calculated by the following formula: 5.11ln(bilirubin) + 11.79ln(creatinine) + 9.44. During a follow-up period of 5.0±4.3 yrs, 75 pts had cardiovascular death (CVD). At multivariate Cox analysis, MELD-XI score
Impact of elevated end-diastolic pulmonary regurgitation gradient on worse clinical outcome in patients with acute heart failure

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Background: Echo-Doppler end-diastolic pulmonary regurgitation (EDPR) gradient (≥ 8mmHg) is associated with poor clinical outcomes in patients with acute heart failure (AHF). However, the prognostic significance of EDPR gradient in HF patients has not been elucidated.

Purpose: To evaluate the prognostic impact of EDPR gradient in HF.

Methods: 477 consecutive patients with AHF in our prospective registry were examined. Those without accessible EDPR gradient data on discharge were excluded. Finally, 454 patients were examined and divided into two groups according to EDPR gradient.

Results: In multivariate Cox proportional hazard model, EDPR was the strongest predictor for mortality hazard ratio [HR] (95% CI) 0.86 (0.75-0.97), p=0.004 among other PPFA. Patients with higher EDPR gradient (>8mmHg) had higher mortality than those with lower EDPR gradient (Figure). After adjustment for potential confounders based on the comparison between lower and higher EDPR, including age, sex, chronic kidney disease, systolic blood pressure (SBP), left ventricular ejection fraction (LVEF), and tricuspid regurgitation pressure gradient, EDPR gradient was an independent predictor of adverse events (HR 1.19, 95% CI 1.02-1.42, p=0.026) among variables including age, sex, chronic kidney disease, SBP, LVEF, and tricuspid regurgitation pressure gradient.

Conclusions: The prognostic impact of EDPR gradient is significant in patients with AHF.

Figure 1

Conclusions: A MELD-XI scoring system could provide the additional long-term prognostic information to hyponatremia in ADHF pts.

P4761 | BEDSIDE
Prognostic impact of plasma phospholipid fatty acid composition and dihomo-gamma-linoleic acid level in patients with acute heart failure

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Background: Malnutrition is an important determinant of poor clinical outcomes in patients with heart failure (HF). Recently, plasma phospholipid fatty acid (PPFA) composition was reported to be altered and especially, the dihomo-gamma-linoleic acid (DHGL) was decreased accompanied with reduced delta-6-desaturase activity in lean HF patients.

Purpose: To investigate the PPFA composition and its impact on clinical outcomes in HF.

Methods: 477 consecutive patients with acute HF (AHF) in our prospective registry were examined. Those without accessible PPFA data on admission were excluded. Finally, 454 patients were examined with median follow-up of 205 (IQR 26-455) days.

Results: In multivariate Cox proportional hazard model, DHGL was the strongest predictor for mortality [HR 0.87 per 1mmol/L, p=0.007] among other PPFA. Patients with lower DHGL had higher mortality than those with higher DHGL (Figure). After adjustment for potential confounders based on the comparison between lower and higher DHGL, including age, serum albumin, creatinine and plasma brain natriuretic peptide levels, and prevalence of statin use, the HR for DHGL was 0.94 (95% CI 0.88-0.98, P<0.001). Furthermore, patients with lower DHGL had higher prevalence of jugular vein distention (P<0.02) and edema of the lower extremities (P<0.01), higher serum bilirubin level (P<0.01), lower serum total cholesterol (P<0.01) and albumin (P<0.01) levels, and lower body mass index (P<0.01) and nutritional risk index (P<0.01) than those with higher DHGL.

Conclusions: Lower plasma DHGL was an independent determinant of mortality in association with right HF sign and malnutrition, suggesting plasma DHGL could be a novel biomarker for risk stratification in AHF patients.

P4762 | BEDSIDE
Prognostic role of growth differentiation factor 15 (GDF-15) in obese patients with systolic heart failure (HF)

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Background: BNP is an established biomarker in patients with HF with excellent predictive power for outcomes. However, obese individuals have generally lower levels of BNP and this may limit its performance. GDF-15 is a new biomarker in HF and its prognostic utility is being investigated. The purpose of this study was to analyze predictive power of BNP and GDF-15 for total mortality in a cohort of HF patients and separately in obese (BMI>30) individuals.

Methods: The prognostic power of BNP, GDF-15 and other parameters, such as routine laboratory test results and echocardiographic and clinical findings was analyzed in a cohort of 290 HF patients (61±10 yrs, LVEF 25±5%, 58% with CAD, 92% on beta-blockers, 97 obese). Patients scheduled for heart transplantation were excluded.

Results: All HF patients were prospective followed for 1283±676 days. A total of 137 patients died during follow-up. Obese patients had lower levels of BNP (511.9±81.9 vs. 917.5±57.9 ng/L, p<0.0001) than non-obese subjects (BMI<30) but similar levels of GDF-15 (1855.5±94.7 vs. 1792.6±139.0 ng/L, p=n.s.). In Cox univariate analysis, systolic blood pressure (SBP), LVEF, furosemide daily dose, NYHA class, sodium level, age, diabetes, resting heart rate, estimated glomerular filtration rate, BNP and GDF-15 were significant predictors of death. In a multivariate analysis encompassing all these variables, only BNP (HR 1.04 per each 100 ng/L, p=0.003) GDF-15 (HR 1.02 per each 100 ng/L, p=0.03), SBP (0.95 per 5mmHg, p=0.04) and sodium (HR 0.90 per 1 mmol/L, p=0.008) were independent predictors of mortality. When this multivariate model was applied to obese patients only, BNP and SBP were no longer significant parameters; only sodium (HR 0.87 per 1mmol/L, p=0.007) and GDF-15 (HR 1.04 per 100 ng/L, p=0.008) had significant predictive power.

Conclusions: GDF-15 and sodium have significant predictive power for all-cause mortality in obese HF patients.
BASIC MECHANISMS, VENTRICULAR FUNCTION, PROGNOSIS II

P4764 | BEDSIDE
Defining prognosis in patients with advanced heart failure
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Introduction: Patients (pts) with advanced heart failure (AHF) constitute a special population of cardiac failure pts, with very specific issues and a particular worrisome prognosis.

