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BEST ABSTRACTS SITZUNG 1

BA I - 1

Subcutaneous treprostinil for the treatment of severe, non-operable chronic thromboembolic pulmonary hypertension: a randomized, double-blind, controlled study (CTREPH)

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Purpose: Treprostinil is a stable prostacyclin analogue approved for the treatment of pulmonary arterial hypertension. A short-term randomized, placebo-controlled trial reported that Treprostinil improved exercise capacity, indices of dyspnea, signs and symptoms, hemodynamics, and quality of life. Recent long-term data suggest that the treatment with subcutaneous Treprostinil (scTRE) is safe and efficacious over many years, in various forms of pre-capillary pulmonary hypertension (PH). The phase III, double-blind, randomized, controlled CTREPH study investigated the efficacy and safety of scTRE in patients with severe non-operable chronic thromboembolic pulmonary hypertension (CTEPH), a PH subset with no approved pharmacological treatment options.

Methods: Patients with severe CTEPH classified as non-operable were assigned in a double-blinded fashion to low-dose scTRE (target dose 3 ng/kg/min—corresponding to a placebo dose) or high-dose scTRE (target dose 30 ng/kg/min at 12 weeks). Primary outcome was the change from baseline in 6-min walking distance (6MWD) at week 24. Secondary endpoints included the change from baseline in pulmonary vascular resistance (PVR), NT-proBNP, WHO functional class (WHOFC), clinical worsening, quality of life (Minnesota questionnaire) and Borg dyspnea score. Ninety-two patients were planned. Interim analysis was performed after 54 patients had been enrolled and subjected to study drug in four European expert centers (Prague, Vienna, Warsaw, Dresden).

Results: Baseline 6MWD was 298.9 ± 83.9 m, and PVR was 843 ± 382 dyn.s.cm-5 (mean age 63.5 years, 48 % female). Three patients (5.5 %) did not tolerate scTRE. Six patients (11 %) were withdrawn due to clinical worsening ($n = 4$), and because of severe concomitant disease (ileus, aortic stenosis, $n = 2$). 6MWD improved by 42.9 m from baseline (95 % CI 11.1–74.8 m, intention-to-treat) in high-dose scTRE-treated patients, compared with a change of 4.5 m in subjects on low-dose scTRE ($p = 0.059$). PVR decreased by 211.6 dyn.s.cm-5 from baseline in patients on high-dose scTRE (95 % −331.04 to −92.24) compared with an increase of 59.2 dyn.s.cm-5 ($p = 0.001$) in the low-dose group. WHOFC significantly improved in patients on high-dose scTRE ($p = 0.01$). Per protocol analysis demonstrated an increase of 6MWD by 57.4 m from baseline (95 % CI 32.4–82.3 m, high-dose scTRE), compared with 5 m ($p = 0.0045$, low-dose scTRE).

Conclusions: In patients with non-operable CTEPH, scTRE significantly improved exercise capacity, WHO FC and PVR.

BA I - 2

Adiponectin as a predictor of increased aortic stiffness in patients after acute ST-segment elevation myocardial infarction

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Introduction: Increased aortic stiffness is an independent predictor of cardiovascular morbidity and mortality. Adiponectin is involved in atherosclerosis and inflammation. In the present study we aimed to explore the relation between adiponectin and aortic stiffness in patients with acute ST-segment elevation myocardial infarction (STEMI).

Methods: Forty-six STEMI patients (mean age: 57 ± 11 years; six females) treated with primary percutaneous coronary intervention were enrolled in the study. Plasma adiponectin was measured 2 days after index event by enzyme-linked immunosorbent assay (ELISA). Aortic pulse wave velocity (PWV), a measure of aortic stiffness, was calculated by the transit-time method with the use of a velocity-encoded, phase-contrast cardiac magnetic resonance protocol.

Results: Median plasma adiponectin concentration was 2,385 ng/mL (Interquartile range: 1,735–5,403). Males had lower values than females and current smokers had lower values than non-smokers (all $p < 0.02$). Adiponectin was associated with PWV ($r = 0.570$, $p < 0.001$), age ($r = 0.471$, $p = 0.001$) and total cholesterol ($r = 0.417$, $p = 0.004$). Multiple linear regression analysis revealed adiponectin as a predictor of PWV independently of relevant covariates (adiponectin: ß = 0.672, $p = 0.001$; model: $R = 0.754$, $p < 0.001$).

Discussion: The current study is the first in investigating the relationship between circulating adiponectin and aortic stiffness in the acute phase after STEMI. The main finding is that plasma adiponectin concentrations are independently associated with increased aortic stiffness in patients with acute STEMI treated by primary percutaneous coronary intervention.

BA I - 3

Time course of heart failure with preserved ejection fraction in a model with compensated renal failure

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Background: Renal impairment and heart failure with preserved ejection fraction (HFPEF) are often associated but the underlying mechanisms are largely unresolved. Therefore we investigated in a rat model with compensated renal failure which developed diastolic dysfunction and HFPEF.

Methods: Fifty-six young male Wistar rats were subjected to subtotal nephrectomy (NXT) or sham operation (SOP) and observed up to 24 weeks. Urine and blood samples for calculating the glomerular filtration rate (GFR) and echocardiography were performed during disease progression. Invasive hemodynamics (P/V-loops) and morphometry analysis of the organs were studied in final experiments at 8 and 24 weeks.

Results: Following NXT rats developed stable compensated renal failure (GFR 22±2 and 16±2 vs. 32±2 and 28±3 mL/min/m^2 at 8 and 24 weeks, resp. $p<0.01$) with preserved urinary excretion and unchanged electrolytes. Arterial pressure was significantly increased in NXT at 8 weeks and remained stable elevated at 24 weeks (148±8 and 154±7 vs. 105±3 and 109±2 mmHg, $p<0.01$). Similarly, LV end-diastolic pressure was increased at 8 weeks (9.2±0.6 in NXT vs. 5.3±0.4 mmHg in SOP, $p<0.01$) and remained elevated with no further increase at 24 weeks (10.4±0.8 in NXT vs. 5.1±0.4 mmHg, in SOP, resp. $p<0.01$). Systolic function was preserved at 8 and 24 weeks (EF 58±3 and 50±5 vs. 60±4 and 56±4%). LV hypertrophy was observed in NXT at 8 weeks (LV mass 708±21 vs. 637±12 mg in SOP, $p<0.05$) and further increased at 24 weeks (866±34 vs. 637±12 mg in SOP, $p<0.05$ vs. SOP and 8 weeks). Lung weight was increased in NXT at 8 weeks (1,494±60 vs. 1,265±57 mg, $p<0.05$) and significantly further increased at 24 weeks (1,816±92 vs. 1,414±39 mg, $p<0.05$ vs. Sham and 4 weeks) indicating progressive cardiac congestion.

Conclusion: Subtotal nephrectomy in rats leads to compensated renal failure, arterial hypertension, LV hypertrophy and impaired diastolic function with elevated LV end-diastolic pressure. While renal function, arterial hypertension and LV function remained stable, cardiac remodeling and congestion worsened, reflecting the progressive nature of myocardial dysfunction in this model of cardio-renal syndrome.

BA I - 4

Multiple autonomic and repolarization investigation of sudden cardiac death (MARIA-SCD): a 10 years prospective, single blinded study in patients with reduced ventricular function and controls

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Background: Left ventricular ejection fraction (LVEF) at a single time point is the standard method to identify patients with risk of sudden cardiac death (SCD). Autonomic evaluation and assessments of cardiac electrical substrate have been introduced successfully to predict mortality. Progression of autonomic dysfunction might help identifying high-risk patients.

Objectives: A combined assessment of autonomic tone and changes in cardiac electrical substrate at multiple time points should add prognostic information to standard methods using LVEF.

Methods: We enrolled patients with ischemic (ICM) and dilated cardiomyopathy (DCM) with LVEF ≤50% and control subjects (CSU) with LVEF >50%. The protocol included initial testing (I1) after establishing an optimal medical treatment, a second testing after 3 years (I2), and a final control (maximum 10 years). We assessed autonomic function by pharmacological baroreflex testing (BRS), by short-term spectral analysis of heart rate variability (LF/HF) and long-term time domain analysis (SDNN). Cardiac electrical substrate was evaluated by exercise Microvolt T-wave alternans (MTWA), signal-averaged ECG (SAECG), and corrected QT-time (QTC). Results were interpreted blinded, and categorized using pre-specified cut-points. The primary outcomes were cardiac death (CD), arrhythmic death (AD) and resuscitated cardiac arrest (RCA). We compared adjusted multivariate models based on combinations of parameters with an univariate "LVEF only" model to identify patients with high risk of CD, AD and RCA using a single time point (I1). We performed similar analysis for multiple time points (I1 and I2) using a time varying covariate model.

Results: We studied 210 patients (age 59±10 years, 82% male): Group 1: $n=120$ ICM, Group 2: $n=60$ DCM, Group 3: $n=30$ CSU. The median follow-up was 7 years (0.4–9.7). CD, AD and RCA was observed in 31, 16 and 18% of ICM and DCM patients, respectively. In the single time point model analysis, MTWA, BRS, SDNN, LF/HF, QTC added significant information regarding CD and AD and MTWA only for AD/RCA. In the time varying covariate model, MTWA ($p<0.001$) and BRS ($p=0.042$) added significant information regarding CD and AD and MTWA only ($p<0.001$) for AD/RCA.

Conclusion: In initial single time point models, MTWA, BRS, SDNN, LF/HF and QTC were significantly related to cardiac and especially arrhythmic mortality. In addition to LVEF, MTWA adds the most powerful information in multiple risk assessment of cardiac patients during ultra-long follow-up.

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BA I - 5

Impact of short-term endothelin-A receptor blockade on plasma markers for remodeling in patients with ST-elevation acute coronary syndrome

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Background: Endothelin (ET) is a pro-fibrotic vasoconstrictor and a mediator of microvascular dysfunction and cardiac remodeling. Animal studies investigating ET receptor blockade in acute myocardial infarction led to conflicting results regarding ventricular remodeling. In-vitro, ET-A receptor blockade decreases neutrophil activation. As part of a randomized clinical trial assessing the safety and efficacy of the ET-A receptor blocker BQ-123 on myocardial perfusion in patients with ST-elevation acute coronary syndrome (STE-ACS), we measured the effect of peri-interventional BQ-123 treatment on plasma markers of remodeling.

Methods: Patients with posterior-wall STE-ACS were randomly assigned to intravenous BQ-123 at 400 nmol/min or placebo over 60 min, starting immediately prior to primary percutaneous coronary intervention (PCI, $n=54$). Peripheral blood samples were drawn upon arrival in the catheterization laboratory (baseline) and at 24 h and 30 days after PCI. Myeloperoxidase (MPO), a marker of neutrophil activation, matrix metalloproteinase 9 (MMP-9) and the procollagen III N-terminal propeptide (PIIINP), a marker of extracellular matrix metabolism, were measured in plasma using commercially available assays.

Results: Patients randomized to BQ-123 demonstrated a greater reduction of MPO levels from baseline to 24 h compared to placebo-treated patients ((177 ng/mL reduction (IQR 103–274) for BQ-123 versus 108 ng/mL (74–147) for placebo-treated patients, $p=0.006$), Fig. 1a). In addition, we observed a significantly greater reduction

of MMP-9 levels in patients treated with study drug (568 ng/mL (44–1,157) versus 117 ng/mL (57–561), $p=0.018$, Fig. 1b).

There was no significant difference in PIIINP values measured at baseline and at 30 days.

Conclusion: Short-term administration of BQ-123 reduces MPO plasma levels as well as MMP-9 plasma levels in patients with STE-ACS. In trials with larger patient numbers this observation may translate into smaller infarct size and improved ventricular remodeling at 6 months.

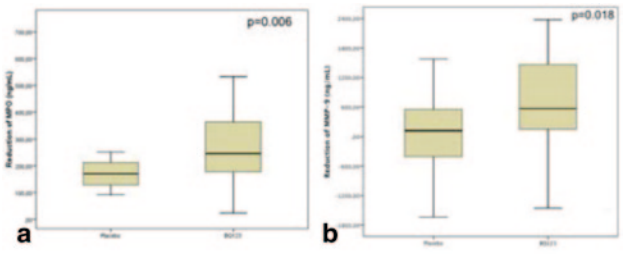

Fig. 1 **a** Reduction of myeloperoxidase (MPO) plasma levels over the first 24 h after percutaneous coronary intervention in patients with STE-ACS receiving an endothelin A receptor antagonist (BQ-123) or placebo. **b** Reduction of matrix metalloproteinase 9 (MMP-9) plasma levels over the first 24 h after percutaneous coronary intervention in patients with STE-ACS receiving an endothelin A receptor antagonist (BQ-123) or placebo

BA I - 6

LVAD implantation in patients with acute myocardial infarction and refractory cardiogenic shock

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Background: Refractory cardiogenic shock (RCS) complicating acute myocardial infarction (AMI) is associated with a poor outcome. Extracorporeal membrane oxygenation (ECMO) is an accepted treatment option to initially stabilize patients in this condition and to decide on escalating therapy concepts. When there is no potential for cardiac recovery and weaning from ECMO is impossible, long-term support as bridge-to-transplant or destination therapy by left ventricular assist device (LVAD) implantation can be provided. This two-step approach might improve overall mortality.

Methods: Retrospective review of 11 patients with RCS after AMI (mean age 52±11 years, 90.9% male) receiving an ECMO followed by permanent LVAD implantation between 07/2004 and 02/2013. Outcomes of interest included 30-day, in-hospital and 1-year mortality.

Results: Cardiopulmonary resuscitation had to be performed in five patients (45.5%), intraaortal balloon pump (IABP) insertion preceded ECMO implantation in seven cases (63.6%). Mean duration of preoperative ECMO support was 7±5 days. VADs to be utilized were the Heartware HVAD in five patients (45.5%), Thoratec Heartmate II in four patients (36.4%) and the DeBakey LVAD in two patients (18.2%). In three cases (27.3%), a sternotomy sparing minimally invasive approach was chosen, cardiopulmonary bypass during implantation was provided by ECMO instead of standard CPB in seven patients (63.3%). In eight patients (72.7) ECMO support had to be continued for temporary right ventricular support (5±8 days). 30-day mortality, as well as in-hospital mortality was low with a percentage of 9.1 and 18.2%, respectively. 1-year survival was 81.8%.

Conclusion: In selected patients with AMI complicated by cardiogenic shock, permanent LVAD implantation is an effective treatment option that leads to excellent results regarding early, as well as late mortality.

BA I - 7

Immunsuppressive Therapie bei virusnegativer inflammatorischer Kardiomyopathie – Wer profitiert am meisten?

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Einleitung: Der Stellenwert der immunsuppressiven Therapie bei Myokarditis wurde in den letzten Jahren kontrovers diskutiert. Rezente Ergebnisse zeigen, dass Patienten mit virusnegativer inflammatorischer Kardiomyopathie (CMP) von einer immunsuppressiven Therapie profitieren. Wir sind der Frage nachgegangen, welche Patienten am besten für diese Therapie geeignet sind.

Methoden: Zwischen 2002 und 2012 wurde an unserer Abteilung bei 86 Patienten per Endomyokardbiopsie (EMB) die Diagnose einer virusnegativen inflammatorischen CMP gestellt. Eine myokardiale Erregerpersistenz wurde mittels PCR ausgeschlossen. Bei 73 Patienten wurde eine immunsuppressive Therapie (Cortsion plus Azathioprin) – zusätzlich zur neurohumoralen Therapie – durchgeführt bzw. eingeleitet. Jeweils sechs Monate nach Therapiebeginn erfolgte eine Kontroll-EMB incl. hämodynamischer Untersuchung. Die Reduktion um zumindest eine NYHA Klasse bzw. der Verbleib in NYHA I und die Abnahme des NTproBNP-Serumspiegels um ≥30% wurde als klinisch relevanter Therapieerfolg definiert.

Ergebnisse: Aktuell liegt von 54 Patienten eine Kontroll-EMB vor (Alter: 46±12,5 Jahre, 32% Frauen, Erkrankungsdauer: Median 1,2 Monate). Nach 6-monatiger Therapie zeigte sich eine deutliche Verbesserung von NYHA-Klasse (vor Therapie: I 13%, II 43%, III 37%, IV 7%, nach Therapie: I 55%, II 43%, III 2%, IV 0%; $p<0{,}001$) und NTproBNP (1449±1542 auf 669±1346 ng/L; $p<0{,}001$) Die LV-EF stieg von 29±12 auf 48±12% ($p<0{,}001$).

Im Vergleich zu Patienten mit fehlendem Therapieerfolg wiesen Patienten mit klinisch relevantem Therapieerfolg ($n=32$ [59%], Alter 45,6±12,5 Jahre, 26% Frauen, Erkrankungsdauer: Median 1 Monat) zu Beginn der Therapie eine höhere NYHA-Klasse (I 0%, II 39%, III 48%, IV 13% vs I 30%, II 48%, III 22%, IV 0%; $p<0{,}001$), ein höheres NTproBNP (1833±1417 vs 948±1545 ng/L; $p<0{,}004$) sowie eine niedrigere LV-EF (24±9 vs 35±13%, $p<0{,}002$) auf. Interessanterweise fand sich zwischen den beiden Gruppen vor Beginn der Therapie kein signifikanter Unterschied hinsichtlich hämodynamischer Parameter und Entzündungsaktivität im Myokard; das Ausmaß der intramoykardialen Fibrose war bei Patienten mit positivem Therapieerfolg sogar größer. Die neurohumorale Therapie war in beiden Gruppen vergleichbar.

Konklusion: Bei gesicherter virusnegativer inflammatorischer CMP profitieren besonders Patienten mit fortgeschrittener Herzinsuffizienz und höhergradig eingeschränkter LV-EF von einer immunsuppressiven Therapie.