Aim: Define predictors of prognosis in the particular case of AHF.

Methods: Retrospective, observational study of pts with AHF with post-capillary reactive group 2 Pulmonary Hypertension (PH), on optimal medical therapy (including sildenafil 20 mg tid), referred for heart transplant (HTx) between 2004 and 2014. Clinical, laboratory and hemodynamic data were evaluated. Primary endpoints were time to all-cause death, HTx and hospitalization for HF after reference to HTx. Composite endpoints included: death or hospitalization, death or HTx and triple endpoint.

Results: A population of 107 pts were studied, with mean age of 55±11 years, 73% were male. Half of the patients were in NYHA class IV, with median BNP 605 (IQR 665) pg/dL and median peak VO2 15.6 (IQR 15) mL/min. Hemodynamic baseline parameters: mean pulmonary artery pressure (mPAP) 45 (IQR 14) mmHg, pulmonary capillary wedge pressure (PCWP) 27 (IQR 13) mmHg, CI 1.8 (IQR 0.7) mL/min/m², PVR 5.5 (IQR 3.8) Wood units, TPQ 17 (IQR 6) mmHg. During follow-up, half of the group had at least one hospitalization during this period, 33.6% underwent HTx and 22.4% died (median days to follow-up: 1658). NYHA functional class did not impact on the prognosis of these pts. However, after beginning of sildenafil therapy this parameter predicted the occurrence of hospitalization (p<0.001). In this specific population of HF pts, BNP was predictor of the composite endpoint death or HTx (p=0.002, HR 1.0; IC 95% 1–1.001). Improvement in functional capacity as predicted by increase in maxVO2 reduced the probability of hospitalization for HF pre-decompensation (p=0.04, HR 0.88; IC 95% 0.78–0.99). With respect to hemodynamic parameters (using univariate Cox Regression analysis) systemic diastolic arterial pressure predicted all-cause death (p=0.035, HR 0.96; IC 95% 0.92–0.99), Cardiac index predicted evolution for HTx (p=0.043, HR 0.47; IC 95% 0.23–0.99). Regarding composite endpoint of death or HTx, systemic hemodynamic profile was determinant: mean systemic arterial pressure (p<0.001, HR 0.96; IC 95% 0.94–0.98), systemic systolic arterial pressure (p=0.006, HR 0.98; IC 95% 0.94–0.99) and systemic diastolic arterial pressure (p=0.001, HR 0.96; IC 95% 0.94–0.99).

Conclusion: AHF is a terminal morbid condition with high index of adverse events. However, there are prognostic predictors which might help improving management of these pts and to increase their survival.

P4765 | BEDSIDE
Elderly heart failure with preserved ejection fraction fraction patients showed different predictors for cardiovascular mortality than younger counterparts
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Background and purpose: Heart failure with preserved ejection fraction (HF-PEF) has been shown to be more common among the elderly population. Nevertheless, little is known about the clinical characteristics and outcomes specific for this population.

Methods: We retrospectively reviewed 1,940 patients who had their first heart failure admission to our institution between January 2005 and April 2012. Clinical characteristics and outcomes of patients who were ≥70 years of age and had HF-PEF, as defined by left ventricular ejection fraction (LVEF) >40%, were compared to those who were <70 years of age. Parameters predictive of cardiovascular mortality were studied in a Cox-regression model.

Results: Among the 569 patients with HFPEF, 109 (19.2%) were ≥70 and 460 (80.8%) were ≥70 years old. Compared with those who were <70, patients who were ≥70 were more likely to be female (60.9% vs 46.8%, p<0.001) and have hypertension (75.4% vs 56.9%, p<0.001), but less likely to have diabetes (35.9% vs 49.5%, p<0.01). At a mean follow-up of 35.8±30.2 months, 175 (38.0%) of those who ≥70 years old and 44 (40.4%) of those who were <70 years old died, of whom 12 (24.3%) and 20 (18.3%) of them died of cardiovascular causes. Regarding cardiovascular mortality (log rank test p=0.05). Multivariate model showed that age (HR 1.88 per decade, 95% CI 1.45–2.43, p=0.006), LVEF <50% (HR 0.50, 95% CI 0.21–1.14), p=0.08), and systolic blood pressure on admission (HR 0.992, 95% CI 0.986–0.999, p=0.02) and aldosterone antagonist (HR 5.79, 95% CI 2.09–16.03, p=0.001) independently predicted cardiovascular mortality among those who ≥70 years old, while only smoking history (HR 3.34, 95% CI 1.39–8.03, p=0.007) was found to be predictive of cardiovascular mortality among those who were <70 years old.

Conclusion: Elderly patients ≥70 years of age who had HFPEF showed similar survival to but different predictors for cardiovascular mortality than their younger counterparts, reflecting potentially different contributing factors to cardiovascular mortality between the two groups of patients. Development of risk model that assesses clinical risk factors and effect of treatment specific for this group of patients can improve their management.

P4766 | BEDSIDE
Regression of sokolow-lyon voltage is associated with higher incidence of cardiac events in patients with chronic heart failure
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Background: Left ventricular hypertrophy (LVH) predicts a new onset of heart failure in hypertensive patients. Sokolow-Lyon (SL) voltage is an easily measured electrocardiographic parameter for assessing LVH. However, the impact of SL voltage for the prognosis in chronic heart failure (CHF) due to LVH remains to be determined.