BEST ABSTRACT – SITZUNG II

BA II - 1

Role of microRNA-223 deficiency in myocardial ischemia-reperfusion injury

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Introduction: MicroRNA-223 (miR-223) is a specific microRNA which acts as a negative modulator of neutrophil activation and degradation. MiR-223 deficient neutrophils exhibit unusual hypermature morphology, are hypersensitive to activating stimuli and thus present an increased inflammatory response. As reperfusion-associated tissue inflammation, induced by neutrophil release of degradative enzymes, is known to be a potential mediator of myocardial reperfusion injury, we aim to investigate the contribution of miR-223 in the regulation of neutrophil infiltration in the myocardial infarct zone. To our knowledge, no in vivo ischemia/reperfusion model has been applied to study the detailed role of miR-223 so far.

Material and methods: MiR-223 knockout (KO) and control wild type (WT) mice were subjected to experimental myocardial ischemia and reperfusion (m I/R). For histological evaluation of cardiac tissue damage, Haematoxylin and Eosin stained sections were scanned using Axio Imager M1 and Tissue-FAXS software package. To evaluate the size of infarction in relation to left ventricle, scar size and left ventricle were determined using Adobe Photoshop CS4 and percentage of infarcted myocardium was calculated. Blood of all animals was collected from the renal vein for measurement of plasma levels of Troponin T. Total RNA was extracted from the area at risk (AAR) and the remote zone, respectively, and RNA quantification of TNF-alpha and IL-6 was performed by quantitative real-time PCR.

Results: After 30 min ischemia and 48 h reperfusion, serum Troponin T levels were significantly increased (3,295.8 vs. 1,226.9 pg/mL, $p=0.000$, $n=15$ per group) in miR-223 KO rodents compared to WT mice. Histological analysis showed that ischemia-reperfusion resulted in marked myocardial injury in all groups of animals, but the cardiac damage was more severe in miR-223-deficient mice after 48 h (21.1 vs. 7.9 %) and 7 d (22.9 vs. 11.7 %) of reperfusion following 30 min of ischemia. Furthermore, serum Troponin T levels were significantly increased (5,476.0 vs. 3,250.5 pg/mL, $p=0.017$, $n=9$ per group) in miR-223 KO rodents compared to WT mice after 3 h of reperfusion following 30 min of ischemia. Quantitative RT-PCR analysis revealed that gene expression of TNF-alpha and IL-6 was significantly higher (both, $p \leq 0.05$) in the AAR compared to the remote zone.

Discussion: So far, our preliminary data indicate that mice lacking miR-223 exhibit an enlarged infarct size following myocardial I/R injury and suggest a contribution of miR-223 in the regulation of neutrophil infiltration in the myocardial infarct zone.

BA II - 2

Albuminuria significantly predicts cardiovascular events in patients with type 2 diabetes independently from the baseline coronary artery state

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Introduction: Albuminuria is an important indicator of cardiovascular risk. We have recently shown that it is also associated with angiographically determined coronary artery disease (CAD). Whether albuminuria predicts cardiovascular events independently of the baseline coronary artery state in patients with type 2 diabetes (T2DM) has not been investigated yet.

Materials and methods: We measured urinary albumin and creatinine concentrations in 211 consecutive patients with T2DM undergoing coronary angiography for the evaluation of suspected or established stable CAD. Albuminuria was defined as a urinary albumin to creatinine ratio (ACR) of 30 µg/mg or greater. Prospectively, we recorded vascular events over 3.2 ± 1.4 years.

Results: During follow up, 24.6 % of our patients suffered cardiovascular events. The cardiovascular event rate was significantly higher in patients with albuminuria ($n=85$) than in those with normoalbuminuria (35.3 vs. 17.5 %; $p=0.003$). Cox regression analysis adjusting for age, gender, BMI, smoking, systolic and diastolic blood pressure, LDL cholesterol, HDL cholesterol, eGFR, and use of ace inhibitors/angiotensin II antagonists confirmed that albuminuria significantly predicted cardiovascular events independently from conventional risk factors (adjusted HR 1.96 [1.11–3.46]; $p=0.021$). Further adjustment for the angiographically determined presence of CAD at baseline did not significantly attenuate the predictive power of the ACR (HR 1.84 [1.04–3.27]; $p=0.037$). Similar results were obtained when the ACR was entered into the final regression model as a continuous variable (standardized adjusted HR 1.30 [1.02–1.65]; $p=0.037$).

Discussion: Albuminuria significantly predicts cardiovascular events in patients with T2DM independently of established cardiovascular risk factors and of the baseline coronary artery state.

BA II - 3

Prognostic value of neutrophil counts in acute coronary syndrome

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Background: Inflammation and thrombosis play crucial roles in the development of acute coronary syndromes (ACS), and consequently, acute myocardial infarction (AMI).

Methods: We have previously described the accumulation of neutrophils at the coronary culprit lesion site. We assessed the prognostic value of culprit site neutrophil accumulation in ACS defined as an increase of neutrophils > 0.5 G/L at the culprit site compared to systemic blood samples.

Results: We followed 417 AMI patients after thrombectomy during primary percutaneous coronary intervention over a median period of 35 months (IQR 18–53 months, 1,217 patient years). Culprit site neutrophil accumulation occurred in 160 patients (38.4 %). After multivariate adjustment for confounders all-cause (18.8 vs. 9.7 %; $p=0.037$) and cardiovascular mortality (15.0 vs. 5.4 %; $p=0.006$) were significantly increased in patients with culprit site neutrophil accumulation (hazard ratio 1.82 (CI 1.06– 3.13, $p=0.03$)). Concordance index for culprit site neutrophil accumulation and all-cause mortality was 0.64 (95 % CI 0.52–0.77; $p=0.014$) and for cardiovascular mortality 0.71 (95 % CI 0.58–0.85; $p=0.001$). Patients with culprit site neutrophil accumulation had a significant higher incidence of non-obstructive lesions compared to patients without neutrophil accumulation (35.9 vs. 26.5 %; $p=0.048$).

Conclusion: Local neutrophil accumulation at the coronary culprit lesion site is a strong and independent predictor of all-cause and cardiovascular mortality in AMI patients. The data suggest that local neutrophils may trigger thrombotic vascular occlusion in patients without obstructive coronary plaque.

BA II - 4

Microvessel loss in degenerative aortic valve disease

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Purpose: Aortic valve disease is the most frequent native valve disease in Europe, and the third most frequent cause of cardiovascular death. The biological mechanisms resulting in calcific aortic stenosis show similarities to atherosclerosis. Because aortic valve degeneration and prosthetic valve degeneration share common features, we hypothesized that a loss of small vessels in the course of an atherosclerotic process is underlying aortic valve stenosis.

Methods: Two hundred and thirty-three aortic valves were collected during aortic valve surgeries and at autopsies, and corresponding patient and echocardiographic data were recorded. Representative tissue samples were used for immunohistochemical analysis. Gene expression profiles of leaflets and rings were analyzed with Microarrays, and confirmed by real-time PCR.

Results: Aortic jet velocities were 1.6 ± 0.4 m/s in aortic sclerosis, versus 4.7 ± 0.9 m/s in aortic stenosis and stenotic valve leaflets were heavier, and more calcified than healthy valve leaflets. Microarray cluster analysis of valve leaflets and rings showed that healthy and sclerotic leaflets have a highly similar gene expression profile whereas in the rings the sclerotic tissue samples grouped together with the stenotic aortic valve rings. VonWillebrand factor stains showed that blood vessel density within the valve rings decreased in parallel with increasing severity of aortic stenosis. Real-time PCR showed that vascular endothelial caherin, as well as the vascular endothelial growth factor A (VEGF) and the VEGF receptor II (KDR) are already down regulated in sclerotic ring samples. Angiopoietin 2 (ANGPT2), endothelial tyrosine kinase (TEK) and platelet/endothelial cell adhesion molecule 1 (PECAM1) showed no expressional difference between healthy controls and sclerotic valves, but all were significantly down regulated in stenotic aortic valve tissues. Lymphatic vessel markers showed no difference in expression compared to healthy controls. In addition KDR knock-out mice showed significantly increased cross-sectional aortic valve leaflet areas ($p=0.01$) and significantly decreased numbers of cells per square millimeter ($p=0.015$) in the aortic valve leaflet compared to control littermates.

Conclusion: Taking these results together there is a strong indication that aortic valve sclerosis/stenosis has its origin in the aortic valve ring. Loss of microvessels within the valve ring may lead to an under-supply of the valve leaflets giving way to protein accumulation and degradation, apoptosis, cholesterol accumulation and matrix degradation, thus contributing to stenosis progression.

BA II - 5

Growth-differentiation factor 15 and osteoprotegerin in acute myocardial infarction complicated by cardiogenic shock: a biomarker substudy of the IABP-SHOCK II-trial

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Background: Growth-differentiation factor 15 (GDF-15), a stress-responsive member of the transforming growth factor beta cytokine superfamily, and osteoprotegerin (OPG), a cytokine of the tumor necrosis factor superfamily have proven prognostic impact in cardiovascular disease including ST-elevation myocardial infarction. In acute myocardial infarction complicated by cardiogenic shock (CS) the impact of these novel biomarkers on outcome has not been investigated, yet.

Methods: In the randomized Intraaortic Balloon Pump in Cardiogenic Shock II (IABP-SHOCK II)-trial 600 patients with CS complicating acute myocardial infarction undergoing early revascularization were assigned to therapy with IABP or no IABP. In 190 patients included at the University of Leipzig- Heart Center blood samples were collected directly during primary PCI. The blood was centrifuged immediately after sample drawing and the serum was immediately frozen at −87 °C. GDF-15 and OPG were measured with standard ELISA-kits. All-cause mortality at 30 days was used for outcome assessment.

Results: Patients with positive 30 day survival had in median significant lower levels of GDF-15 (6,382 [interquartile range IQR 2,945; 10,195] vs. 10,926 [IQR 6,141; 14,696] pg/mL; $p<0.001$) and OPG (546 [IQR 329; 1,178] vs. 868 [IQR 438; 2,574] pg/mL; $p=0.002$). GDF-15 and OPG levels > median showed higher rates of death at 30 days in χ^2-testing (51.6 vs. 29.5 %, $p=0.008$ for both) and log-rank-testing (GDF-15: hazard ratio [HR] 1.93 [95 % confidence interval CI 1.24–3.03]; $p=0.004$; OPG: HR 1.79 [CI 1.15–2.80]; $p=0.004$). Patients with GDF-15 and OPG < median had a mortality of 27.6 %, with either GDF-15 or OPG > median mortality was 35.1 % and with both > median 60.3 % (p for trend < 0.001). In univariable logistic regression modeling a 10 % increase of GDF-15 resulted in HR of 4.74 (CI 1.99–11.28, $p<0.001$) and of OPG in HR of 2.86 (CI 1.43–5.69, $p=0.003$) for probability of death. In a multivariable logistic stepwise regression model including both biomarkers age, diabetes, body mass index, baseline serum creatinine and serum lactate, use of IABP and sex GDF-15 and serum lactate remained significant predictors of 30 day mortality (HR for 10 % increase of GDF-15 5.45 [CI 2.04–14.58, $p<0.001$]; serum lactate per 10 % increase 5.39 [CI 1.82–15.98, $p=0.002$]).

Conclusion: GDF-15 and OPG levels at baseline are predictors of short term mortality in acute myocardial infarction complicated by CS. GDF-15 remained even significant in multivariable modeling.

BA II - 6

Which endurance training protocol works best in coronary artery disease: interval vs. pyramid vs. continuous training?

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Introduction: Endurance training is a key component of cardiac rehabilitation and recommended in treatment guidelines of all major professional societies. During the past decades different endurance training protocols have been studied, however, a head-to-head comparison between the most effective modes, i.e. continuous endurance training (CET), high-intensity interval training (HIIT), and pyramid training (PYR), has not yet been performed in patients with coronary artery disease (CAD).

Methods: In this prospective, randomized study three isocaloric training protocols (see Fig. 1) were compared on 54 coronary artery disease patients: (1) CET ($n=18$): 31 min at 65–75 % HRpeak according to the European Guidelines of Cardiac Rehabilitation; (2) HIIT ($n=17$): 4 × 4 min intervals at 85–95 % HRpeak, each followed by 3 min of active recovery at 60–70 % HRpeak (25 min total); and (3) PYR ($n=19$): three repetitions (each 8 min) of gradual load increase and subsequent decrease from 65–95–65 % HRpeak, supplemented by 2 min recovery in between pyramids at 65 % HRpeak (28 min total). All protocols included 5 min of warm-up and cool-down at 60–70 % HRpeak. Supervised training was performed 3x/week for 6 weeks on cycle ergometers. Primary endpoint was physical work capacity during maximal ergometry.

Results: All protocols led to highly significant increases ($p<0.001$) of exercise capacity (begin vs. end: CET: 132 vs. 160W (21.2 % increase); HIT: 148 vs. 180W (21.6 %); PYR: 130 vs. 160W (23.1 %)), without statistically significant differences between protocols (see Fig. 2).

Discussion: Our data clearly show that 6 weeks of exercise training lead to significant improvement in exercise capacity by >20 % in coronary artery disease patients, regardless of the mode of endurance training. Therefore exercise training can be even more individualized and thus tailored to the specific preferences and needs of patients, which might have a positive impact on patients' compliance.

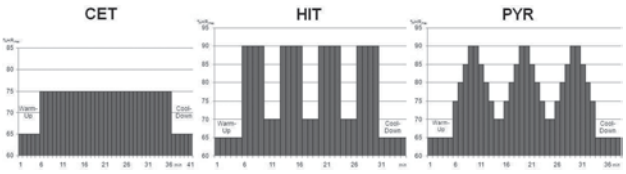

Fig. 1 Training protocols

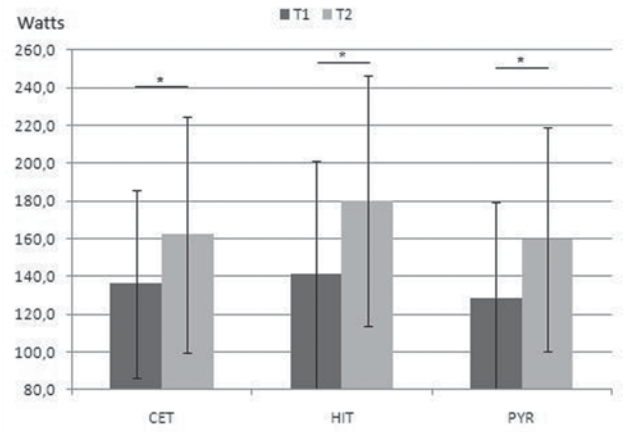

Fig. 2 Exercise capacity of initial ergometry (T1) and after six weeks of exercise training (T2)

BA II - 7

Influence of high-dose highly efficient statins (atorvastatin and rosuvastatin) on short-term clinical outcome in patients undergoing percutaneous coronary interventions plus coronary stenting for acute coronary syndrome

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Background: Statins are recommended for prevention of progression of cardiovascular disease after percutaneous coronary intervention (PCI) and stenting and a dose-dependent improvement of the lipid profile is observed with all statins. Despite the fact that high-dose, highly efficient statins (atorvastatin 80 mg or rosuvastatin 20 mg) are recommended especially in high-risk patients, clinical data are scarce and further investigation in "real-world" settings are needed.

Methods: One thousand five hundred and twenty-eight consecutive patients, who underwent PCI for acute coronary syndrome (ACS), were included in a prospective registry from January 2003 until January 2011. In a retrospective analysis cardiovascular risk factors, co-morbidities and basal circulating lipid variables (total cholesterol (T-C); LDL-cholesterol (LDL-C); were evaluated. Moreover, all-cause mortality after a follow-up period of 3 months (the period, in which the patients were documented to be constantly on therapy) was evaluated. Results were compared between patients receiving high-dose, highly effective statins (atorvastatin 80 mg or rosuvastatin 20 mg) versus patients receiving low-dose statins or without lipid-lowering therapy.

Results: Nine hundred and twenty-six (60.6 %) patients received high-dose atorvastatin or rosuvastatin and 602 (39.4 %) patients received low-dose statin therapy or were not on statins at discharge due to normal cholesterol levels. Their mean plasma levels of lipid variables were for T-C: High-dose statin: 197 ± 60 mg/dl; low-dose/without statin: 172 ± 45 mg/dl ($p<0.001$), and for LDL-C: High-dose statin: 124 ± 53 mg/dl; low-dose/without statin: 98 ± 84; ($p<0.001$), respectively.

Out of a series of clinical characteristics the following were significantly different between the study groups: age ($p<0.001$)

current smoking ($p<0.001$), cerebrovascular disease ($p=0.002$), peripheral vascular disease ($p<0.001$), previous myocardial infarction ($p=0.03$), previous CABG ($p=0.04$) and renal dysfunction ($p<0.001$).

Eight (0.9 %) patients under high-dose statin therapy and 21 (3.5 %) patients on low-dose/without statins at discharge died during the follow up (HR =0.244; 95 % CI, 0.108–0.551; $p=0.001$). After adjustment with propensity score the results remained consistent (adjusted HR for high-dose statins 0.405, 95 % CI 0.176–0.931; $p=0.033$).

Conclusion: In this small single-center series of 1,528 "real world" patients undergoing PCI and coronary stenting for ACS a significant reduction in short-term all-cause mortality could be demonstrated in patients under high dose, highly efficient statins compared to patients receiving low-dose statins or no lipid lowering therapy at all based on slightly elevated or normal cholesterol levels at admission. This study in a real-world population confirms the necessity of the "the lower-the better" lipid treatment strategy in patient with ACS referred for PCI and stent implantation.

Postersitzung I: Akutes Koronarsyndrom

I-1

Kardiogener Schock bei Patienten mit Nicht-ST-Hebungsinfarkt

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Einleitung: Über kardiogenen Schock (KS) im Akutverlauf von Nicht-ST-Hebungsinfarkten (NSTEMI) gibt es wenig verfügbare Daten. Wir berichten über unsere Erfahrungen aus einem Akut-PCI Spital des Wiener Infarkt-Netzwerkes.