Method and results: We performed standard 12-lead electrocardiography and calculated SL voltage in consecutive 303 CHF patients with echocardiography. LVH. SL voltage was positively correlated with left ventricular mass index (LVMI) (R=0.37, p<0.0001). However, SL voltage was significantly decreased with advancing New York Heart Association functional class. During median follow-up period of 467 days, there were 100 major adverse cardiac events (MACE). Multivariate Cox proportional hazard analysis showed that SL voltage was an independent predictor of cardiac events (Hazard ratio [HR]: 0.82, 95% confidence interval [CI]: 0.70–0.96, p=0.01). Moreover, patients were divided into two groups according LV geometry defined as follows: concentric hypertrophy (high relative wall thickness [RWT]); and eccentric hypertrophy (low RWT). Multivariate Cox proportional hazard analysis demonstrated that SL voltage was an independent predictor of cardiac events in patients with eccentric hypertrophy (HR: 0.79, 95% CI: 0.62–0.96, p=0.03). In contrast, there was no association between SL voltage and MACEs in patients with concentric hypertrophy (HR: 1.10, 95% CI: 0.96–1.24, p=0.14), which means that regression of SL voltage is associated with a higher incidence of MACEs among CHF patients with LV eccentric hypertrophy.

P4767 | BEDSIDE
Soluble ST2 predicts cardiovascular events, infectious and all-cause mortality in diabetic hemodialysis patients
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Background: Soluble suppression of tumorigenesis 2 (sST2) has emerged as a strong prognostic biomarker in patients with underlying cardiovascular (CV) disease. Enlarged kidney disease patients are at high mortality risk due to CV events and infections but the predictive value of sST2 in these patients is unknown.

Objective: The aim of the present study was to investigate the effect of plasma concentrations of sST2 on CV events, all-cause death and death due to infections in diabetic hemodialysis patients.

Methods: We analyzed sST2 concentrations in plasma samples of 1196 diabetic hemodialysis patients who participated in the German Diabetes and Dialysis Study (4D Study). Hazard ratios (HR) for pre-specified, adjudicated endpoints: sudden cardiac death (HR: 0.27, 95% CI: 0.10–0.72), death due to heart failure: HR: 0.49; myocardial infarction (fatal and non-fatal): HR: 0.52, stroke (fatal and non-fatal): HR: 0.64; combined cardiovascular events (CV death, stroke, myocardial infarction): HR: 0.44; death due to infections: HR: 0.56; all-cause mortality: HR: 0.56) were determined according to sST2 levels at baseline by Cox proportional hazards regression analysis. The Presage ST2 assay was used for measurement of sST2 concentrations.

Results: Patients (mean±SD; age: 66±8.3 years, 54% male) had a median sST2 of 25 ng/ml (interquartile range, 20.1–32.6) and were followed up for 4 years. After adjustment for possible confounders, patients with sST2 concentrations in the highest quartile compared to the lowest showed a more than two fold increased risk of sudden cardiac death (hazard ratio [HR]: 2.24 [95% confidence interval (CI): 1.33–3.77]), a more than 3 fold increased risk of death due to heart failure
P4768 | BESIDE
Low plasma albumin at admission is associated with worse outcomes in cardiacogenic shock

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Aims: In this cohort of diabetic hemodialysis patients, high concentrations of sST2 were a strong predictor of fatal and non-fatal CV events, death due to infections and all-cause mortality.

Acknowledgement/Funding: Present ST2 assays were provided by Critical Diagnostics.

P4770 | BESIDE
Slovak acute heart failure survey II - predictors of in-hospital mortality

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Purpose: To identify predictors of in-hospital mortality in a non-selected population of pts hospitalised with AHF.

Methods: Among patients hospitalised with AHF during 2013, we identified patients hospitalized between January 1st and December 31th.

Materials and methods: We excluded patients with a history of heart transplantation, ventricular fibrillation, primary or secondary prevention of heart failure.

Results: During the inclusion period, 940 patients were evaluated. The median age was 70 (interquartile range 60–80) years. The majority of patients were male (70%). The most frequent comorbidity was hypertension (59.9%), followed by diabetes (42.8%), chronic obstructive pulmonary disease (34.6%), and ischemic heart disease (27.7%). The in-hospital mortality rate was 9.6%.

Conclusions: This study showed that age, gender, and comorbidities such as hypertension, diabetes, chronic obstructive pulmonary disease, and ischemic heart disease were significant predictors of in-hospital mortality in patients hospitalised with AHF.

P4771 | BESIDE
Comparison of characteristics and outcomes in patients with HFpEF and HFrEF: result from KorAHF registry

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Purpose: The aim of the study is to investigate the differences in short-term outcomes and predictors of in-hospital mortality between HFrEF and HFpEF in Asian population.

Methods: We analyzed data from the Korean Acute Heart Failure (KorAHF) which is a nationwide prospective registry of patients hospitalized for acute heart failure syndrome in ten regionally-representative tertiary university hospitals in Korea. Clinical characteristics, all-cause in-hospital mortality and predictors of mortality were compared between patients with HFrEF (LVEF<50%) and HFpEF (LVEF>40%).

Results: In total, 5,627 patients were included in the analysis. The median age of patients was 72 years. The majority of patients were male (61%). The most common comorbidity was hypertension (64% vs 56%) and atrial fibrillation (36% vs 23%).

Conclusions: In-hospital mortality in unselected AHF pts remains high. Short term mortality can be predicted by easily available variables. Referral to heart failure centre should be considered in pts with predictors of higher in-hospital mortality for advanced treatment options assessment.
influence of old age (>70 years), pulmonary congestion, poor functional capacity (NYHA functional class III or IV) and Q wave in electrocardiogram on the risk of mortality was significantly greater in HFrEF than HfPef. In contrast, the influence of lower BMI (<25 kg/m²) on the risk of mortality was significantly greater in HFrEF than HfPef.

Conclusions: Compared with HfPef, HFrEF showed better in-hospital outcome and different predictors of mortality.

P4772 | BEDSIDE
Hepatic dysfunction - an important prognostic indicator for mortality in heart failure; a population based study
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Introduction: Hepatic dysfunction has always been considered as a sequel of chronic heart failure (CHF), however there has been recent interest in it being used as a marker of disease severity in CHF. Previous studies have demonstrated this among patients in clinical trial settings but no population based studies have been conducted thus far. We aim to determine the impact of hepatic dysfunction on a composite of cardiovascular (CV) mortality and heart failure hospitalization in patients treated for CHF.