Methodik: Im Rahmen von Akutinterventionen an unserer Abteilung wurden in den Jahren 2005–2010 insgesamt 848 Patienten akut koronarangiografiert, davon 215 Patienten wegen Verdachts auf NSTEMI. Es wurden anhand von EKG und Troponinerhöhung 181 Patienten mit NSTEMI identifiziert. Kardiovaskuläre Risikofaktoren (HTN, DM, Nikotinabusus), bekannte KHK (vorangegangene PCI, CABG oder Myokardinfarkt) und klinische Parameter (Alter, Kreatinin, kardiogener Schock) wurden zueinander in Beziehung gesetzt und statistisch ausgewertet.

Ergebnisse: Unter den subtotal und total verschlossenen Gefäßen ($n=116$/64,1 % der Patienten) fand sich ein signifikanter Unterschied in der Gefäßverteilung ($p<0{,}001$), der durch die geringe Zahl der Patienten mit Hauptstamm ($n=8$ bzw. 6,9 %) oder Bypass ($n=6$ bzw. 5,2 %) als Culprit Lesion bzw. ohne eindeutig identifizierbares schuldiges Gefäß ($n=1$ bzw. 0,9 %) erklärbar ist. Die Verteilung der Gefäßverschlüsse auf die 3 Hauptgefäße war gleichmäßig ohne signifikanten Unterschied (LAD: $n=33$ oder 28,4 %, RCA: $n=31$ oder 26,7 %, RCX: $n=37$ oder 31,9 %).

Von allen akut koronangiografierten NSTEMI-Patienten erlitten 13 (7,2 %) während des stationären Aufenthaltes einen kardiogenen Schock und wurden intensivmedizinisch betreut. Davon wurden 11 Patienten (84,6 %) reanimiert. 4 Patienten (30,8 %) erhielten eine intraaortale Ballonpumpe. 6 Patienten (46,2 %) verstarben während des Spitalsaufenthaltes (MOV, hypoxischer Hirnschaden, kardiogener Schock, thromboembolische Komplikationen, Blutungskomplikationen). Bei den Patienten mit kardiogenem Schock war die RCA das am häufigsten betroffene Gefäß ($n=5$ oder 38,5 %, $p=0{,}009$). Ein kardiogener Schock war häufiger bei Patienten ohne anamnestischen Myokardinfarkt ($n=8$ oder 61,5 %; $p=0{,}017$) und ohne anamnestische Koronarintervention wie PCI oder CABG ($n=10$ oder 76,9 %; $p=0{,}513$). Weiters zeigte sich ein signifikant höheres Durchschnittsalter in der Schockgruppe (70,69 ± 14,44 vs 61,06 ± 11,83 a; $p=0{,}035$) sowie ein Trend zu erhöhten Aufnahme – Kreatininwerten (1,43 ± 0,70 vs 1,062 ± 0,97 mg/dl; $p=0{,}097$).

Schlussfolgerung: 1) Pat. mit KS im Rahmen eines NSTEMI haben häufig Verschlüsse in allen 3 Hauptgefäßen. 2) Der kardiogene Schock bei NSTEMI hat keine geringere Mortalität als nach STEMI. 3) Patienten mit NSTEMI ohne kardiale Vorgeschichte könnten durch verzögerte Diagnose und Therapie prognostisch benachteiligt sein.

I-2

Endothelin-A receptor blockade and long-term outcome in patients with ST-elevation acute coronary syndrome

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Background: ST-elevation acute coronary syndrome (STE-ACS) is characterized by thrombotic coronary occlusion compromising blood flow at the epicardial and microvascular levels. Coronary thrombi are a source of large amounts of endothelin-1 (ET-1), a profibrotic vasoconstrictor and a mediator of microvascular dysfunction and cardiac remodeling. As part of a randomized clinical trial where we assessed the effect of the ET-A receptor blocker BQ-123 on myocardial perfusion in patients with STE-ACS, we conducted a long-term substudy to assess the effect of BQ-123 treatment on the predefined combined endpoint survival or cardiovascular rehospitalisation.

Methods: Patients with posterior-wall STE-ACS were randomly assigned to intravenous BQ-123 at 400 nmol/min or placebo over 60 min, starting immediately prior to primary percutaneous coronary intervention (PCI, $n=54$). During a 3-year follow-up period, patients were followed and kept on optimal medical treatment by an investigator who was blinded to the acute treatment allocation.

Results: During the median follow-up period of 3.3 years (IQR 2.9–3.7), no deaths occurred. The reasons for rehospitalisation ($n=20$) were unplanned coronary revascularization ($n=10$, 50 %), worsening angina ($n=3$, 15 %), hypertensive urgency ($n=2$, 10 %), dyspnoea ($n=2$, 10 %), as well as stroke ($n=1$), ventricular tachycardia ($n=1$) and cerebrovascular disease ($n=1$). We observed a longer event-free survival in patients randomized to receive BQ-123 compared with patients randomized to placebo (3.8 years (95 % CI: 3.3–4.2) for BQ-123 versus 2.8 years (2.1–3.4) for placebo, $p=0.032$, Fig. 1).

Conclusion: Short-term administration of BQ-123 in patients undergoing primary PCI for STE-ACS leads to a longer cardiovascular event-free survival.

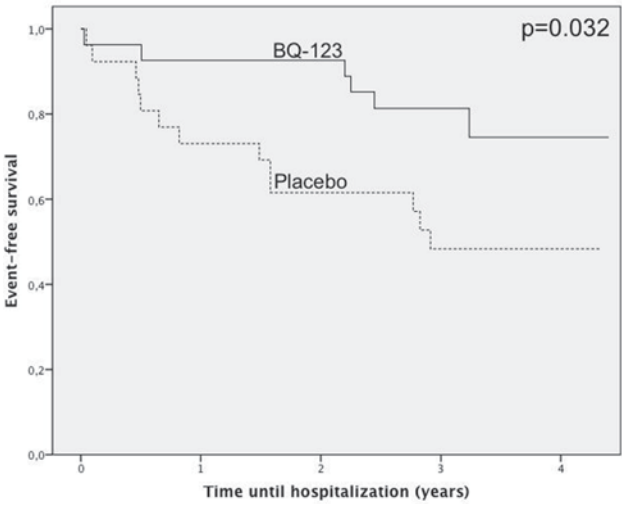

Fig. 1 Kaplan–Meier plot displaying time until death or first re-hospitalization for cardiovascular reasons in patients with STE-ACS receiving an endothelin A receptor antagonist (BQ-123) or placebo

I-3

Copeptin as a part of the dual biomarker strategy for early diagnosis of NSTEMI-WILCOP study

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Introduction: At present, the detection of non-ST-segment elevation myocardial infarction (NSTEMI) is greatly based upon the cardiac troponin as a conventional and established biomarker in the diagnostic process. However, the major disadvantage of cTn is its incapability to generally detect an Acute coronary syndrome (ACS) in the early hours after symptom onset, due to the delayed increase of its circulating levels after the actual ACS occurrence (so-called 'silent Troponin time'). We have investigated the effect of combined measurement of copeptin and high-sensitivity cardiac troponin I (hs-cTnI) levels for early identification of patients with NSTEMI.

Methods: This is an ongoing prospective single-centre study of consecutive patients admitted to the emergency department (ED) of the Wilhelminen hospital with chest pain suggestive of ACS. This study began in March 2011 and present analysis reports the data of the first 577 consecutive patients. All patients had copeptin and hs-cTnI determinations at admission to ED. Cutoff value for Copeptin was set at 14 pmol/L and for hs-cTnI at 0.056 ng/mL. Copeptin concentrations were measured using a novel, commercially available, chemiluminescence assay (Copeptin Kryptor® developed by BRAHMS AG, Hennigsdorf, Germany).

Results: In total, 82/577 (14.2 %) patients had the final diagnosis of acute myocardial infarction (AMI). Copeptin and hs-cTnI at admission were significantly higher among patients with proven AMI then in patients with other diagnosis, with copeptin levels being significantly higher in STEMI patients in comparison to NSTEMI and non-AMI pats. (75.07 pmol/L±98.53 vs. 41.13 pmol/L±87.08; $p<0.01$ and vs. 24.51 pmol/L±63.84; $p<0.001$). Copeptin levels in NSTEMI pats., though lower than in STEMI pats., were sign. higher than in non-AMI patients (41.13 pmol/L±87.08 vs. 24.51 pmol/L±63.84; $p<0.05$).

From the entire AMI population, 44/82 (53.6 %) pats. had an angiography-proven diagnosis of NSTEMI. The diagnostic accuracy of cTnI for diagnosis of NSTEMI for the entire study population was convincingly higher (AUC 0.916; $p<0.001$) than the one of Copeptin (AUC 0.610). Utilization of the 'dual biomarker strategy' in overall study population by combining the both biomarkers increased considerably the diagnostic accuracy for NSTEMI with AUC 0.926; $p<0.001$ and NPV of 98.6 % (98.32–99.34; 95 % CI).

Nevertheless, the group of patient that presented to ED inside the 6 h after onset of symptoms (so-called 'early presenters to ED') comprised 45.4 % of the total study population (262/577 pats.). In this group of patients diagnostic accuracy of cTnI alone for NSTEMI was lower (AUC 0.870; $p<0.001$) than in the overall study population (AUC 0.916). The additional use of copeptin levels in this 'early presenters' group regained and increased the diagnostic precision for identifying the patients with NSTEMI, quantified with AUC of 0.920 ($p<0.001$).

Conclusion: Observed in the whole study population, levels of hs-cTnI at admission to ED have fairly good diagnostic accuracy for early identification of patients with NSTEMI. However, among the patients with initially normal hs-cTnI levels presenting early after the onset of symptoms (inside 6 h after symptom onset), there obviously exists a significant diagnostic relevance of additional determination of copeptin levels (dual marker strategy), which results in a prompt and reliable diagnosis of NSTEMI.

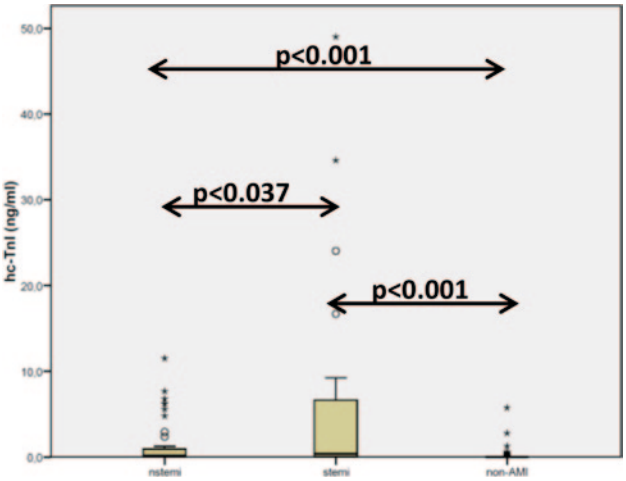

Fig. 1 hs-cTnI levels at presentation to ED in all patients according to final diagnosis

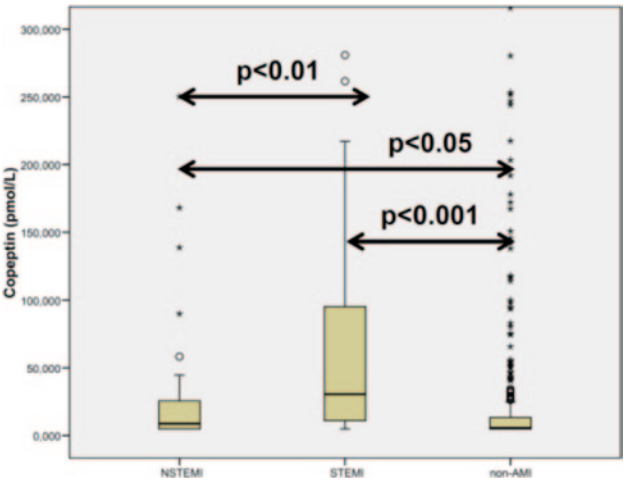

Fig. 2 Copeptin levels at presentation to ED in all patients according to final diagnosis

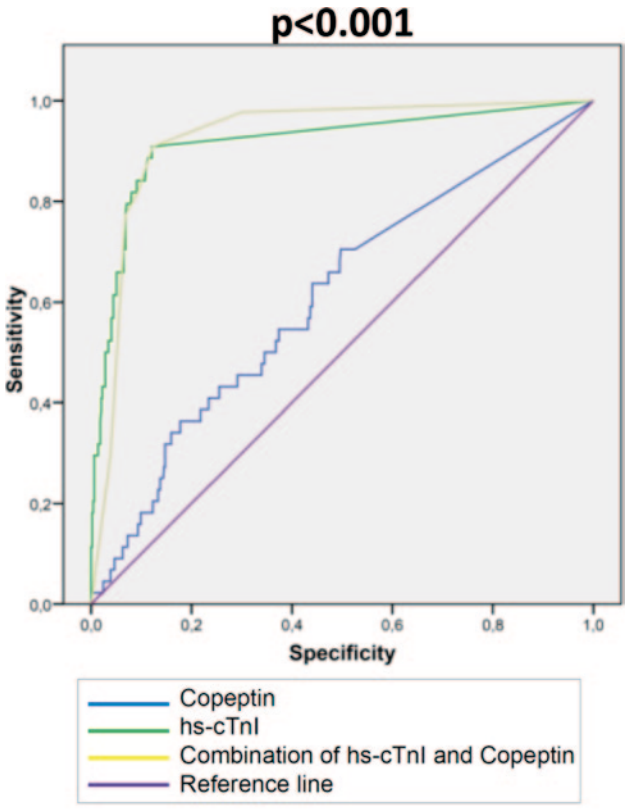

Fig. 3 ROC curves at presentation for the diagnosis of NSTEMI in overall study population

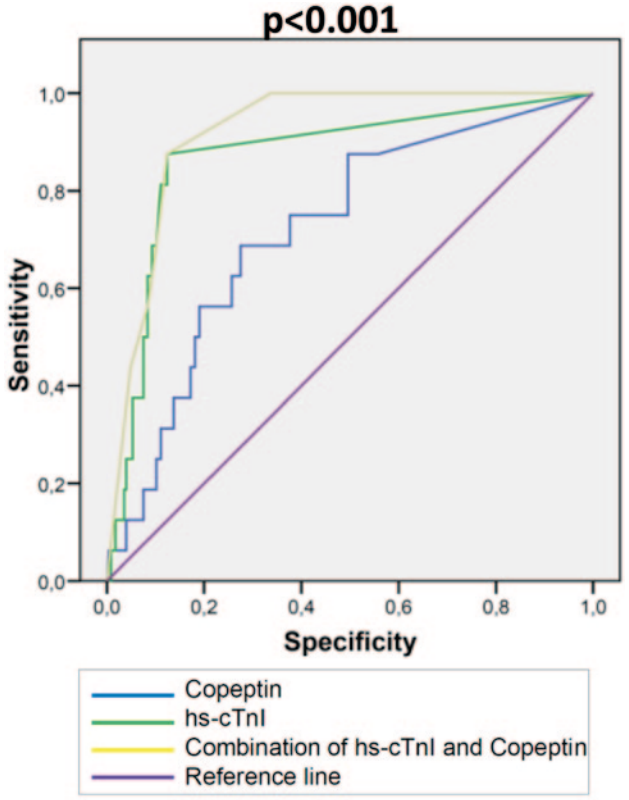

Fig. 4 ROC curves at presentation for the diagnosis of NSTEMI in the 'early presenters' group (patients presenting in ED within 6 h since symptom onset)

I-4

Copeptin in everyday clinical practice of an emergency department

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Background: Copeptin has been proposed for the early exclusion of acute myocardial infarction (AMI). We investigated the additional value of copeptin to high-sensitivity cardiac troponin T (hs-cTnT) in everyday clinical practice of an emergency department (ED).

Methods: Copeptin was measured on ED admission in 258 patients (135 males, age 62±19 years). At first 171 chest pain patients (93 males, 62±18 years, median delay 24 h, interquartile range 3 168 h, 34 not exactly known) seen by SA during regular working hours were enrolled, and subsequently 87 all-comers (41 males, 59±20 years; median delay 72 h, interquartile range 24 168 h, 44 not exactly known) with various key symptoms were enrolled to test the clinical specificity of the marker. Copeptin and hs-cTnT were measured with routine assays from BRAHMS® and ROCHE® Diagnostics. Only hs-cTnT values were reported to the treating physician. Patients were followed-up for ED readmissions and mortality by reviewing hospital charts for a period up to 14 months.

Results: The chest pain patients comprised of 16 AMIs (5 STEMI and 11 non-STEMI, delay 18.5, interquartile range 2–108 h), 54 other cardiac diseases and 100 various non-cardiac diseases (mostly musculoskeletal). Copeptin concentrations in AMI patients presenting within 14 h from onset (median 63, interquartile range 26–214 pmol/L) were significantly higher than in the remaining patients, whereas AMIs presenting thereafter did not differ significantly. By contrast hs-cTnT of both AMI groups were significantly different from non-AMIs. In the whole study population, chest pain patients and chest pain patients presenting within 14 h from onset hs-cTnT was significantly superior to copeptin for AMI diagnosis and the combination of copeptin and hs-cTnT did not significantly improve the diagnostic performance for AMI diagnosis. For example, areas under Receiver Operating Characteristics in chest pain patients with delay <14 h: 0.82 (copeptin), 0.90 (hs-cTnT), 0.94 (copeptin and hs-cTnT, no significant difference from hs-cTnT). In cox regression analysis for the prediction of ED readmission only age and gender remained significant, hs-cTnT was a significant predictor of readmissions in Kaplan-Meier analysis only in the whole study population, copeptin was not significant. In cox regression analysis for mortality prediction age and copeptin (hazard ratios 1.0035—whole population, 1.0064 chest pain patients, 1.0054 chest pain patients with delay< 14 h) were significant predictors of outcome

Conclusion: In our every-day ED population copeptin did not add to AMI diagnosis when using a high-sensitivity cardiac troponin assay for cardiac troponin determination. A limitation of our investigated population is that only 25 % of chest pain patients presented within 3 h from chest pain onset. We confirm the limited clinical AMI specificity of the marker in our study population which restricts copeptin testing to highly clinically pre-selected chest pain patients presenting very early after symptom onset.