Methods: We analysed data from the Systems Biology Study to Tailored Treatment in Chronic Heart Failure (BIOSTAT-CHF) database which prospectively tracks treatment, comorbidity, blood investigations, hospitalization and death information of patients with heart failure from a single region in Scotland. Cox proportional hazard models were used to assess the prognostic impact of liver dysfunction on heart failure outcomes, while controlling for covariates like treatment regime, previous history of myocardial infarctions, atrial fibrillation, renal disease and CHF duration.

Results: Out of a total 1805 patients, there were 1200 (66.5%) males, with a mean age of 73.6 ± 10.7 years, and mean duration of HF 39.9 ± 54.1 months with a total of 414 CV death or heart failure hospitalization. We found low serum albumin levels (less than 30 g/L) to be an independent predictor of CV death or hospitalization with a hazard ratio of 2.05 (95% CI 1.51–2.79, p < 0.001). Similarly, elevated bilirubin (more than 20 μmol/L) and alanine aminotransaminase (ALT) (more than 35 U/L) increased the risk of outcomes by 1.97 (95% CI 1.56–2.50, p < 0.001) and 1.31 (95% CI 1.04–1.66, p = 0.024) respectively.

Conclusions: The mechanisms by which hepatic derangement can worsen CHF is beyond the scope of this study. Our findings demonstrate lower serum albumin, elevated total bilirubin and ALT were independent predictors of CV death or hospitalization among ambulatory CHF patients.

Acknowledgement/Funding: European commission Seventh Framework Programme (FP-7)

P4773 | BEDSIDE
Pre-operative serum sodium and atrial fibrillation predict improvement in cognitive function following left ventricular assist device implantation
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Cognitive impairment is common in heart failure patients and can negatively impact quality of life, functional capacity, and survival. Though the effects of hepatic dysfunction on cognitive function (CF) remain poorly investigated, a recent pilot study indicated improvement following left ventricular assist device (LVAD) implantation. We investigated pre-operative predictors of improvement in CF following LVAD implantation.

The Montreal Cognitive Assessment (MoCA) was used to evaluate CF in 56 patients prior to and 8 months after LVAD implantation. Demographic, hemodynamic, echocardiographic, and laboratory data were collected concurrently. Patients were divided into two groups - those with improved and non-improved MoCA scores.

Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Non-improved MoCA (n=20)</th>
<th>Improved MoCA (n=36)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-Implant MoCA</td>
<td>25.0±2.7</td>
<td>22.8±3.7</td>
<td>0.049</td>
</tr>
<tr>
<td>Post-Implant MoCA</td>
<td>23.5±3.5</td>
<td>25.0±3.5</td>
<td>0.008</td>
</tr>
<tr>
<td>Age (years)</td>
<td>65.05±12.03</td>
<td>65.76±14.05</td>
<td>0.850</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>30.66±1.78</td>
<td>27.67±5.86</td>
<td>0.099</td>
</tr>
<tr>
<td>Mean pulse pressure (mmHg)</td>
<td>90.9±14.4</td>
<td>37.95±10.74</td>
<td>0.038</td>
</tr>
<tr>
<td>Sodium (mEq/L)</td>
<td>135.7±3.52</td>
<td>133.2±14.57</td>
<td>0.011</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>3.25±0.50</td>
<td>2.93±0.47</td>
<td>0.040</td>
</tr>
<tr>
<td>BNP (ng/mL)</td>
<td>350.55±23.32</td>
<td>854.74±60.23</td>
<td>0.020</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>4 (20%)</td>
<td>46 (17.1%)</td>
<td>0.047</td>
</tr>
</tbody>
</table>

When the cohort was subdivided based on change in MoCa score, 20 (35.7%) patients did not improve at follow up while 36 (64.3%) improved. Within these groups, those with improved MoCA had significantly lower MoCA pre-implant than those who did not improve postoperatively (22.8 vs 25.0, p = 0.049). Mean pulmonary artery pressure, serum sodium, albumin, B-type natriuretic peptide (BNP), and incidence of atrial fibrillation (A. Fibr.) indicated a trend towards a more advanced disease state in the group whose MoCA scores improved compared to those in the non-improved group (Table 1). Noting these worsened clinical indicators in the group with improved MoCA, a multivariate logistic model was tested using these variables. Pre-operative serum sodium levels and history of A. Fibr. were found to be independent predictors for improvement in MoCA score after LVAD implantation (OR: 0.84 CI: 0.71–0.99 p=0.02; OR: 0.28 CI: 0.08–1.02 p=0.05, respectively).

HAEMODYNAMICS AND AUTONOMIC NERVOUS SYSTEMS IN HYPERTENSION

P4774 | BEDSIDE
Impact of hypertension on myocardial salvage assessed by cardiac magnetic resonance in patients with reperfused acute myocardial infarction
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Introduction: Controversy exists on whether hypertension has a cardioprotective effect in patients with acute myocardial infarction (MI). We sought to assess the influence of hypertension on cardioprotective effects, measured as myocardial salvage index (MSI) by using cardiac magnetic resonance (CMR), in patients with reperfused acute MI.

Methods: A total of 31 patients with acutely reperfused first ST-segment elevation MI caused by proximal coronary culprit lesions and pre-procedural Thrombolysis in Myocardial Infarction (TIMI) flow 0/1 underwent CMR within 2 weeks. Area at Risk (AAR), MI size and MSI were determined by T2-weighted and late gadolinium enhanced CMR.

Results: AAR, MI size normalized by LV mass was 36±14% and 27±15%, respectively (P<0.05), yielding a mean MSI of 28±20% (range 0–69%). Seventeen patients (55%) had hypertension. Hypertensive patients had significantly lower MSI than non-hypertensive patients (20±16% vs 38±20%, p<0.05). However, there was no significant differences in AAR and MI size between both groups (37±15% vs 35±15%, p=0.7, 30±15% vs 23±14%, p=0.2). Univariate analysis demonstrated that MSI was associated with MI size. TIMI flow, LV mass index (LVMi) and peak CPK level (r=−0.38, 0.62, −0.40, −0.46, respectively, all p<0.05). The presence of hypertension was a significant predictor of lower MSI (b coefficient=−0.34, p<0.05).

Conclusion: The current results demonstrated that myocardial salvage was attenuated in hypertensive patients with acute MI and inversely related with LVMi. Thus, cardioprotective effects may be impaired in patients with hypertension through increased LV mass.

P4775 | BEDSIDE
Association between diffuse myocardial fibrosis and decreased myocardial strain in hypertensives with preserved ejection fraction. A pilot study with cardiovascular magnetic resonance
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New cardiovascular magnetic resonance (CMR) T1 mapping sequences have been developed that can be applied to quantify diffuse myocardial fibrosis. Novel analysis softwares allow for the accurate and reproducible measurement of myocardial strain. We aimed to use these two new developments in a pilot study in order to assess the association between presence of diffuse fibrosis and changes in myocardial strain.

Methods: 15 hypertensive patients (HT, 51±7ys, 12 males) with preserved ejection fraction and 15 controls (NT, 49±13yrs, 9 males) underwent a CMR protocol at 3T that included black blood sequences, cine sequences in the 2,3,4-chamber views and short axis series with typically 40 phases for each acquisition, T1-mapping with two MOLLI acquisitions (3–3-5), before and 15 min after administration of gadolinium (0.1mM/kg), and late gadolinium sequences. The current results demonstrated that myocardial salvage was at-tenuated in hypertensive patients with acute MI and inversely related with LVMi. Thus, cardioprotective effects may be impaired in patients with hypertension through increasing LV mass.
diffuse myocardial fibrosis. Also, longitudinal and radial global myocardial systolic strain and strain rate, as well as epicardium-endocardium strain gradient were measured.

**Results:** All subjects had preserved systolic function. Global longitudinal and radial strain (GLS, GRS), longitudinal strain rate (GLSR) and precontrast T1 were all lower in HT, while radial strain gradient between subendocardium and subepicardium (GRS endo-epi) was increased in HT and there was a trend towards increased ECV in HT. There was a significant inverse correlation of GLS and GRS with ECV, and of radial strain rate (GRSR) with ECV (all p < 0.05).

**Conclusion:** In this study we have found that there is an inverse correlation between global strain, a sensitive indicator of regional contractility, and myocardial extracellular volume fraction, a marker of diffuse fibrosis. This finding may have implications for early diagnosis of target organ damage in hypertensive patients.

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**P4777 | BEDSIDE**

**Comparison of methodology to evaluate arterial stiffness in elderly males**

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**Background:** The Sphygmocor device (S) is the established method for evaluating arterial stiffness. A new cuff-based method (Vicorder [V]) shows promise, but large comparative studies are lacking, especially in the elderly where arterial stiffening is most prevalent.

**Purpose:** To assess the ability of S and V to obtain pulse wave velocity (PWV) measurements and compare data from both devices.

**Methods:** We studied 1720 men in the British Regional Heart Study. Carotid (C) to femoral (F) PWV measurements were derived from path length (PL)/transit time (TT) for both devices. For S, PL was calculated as distance from: (stenotic notch [SN] to F) minus (SN to C) for F. PL = distance from SN to centre of thigh cuff. TT with S (TTs) was calculated as time from: (ECG R wave to F pulse wave onset) minus (ECG R wave to C pulse wave onset). TTv was measured between the onset of the C and F pulse waves in the same cardiac cycle.

**Results:** Acceptable PWV data were obtained with S (PWVs) in 1180 men (69%) and 1577 (92%) with V (PWVv). In 1122 men with both PWVs and PWVv, mean PWVs was > PWVv (10.3±2.6 m/s vs 10.0±1.7 m/s; p < 0.001) and values were positively correlated (r=0.519, P<0.001). Figure 1A. However, S tended to give faster readings than V at higher PWV and slower readings at lower PWV. The slope of the regression line for FT Ts vs TTv was steeper than for C TTs vs TTv faster readings than V at higher PWV and slower readings at lower PWV. The positively correlated (r=0.519, P<0.001).

**Conclusion:** In this study we have found that there is an inverse correlation between global strain, a sensitive indicator of regional contractility, and myocardial extracellular volume fraction, a marker of diffuse fibrosis. This finding may have implications for early diagnosis of target organ damage in hypertensive patients.

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**P4778 | BEDSIDE**

**The relationship between right ventricular mechanics and different geometric patterns according to the updated criteria: findings from the hypertensive population**


**Purpose:** To investigate right ventricular (RV) mechanics in hypertensive patients with different geometric patterns by using two-dimensional (2DE) strain analysis.

**Methods:** This cross-sectional study included 184 hypertensive subjects. All subjects underwent complete 2DE examination. We applied the new Dallas classification of LV geometry that considers LV mass index, LV end-diastolic diameter and relative wall thickness. According to this classification all subjects were divided into the six different groups: normal LV geometry, concentric remodeling, eccentric non-dilated LV hypertrophy (LVH), concentric LVH and dilated LVH.

**Results:** Global RV longitudinal strain progressively reduced from the patients with normal LV geometry to the subjects with concentric-dilated LVH. RV global systolic and early diastolic strain rates were lower in the subjects with concentric, dilated and concentric-dilated LVH than in other groups (Table). However, the difference was more pronounced in cases of eccentric diastolic strain rate that gradually decreased from the normal LV geometry pattern to concentric, dilated, concentric-dilated LVH. On the other hand, late diastolic strain rate was significantly lower in the eccentric non-dilated LVH group.

**Conclusion:** In this study we have found that there is an inverse correlation between global strain, a sensitive indicator of regional contractility, and myocardial extracellular volume fraction, a marker of diffuse fibrosis. This finding may have implications for early diagnosis of target organ damage in hypertensive patients.