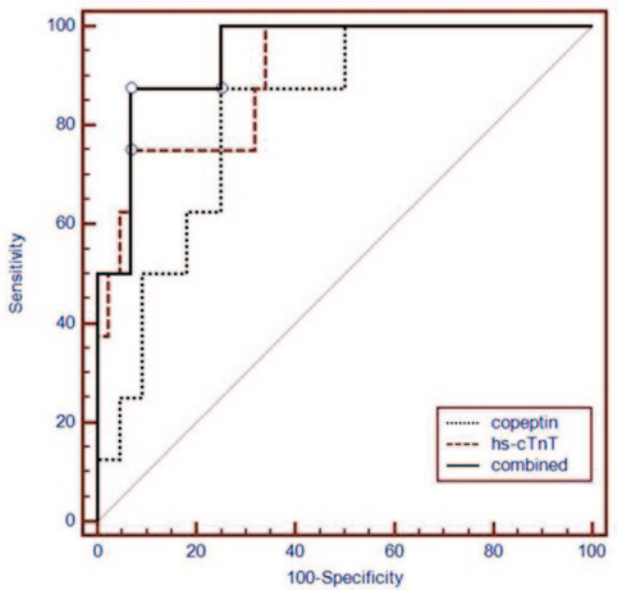

Fig. 1 ROC curves of copeptin, hs-cTnT and their combination by logistic regression in chest pain patients with delay <14 h

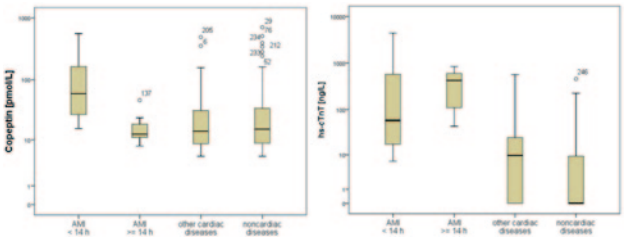

Fig. 2 Boxplots of logarithmised copeptin (*left*) and hs-cTnT (*right*) concentrations grouped by discharge diagnosis of the whole study population. * indicate sig. differences from other cardiac and noncardiac diseases

I-5

Plasma osmolality predicts clinical outcome in patients admitted with acute coronary syndrome undergoing percutaneous coronary intervention and stent implantation

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Background: The utilization of plasma osmolality as unspecific marker for endogenous stress, predicting clinical outcome in the context of acute coronary syndrome (ACS), has not been investigated so far.

Methods: In a retrospective analysis, we included 985 consecutive patients with ACS, who were referred to our tertiary referral center for percutaneous coronary intervention (PCI) with stent implantation.

Plasma osmolality was calculated using concentrations of sodium, plasma glucose and blood urea nitrogen at admission.

Furthermore, peak levels of creatine kinase-myocardial band isozyme fraction (CK-MB) were measured.

All-cause mortality was evaluated for each quartile of plasma osmolality at admission and compared between groups.

Primary endpoints were in-hospital mortality and 1-year mortality. As secondary endpoint, myocardial injury during the index hospitalization was evaluated comparing peak levels of CK-MB between the groups.

Results: Median osmolality was 283 mosmol/kg (IQR 279–287), rates of in-hospital death were 9 (3.7 %), 9 (3.7 %), 6 (2.4 %) and 41 (16.6 %) for Quartile (Q1–Q4), respectively.

Since similar rates of death for Q1–Q3 could be observed ($p=0.8$), those groups were combined for further analysis.

Univariate analysis in the cox proportional-hazards model revealed significantly higher rates of in-hospital death for patients with osmolality in the 4th quartile, as compared to patients with osmolality in Q1–Q3 (HR 5.4, 95 % CI 3.3; 9.0, $p<0.01$).

After adjustment for confounding baseline variables (presentation (myocardial infarction with or without ST-segment elevation), shock, age, renal failure, diabetes, peripheral vascular disease, smoking, heart failure and history for malignant tumors) osmolality in Q4 was associated with a 2.8-fold hazard of in-hospital death (HR 2.8, 95 % CI 1.4; 5.5, $p<0.01$).

Significantly higher rates in all-cause death within 1 year could be observed for patients with osmolality in Q4 vs. Q1–Q3 (HR 1.82, 95 % CI 1.09; 3.06, $p=0.02$).

Moreover, peak levels of CK-MB were significantly higher in Q4, as opposed to Q1–Q3 (median 150.0 U/L vs. 187.5 U/L, $p=0.02$).

Conclusion: Using the fourth quartile of plasma osmolality at admission as a natural cut-off point, osmolality in Q4, as compared to Q1–Q3, was highly significantly predictive of clinical outcome in ACS patients undergoing coronary stenting.

Our data suggests osmolality to be a feasible and cost-effective marker for predicting in-hospital and 1-year outcome in patients presenting with ACS. Keeping in mind all limitations of a retrospective analysis performed in a single center, further investigations are needed to confirm these results and to determine underlying mechanisms.

I-6

Depressive disorders in patients with primary and recurrent myocardial infarction

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Increasing interest in the problem of the relationship of anxiety, depression and heart disease due to their wide distribution, social importance and influence on the ability to work. Studies of the last decade suggests that the presence of comorbid affective spectrum have a negative impact on the course and prognosis in patients with AMI. At the same time, acute myocardial infarction (AMI) can act as a factor provoking affective disorders, and they, in turn, can worsen the disease process in the cardiovascular system.

The purpose of this study was to investigate affective disorders in patients with primary and recurrent acute myocardial infarction (AMI) on the basis of the constitutional approach, the analysis of age changes and sex.

Materials and Methods: The study involved 125 patients with acute myocardial infarction: 68 patients with primary AMI (46 men and 22 women, average age 53.4±11.2 years) and 57 patients with recurrent MI (31 men and 26 women, average age 62.7±9.3 years). For estimation of the degree of anxiety and depression Beck Depression Inventory and the Hamilton Anxiety Scale were used. The evaluation was conducted on 2–3rd day from the onset of AMI and the 14–15th day on a background of standard therapy of the underlying

disease. All patients were examined according to laboratory and instrumental standards of AMI diagnostics, on 14–15th day from the onset of the disease the patients underwent a 6 min walk test to assess exercise tolerance.

Results and discussion: Among the patients of group 1 on 2–3rd day patients with anxiety disorders dominated. The prevalence of clinically significant anxiety (>11 points on the Hamilton anxiety scale HARS) and mild depression (13±2 points on a scale Beck) was observed mostly in female. At 14–15th day in 1st group the severity of anxiety disorders had reduced. Patients of the 2nd group on 2–3rd day revealed symptoms of moderate depression (18±1 by Beck scale) in 21 patients and major depression (23±3 points by Beck scale)—in 36 patients with a prevalence of women over 65 years old. At 14–15th day the ratio of moderate to severe depression in the 2nd group was 57 and 43 %, respectively. In 82 % of patients with severe depression EF was <40 %, this subgroup of patients showed a significant decrease in exercise tolerance according to the 6 min walk test. Among patients with severe depression in 47 % of cases, there was complicated course of myocardial infarction compared with patients with mild depression—32 %, and 1st group—26 %. The degree of severity of affective disorders was more significant in men of asthenic body type and was independent of constitutional features in women.

Conclusions:

1. Patients with primary AMI were suffering mainly of anxiety disorders compared with patients with recurrent AMI which suffered mainly from depression.
2. The increase of depression severity was associated with the presence of LV systolic dysfunction, reduced exercise tolerance, with elderly age and a rising up of the percentage of complicated myocardial infarction.
3. Among men, affective disorders were more significant in men of asthenic body type.
4. Anxious and depressive disorders are more substantial in women comparing to men regardless of their somatotype.
5. The study of these aspects is important to optimize the treatment and rehabilitation of patients with AMI and improve their prognosis.

I-7

Comparison of outcome of patients with STEMI treated with Taxus drug-eluting stents or Genous endothelial progenitor cell capturing stents in a real-world setting

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Background: The aim our study was to compare the long-term safety and efficacy of Genous endothelial progenitor cell capturing stents with Taxus drug-eluting stents in patients undergoing primary percutaneous coronary intervention (pPCI) due to STEMI in a "real-world" setting.

Methods: Between February 2006 and November 2008, One hundred and two patients (62±12 years, 80.4 % male) with STEMI received Genous stent durint pPCI. Patients receiving Taxus stents during the same time period undergoing pPCI were matched (76.2 % male, 61±13 years) as controls. Patients were followed up up to 1 year. The primary endpoint of the study was the cumulative incidence of major adverse cardiac and cerebrovascular adverse event (MACCE, all-cause death, re-STEMI, target vessel revascularization/TVR/, and stroke). Secondary endpoints were the in-hospital death, procedure-related complications and stent thrombosis. Kaplan–Meier and multivariate Cox regression analyses concerning primary endpoint were performed.