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**Table 1. Reservoir pressure parameters**

<table>
<thead>
<tr>
<th>Aortic position</th>
<th>Systolic pressure (mmHg)</th>
<th>Diastolic pressure (mmHg)</th>
<th>Reservoir pressure integral (mmHg s)</th>
<th>Maximum reservoir pressure (mmHg)</th>
<th>Rate (s⁻¹)</th>
<th>kₚ (ms⁻¹)</th>
<th>kᵩ (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascending aorta</td>
<td>131.6 (27.4)</td>
<td>65.5 (11.5)</td>
<td>20 (6.2)</td>
<td>49.2 (14.5)</td>
<td>5.9 (2.8)</td>
<td>15.5 (4.7)</td>
<td>2.6 (0.9)</td>
</tr>
<tr>
<td>Aortic arch</td>
<td>130.8 (25.4)</td>
<td>65.4 (10.9)</td>
<td>19.6 (6.3)</td>
<td>47.8 (13.7)</td>
<td>6.0 (2.8)</td>
<td>13.9 (3.8)</td>
<td>2.6 (0.8)</td>
</tr>
<tr>
<td>Daphragm</td>
<td>140.4 (20.5)</td>
<td>65.9 (18.3)</td>
<td>19.7 (6.5)</td>
<td>48.9 (11.6)</td>
<td>7.0 (2.8)</td>
<td>12.1 (2.3)</td>
<td>2.8 (0.7)</td>
</tr>
<tr>
<td>Renal arteries</td>
<td>128.7 (23.2)</td>
<td>67.2 (9.7)</td>
<td>18.5 (5.7)</td>
<td>46.9 (12.2)</td>
<td>7.6 (2.7)</td>
<td>10.4 (1.5)</td>
<td>2.9 (0.7)</td>
</tr>
<tr>
<td>Bifurcation</td>
<td>141.3 (24.8)</td>
<td>67.6 (18.3)</td>
<td>18.3 (5.7)</td>
<td>46.9 (12.3)</td>
<td>8.2 (2.8)</td>
<td>54.6 (2.5)</td>
<td>9.7 (1.4)</td>
</tr>
</tbody>
</table>

kᵩ, systolic pressure constant; kₚ, diastolic pressure constant. *P<0.01; **P<0.001.

**Table 2.** Normal LV geometry remodeling Concentric LVH Dilated LVH Dilated LVH

| Longitudinal RV strain (%) | -24.7±3.3 | -20.3±3.5 | -21.3±2.3 | -20.1±2.8 | -0.001 |
| RV systolic pressure rate (rate s⁻¹) | -1.5±0.3 | -1.5±0.3 | -1.4±0.4 | -1.2±0.4 | 0.001 |
| RV early diastolic strain rate (rate s⁻¹) | 1.8±0.4 | 1.7±0.4 | 1.5±0.3 | 1.4±0.3 | 0.001 |
| RV late diastolic strain rate (rate s⁻¹) | 1.6±0.4 | 1.6±0.4 | 1.8±0.5 | 1.9±0.5 | 2.6±0.4 | 0.002 |

LV, left ventricle; LVH, left ventricular hypertrophy; RV, right ventricle.

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**Abstract P4777 – Table 1. Reservoir pressure parameters**

<table>
<thead>
<tr>
<th>Aortic position</th>
<th>Systolic pressure (mmHg)</th>
<th>Diastolic pressure (mmHg)</th>
<th>Reservoir pressure integral (mmHg s)</th>
<th>Maximum reservoir pressure (mmHg)</th>
<th>Rate (s⁻¹)</th>
<th>kₚ (ms⁻¹)</th>
<th>kᵩ (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascending aorta</td>
<td>131.6 (27.4)</td>
<td>65.5 (11.5)</td>
<td>20 (6.2)</td>
<td>49.2 (14.5)</td>
<td>5.9 (2.8)</td>
<td>15.5 (4.7)</td>
<td>2.6 (0.9)</td>
</tr>
<tr>
<td>Aortic arch</td>
<td>130.8 (25.4)</td>
<td>65.4 (10.9)</td>
<td>19.6 (6.3)</td>
<td>47.8 (13.7)</td>
<td>6.0 (2.8)</td>
<td>13.9 (3.8)</td>
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</tbody>
</table>
toxic strain rate was increased in subjects with concentric and dilated-concentric LVH in comparison with normal LV geometry patients (Table). Nevertheless, statistically significant importance was found only in comparison between normal LV geometry subjects and concentric LVH individuals.

Conclusion: RV myocardial deformation in hypertensive patients is significantly impaired by LV geometry. Concentric and eccentric LVH patterns have the greatest unfavorable effect on LV mechanics. The new classification of LV geometry provides valuable and comprehensive information about RV mechanical function in hypertensive population.

P4779 | BEDSIDE
Relationship between left ventricular systolic stress and systolic strain or strain rate by speckle tracking echocardiography with high volume rate
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Purpose: Left ventricular hypertrophy (LVH) is known as a compensative mechanism of LV against pressure overload to reduce LV stress and maintain systolic pump function of LV. Significant increase may be more deteriorated by pressure overload in hypertension (HTN). However, the relationship between LV systolic stress and LV peak systolic stress or strain or strain rate (SR) assessed by 3-dimensional speckle tracking echocardiography (3D-STE) as an index that reflects contractility has not been examined. Therefore, we examined the relationship between LV systolic stress and strain or SR in HTN using one-beat real-time 3D-STE with high volume rates and sought to evaluate the impact of LV systolic stress on contractility in HTN.

Methods: A total of 168 subjects (114 patients with HTN and 54 controls (age 69±9) were enrolled. Patients with HTN were divided into 3 groups: 50 HTN patients without LVH (age 70±9), 40 HTN patients with LVH (age 69±6) and 24 patients with hypertensive heart failure (HHF) (age 71±11). We examined LV longitudinal, circumferential and radial peak strain at endocardium and SR during systole at both endocardium and epicardium by the novel 3D-STE with 60–80 vps. LV systolic stress was calculated as LV end systolic radius x systolic blood pressure/LV end systolic thickness.

Results: LV systolic stress in 3 directions and SR at endocardium were reduced in HTN and further reduced in HHF (longitudinal stress: control; +19±4, HTN without LVH: +17±4, HTN with LVH: +15±4, HHF: +13±3*, P<0.05 vs control). There was a significant correlation between LV systolic stress and longitudinal and circumferential peak stress (r=0.17, P=0.031 and r=0.19, P=0.014, respectively) and between LV stress and LV SR during systole at both endocardium and epicardium in total subjects (r=0.28, P<0.001 and r=0.20, P=0.01, respectively).

There was a significant correlation between LV systolic stress and circumferential stress in HHF (r=0.48, P=0.018), but no relation between stress or longitudinal or radial strain. Significant correlation was not found between LV stress and LV strains in 3 directions in controls or HTN.

Conclusion: LV contractility assessed by LV strain and SR was reduced associated with increased LV stress. Only LV circumferential strain was reduced in HHF associated with further reduction in longitudinal and radial strain, suggesting that LV longitudinal and radial strain had been already deteriorated and the beginning of reduction in circumferential strain after deterioration of longitudinal and radial contractility may be responsible for HHF.

P4780 | BEDSIDE
Myocardial fibrosis correlated with sub-endocardial but not global circumferential strain in hypertension
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Background: Hypertension causes myocardial fibrosis. However, effects of myocardial fibrosis on circumferential deformation of myocardium have not been well elucidated.

Methods: This study included 90 patients (34 female, age 65±12 years) with uncomplicated hypertension who have been regularly treated for more than 1 year. Degree of myocardial fibrosis was assessed by measuring serum carboxy-terminal propeptide of procollagen type I (PICP). Circumferential and longitudinal deformations of left ventricle were measured by speckle tracking echocardiography.

Results: Levels of PICP were not correlated with global longitudinal strain (r=−0.178, P=0.144) and global circumferential strain (CS) (r=0.169, P=0.118). We further divided CS into sub-endocardial and sub-epicardial CS. Only sub-endocardial CS was significantly correlated with PICP (r=0.225, P=0.036) but not sub-epicardial CS (r=0.035, P=0.613). Multivariate analysis showed sub-endocardial CS was still significantly correlated with PICP (B = −0.464, P = 0.022) after controlling age, systolic blood pressure, and left ventricular mass index. Sub-endocardial CS was significantly correlated with early mitral velocity to lateral annulus velocity ratio (E/e′) (r=−0.299, P=0.034).

Conclusion: Serum PICP was correlated with only sub-endocardial CS. Myocardial fibrosis occurred mainly in sub-endocardial myocardium in hypertension.

Decreased sub-endocardial CS contributed to increased filling pressure of left ventricle.

P4781 | BEDSIDE
Effects of iron overload on sympathetic nervous system in essential hypertensive patients
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Background and aims: A recent hypothesis claims that iron metabolism directly or indirectly, i.e. throughout metabolic (insulin resistance) or inflammatory/autoimmune mechanisms is linked to the sympathetic nervous system. We tested this hypothesis by recording central sympathetic neural outflow in hypertensive patients with normal or elevated circulating plasma levels of ferritin (FE), i.e. a marker of iron load.

Methods: In 8 untreated male essential hypertensives with elevated plasma Fe (HFTE+), age 46.9±2.6 yrs, mean±SEM, we measured, along with Fe levels and transferrin saturation, clinic blood pressure (BP), heart rate (HR, EKG), muscle sympathetic nerve traffic (MSNA), HOma index and glucose. Data were compared to those from 7 untreated male essential hypertensives with normal Fe levels (HFTE−) age matched with HFTE+.

Results: For example, HFTE+ displayed Fe values significantly greater than those seen in HFTE−: (44.3±1.01 vs 13.5±4.98 μg/ml, P<0.05). This was the case also for transferrin saturation (38.9±24 vs 24.2±19.9%, HR HFTE+ the increased iron load was accompanied by Homa index values significantly greater than in HFTE−: (2.1±0.4 vs 1.2±0.2 au, P<0.05). This was accompanied by significantly greater values of MSNA, both when expressed as frequency over time (48.5±4.3 vs 39.7±3.5, P<0.05) and when corrected for HR (66.4±5.0 vs 54.1±3.7 bursts/min; P<0.05). In the group as a whole there was a significant relationship between MSNA and Fe (r=0.6, P<0.01), whose level of statistical significance was greater than the one related to the relationship MSNA and HOma index (r=0.53, P<0.05). Homa index and Fe were also significantly and directly related each other (r=0.58, P<0.05).

Conclusions: These data provide the first evidence that in hypertensive males iron overload exerts marked sympathoexcitatory effects associated with a decrease in insulin sensitivity. It is likely that the iron overload directly or through the concomitant hyperinsulinemia may be responsible for this neuroadrenergic response.

P4782 | BEDSIDE
Prolonged heart rate recovery as predictor of incidental hypertension and survival
C. Hjalmarsson1, L. Holmlund2, B. Andersson2, K. Manhem3, L. Bergfeldt4, 1 Sahlgrenska University Hospital, Department of Cardiology, Gothenburg, Sweden; 2 Sahlgrenska University Hospital, Department of Internal Medicine, Gothenburg, Sweden; 3 Sahlgrenska Academy, Department of Internal Medicine, Gothenburg, Sweden; 4 Sahlgrenska Academy, Department of Cardiology, Gothenburg, Sweden

Background: Heart rate recovery (HRR) defined as the decline in heart rate immediately following cessation of exercise, is influenced by autonomic function. Prolonged HRR has been associated with poor survival, typically in patients with heart failure or diabetes mellitus, but less is known about its relation to hypertension.

Purpose: To study the relation between HRR and ongoing and incidental hypertension as well as the association of HRR with long-term survival.

Methods: 1047 consecutive patients (mean age 56±14 years, 43% women) were referred for an exercise ergometry test at a university hospital between May 1996 and December 1997. N=708 patients (68%) remained after excluding patients on beta-blockers, or with a pacemaker, established cardiac morbidity, stroke, and diabetes. N=95 patients had ongoing hypertension (defined as diagnosis of hypertension identified in a medical board’s patient register or as use of antihypertensive medication). HRR was defined as the decrease in HR during the first minute after peak exercise.

Information about incidental cardiovascular morbidity and mortality, as well as all-cause mortality, was collected during a mean follow-up of 15±4 years. N=157 patients with incidental hypertension were identified at follow-up.

Results: There was no difference in HRR between men (32±13 beats/min) and women (31±12 bpm), P=0.104. The mean HRR was significantly less in patients without hypertension (5±4, P<0.001) than in those with hypertension (12±3±12 bpm, P<0.001). The patients who eventually developed hypertension also had significantly lower HRR than those without hypertension (3±11 vs. 34±11 bpm; P=0.012).

In a survival analysis by Cox proportional model of the whole cohort, the HRR was a significant predictor of survival (HR 0.97, 95% confidence interval 0.95–0.98; P<0.001) after adjusting for relevant covariates (age, gender, smoking, previous cardiovascular morbidity, and diabetes).

Conclusion: Heart rate recovery after an exercise test is associated with both ongoing and incidental hypertension. Thus, this exercise parameter might be useful for predicting both survival and the risk of hypertension.

Acknowledgement/Funding: Svenska Läkarälskapsfond
P4783 | BEDSIDE
Reduced baseline heart rate and increased exercise-induced heart rate response as characteristic features in patients with orthostatic hypotension
M. Noda, S. Watanabe, T. Murakami, T. Nakamura, T. Ikenouchi, Y. Yamamoto, K. Ichikawa, M. Usui. JCHO Tokyo Yamate Medical Center, Internal Medicine, Tokyo, Japan

Background: The orthostatic hypotension (OH) is a rare but not so uncommon disease in elderly individuals. Recent attention has been paid to the increase in serious cardiovascular risk in pts with OH and clinical extreme. However, underlying baroreflex dysregulation and clinical features are still unknown during exercise (Ex).

Purpose and methods: To examine the vital and clinical features, consecutive 802 patients (pts) requiring routine treadmill Ex-test (Bruce protocol, symptom-limited) were examined and 15 OH (a fall in systolic blood pressure [sBP] at least by 15mmHg; [ΔsBP; −17±5 mmHg]) pts and 94 control (no medication/no organic disease) pts were included. All pts with orthostatic hypotension were excluded. Heart rate (HR; bpm), heart rate variability (HRV) [MemCalc™(maximum entropy) method] and baseline clinical features (body mass index [BMI; kg/m²], low-density lipoprotein cholesterol [LDL-C; mg/dl]) were selected. Pts with neurogenic disease, diabetes mellitus, Parkinson disease and current oral medication were excluded. Heart rate (HR; bpm) and HR-variability (HRV) [MemCalc™(maximum entropy) method] and baseline clinical features (body mass index [BMI; kg/m²], low-density lipoprotein cholesterol [LDL-C; mg/dl], ultrasound echocardiogram-guided left ventricular diastolic dimension [LVDd:mm] and ejection fraction [LVEF;%]) were compared between OH and control groups. Based on the resting HR, a ratio of HR in each Ex-period was estimated as “Ex/rest”, “peak-Ex/rest” and “recovery (Rec)/rest”, respectively. The degree of a BP fall (ΔsBP) in OH was compared to that of HR in each Ex period (rest, Ex, peak-Ex and recovery) by regression analysis.

Results and conclusion: Clinical (BMI, LDL-C, LVDd, LVEF) and autonomic features (HR and high frequency components [log HF; msec²] in each Ex period) were similar in 2 groups but exaggerated HR response during Ex was observed only in pts with reduced baseline HR in a dose-response manner. Therefore, not reduced but exaggerated HR response may be a common autonomic feature in OH pts.

P4784 | BENCH
High sodium enhances non-neuronal acetylcholine release in the renal cortex

Background: In the renal arteries, acetylcholine (ACH) activates endothelial nitric oxide synthesis and causes endothelium-dependent vasorelaxation, resulting in an increased renal blood flow. In the kidney of salt-sensitive hypertensive subjects, exogenous ACH-induced vasodilatation is reported to be impaired. Therefore, there may be a close relationship between the onset of salt-sensitive hypertension and endogenous ACH release in the kidney. However, the mechanism of endogenous ACH release in the kidney remains unclear.

Purpose: To clarify the mechanism of endogenous ACH release in the kidney, we introduced a microdialysis technique to the kidney.

Methods: A microdialysis probe was implanted into the renal cortex of the chloralose-urethane anesthetized rabbits. (1) High potassium (200 mM), (2) high sodium (500 or 900 mM), (3) Na+K+-ATPase inhibitor, ouabain (100 μM), and (4) epithelial Na+ channel blocker, benzamil (300 μM) were locally administered through the microdialysis probe and dialysate samples were collected. Dialysate ACh concentrations were analyzed using high-performance liquid chromatography (HPLC). Results: (1) High potassium did not affect dialysate ACh concentration (1±0.02 to 1±0.03 nM, not significant). (2) Both doses of high sodium significantly increased dialysate ACh concentrations (500 mM: 1±0.04 to 2±0.04 nM, P<0.05; 900 mM: 1±0.03 to 5±0.11 nM, P<0.01). (3) Ouabain significantly increased dialysate ACh concentration (1±0.02 to 2±0.03 nM, P<0.01). (4) Benzamil significantly decreased dialysate ACh concentrations in both baseline and high sodium (900 mM) conditions (benzamil, P<0.01; high sodium, P<0.01; interaction, P<0.01 by two-way ANOVA).

Conclusions: High sodium-induced depolarization did not affect endogenous ACh release. This result suggests that renal ACh release is mainly dependent on non-neuronal mechanism. High sodium and Na+K+-ATPase inhibitor significantly increased endogenous ACh release, but epithelial Na+ channel blocker significantly decreased ACh release. These results suggest that an increase in intracellular sodium level enhances non-neuronal ACh release in the renal cortex. Endogenous ACh in the kidney may increase renal blood flow against high sodium and act as a renoprotective agent.