Results: No difference between the Genous vs Taxus stent groups was documented regarding cardiac risk factors, such as incidence of diabetes mellitus (14 vs 19 %), hypertension (65 vs 70 %), hypercholesterolaemia and smoking, respectively. Fifty-eight percent of patients receiving Genous stent had previous statin therapy. The initial troponinT (0.98±0.14 vs 0.95±0.22 ng/mL) and the door-to-balloon time (195±213 vs 188±186 min) were similar in the Genous vs Taxus groups, respectively. No difference between the implanted stent size, length or other procedural parameters, such as total inflation time or number of implanted stents were observed. During the FUP, mortality was significantly higher in the Genous group vs Taxus group (11.8 vs 1 %, $p<0.01$), with trends toward higher rate of TVR in the Genous group. The cumulative MACCE was 20.6 vs 5.9 % ($p<0.01$) in the Genous vs Taxus group. Univariate Kaplan–Meier analysis showed a time-dependent benefit of Taxus over Genous stent concerning the primary end-point MACCE ($p<0.01$). When adjusting for classic risk factors and additional factors that affect the outcome of coronary intervention (number of implanted stents and total stent length) Taxus was found to be associated with significantly lower risk to MACCE as compared with Genous (hazard ratio 0.059, 95 % confidence interval 0.007–0.512, $p<0.05$).

Conclusion: Treatment with Genous stent in primary PCI in STEMI is associated with increased risk of mortality and composite of MACCE. The pre-treatment with statins seems to be mandatory before use of Genous stent in STEMI.

I-8

Circumflex artery-related ST-elevation myocardial infarction is associated with an increased delay in primary PCI: data from the Austrian Acute PCI Registry

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Purpose: Standard 12-lead ECG shows low sensitivity to detect acute myocardial infarction (MI) related to the circumflex artery and data on primary PCI in affected patients (pts.) is rare. We aimed to investigate characteristics and outcome in pts. with ST-elevation MI undergoing primary PCI according to the infarct-related artery (IRA).

Methods: Within a prospective nationwide registry of myocardial infarction we identified 4,846 pts. treated with primary PCI from July 2009 to October 2012. These patients were subdivided according to the IRA (LAD 43.7 %, RCA 42.8 %, CX 13.5 %). Characteristics, time delays, treatment and outcome were compared between the three groups.

Results: Baseline characteristics were similar except a higher rate of current smokers, higher BMI and age in the pts. with CX-related MI. Total ischemic time was highest in the CX group (3.7 h, IQR 2.3–7.2) and lowest in the LAD group (3.2 h, IQR 2.1–6.2; $p<0.01$). The rate of field triage was lowest in the CX group (LAD 59.1 %, RCA 59.9 %, CX 52.9 %; χ^2 $p=0.01$). ST-segment depression in left precordial leads (V1–V3/4) were more often documented in the CX (59.8 %) and the RCA groups (50.4 %) than in the LAD group (13.2 %; χ^2 $p<0.01$). Overall in-hospital mortality was 5.0 % and higher in the LAD-group (6.4 %) than in the RCA (3.9 %) or CX group (3.7 %; χ^2 $p<0.01$).

Conclusion: CX-related STEMIs show similar in-hospital mortality rates compared to STEMIs with the RCA as the culprit artery. These data underline the importance of critical initial assessment and ECG diagnosis in order to shorten delays, to increase the number of direct transfers and to improve outcome in patients with CX-related STEMI.

I-9

Relevance of copeptin for employment of dual biomarker strategy in diagnosis of ACS: WILCOP study

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Introduction: Cardiac troponin is an established biomarker in diagnosis of ACS. However, the major disadvantage of cTn is its incapability to detect an acute coronary syndrome (ACS) in the early hours after symptom onset, due to the delayed increase of its circulating levels after the actual ACS occurrence (so-called 'silent Troponin time'). We have investigated the effect of combined measurement of copeptin and high-sensitivity cardiac Troponin I (hs-cTnI) levels for early identification of patients with ACS.

Methods: This is an ongoing prospective single-centre study of consecutive pats. admitted to the emergency department (ED) of the Wilhelminen hospital with chest pain suggestive of ACS. The study started in March 2011 and the present analysis reports the data of the first 577 consecutive pats. All pats. had copeptin and hs-cTnI determinations at admission to ED. Cutoff value for Copeptin was set at 14 pmol/L and for hs-cTnI at 0.056 ng/mL.

Results: Overall, 82/577 (14.2 %) pats. had the final diagnosis of AMI. Copeptin and hs-cTnI concentrations at admission were significantly higher among pats with proven AMI. Levels of hs-cTnI in STEMI (5.097 ng/mL ±10.31; $p<00.1$) and NSTEMI (1.388 ng/mL ±2.62; $p<0.001$) pats. were significantly higher than in pats. with non-AMI diagnosis (0.049 ng/mL ±0.29). In comparison, Copeptin levels were significantly higher in STEMI pats. in comparison to NSTEMI and non-AMI pats. (75.07 pmol/L ±98.53 vs. 41.13 pmol/L ±87.08; $p<0.01$ and vs. 24.51 pmol/L ±63.84; $p<0.001$). Copeptin levels in NSTEMI pats., though lower than in STEMI pats., were sign. higher than in non-AMI pats. (41.13 pmol/L ±87.08 vs. 24.51 pmol/L ±63.84; $p<0.05$).

Accordingly, in all pats. with AMI both biomarkers had good diagnostic accuracy, although c-statistics of hs-cTnI (AUC 0.918) were significantly higher than that of copeptin (AUC 0.678). In addition, also in overall study population, negative predictive value (NPV) of hs-cTnI for AMI diagnosis was better than the NPV of copeptin (97.96 vs. 91.28 %; 95 % CI).

At admission, 8/82 (12.5 %) pats. with AMI had hs-cTnI levels under the detection limit of the assay (0.017 ng/mL) and 15/82 (18.3 %) pats. had hs-cTnI within the reference range (≤0.056 ng/mL). This was the group of so-called 'early presenters to ED'. In this 'early presenters' group with normal hs-cTnI concentrations, copeptin levels had good diag. accur. for AMI (AUC 0.753; $p=0.001$) and was in fact, more beneficial than c-statistics of hs-cTnI in the same patient group (AUC 0.704; $p=0.007$), with copeptin also demonstrating a higher NPV (98.37 %; 96.31–99.34; 95 % CI) than hs-cTnI (96.44 %; 94.24–97.84; 95 % CI) for AMI diagnosis in this subgroup. However, among pats. with already elevated levels of hs-cTnI at admission ('late presenters' group) copeptin had no diagnostic relevance (AUC 0.457; $p=0.06$).

When employed in entire population, combination of both markers (dual marker strategy) resulted in an increase of diagn. accur. with an AUC of 0.932 and NPV of 98.10 % (95.96–99.17; 95 % CI), compared to the c-statistics of hs-cTnI alone (AUC 0.918).

Conclusion: Levels of hs-cTnI at admission to ED have excellent accuracy for early diagnosis of AMI. However, among pats. with initially normal hs-cTnI levels presenting early after the onset of symptoms, there obviously exists a sign. diagn. relevance of additional determination of copeptin levels (dual marker strategy), which might result in a rapid and reliable diagnosis of AML.

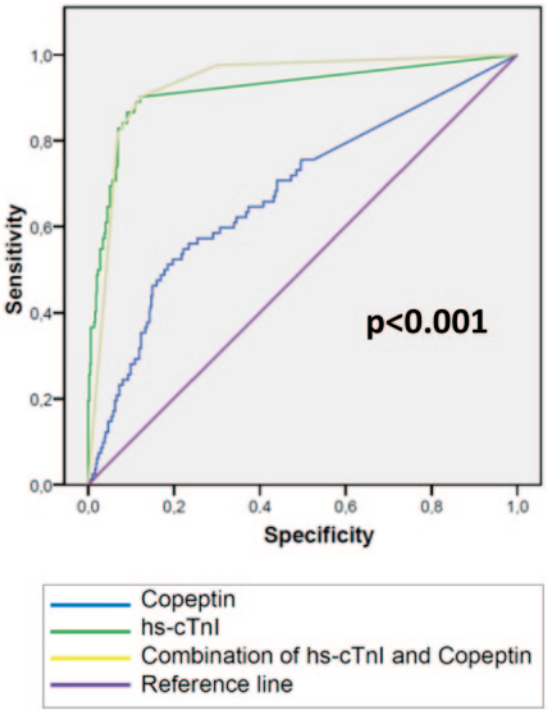

Fig. 1 ROC Curves at presentation for the diagnosis of ACS

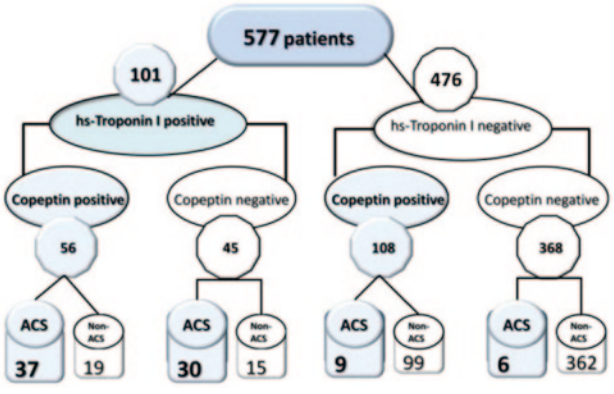

Fig. 2 Copeptin levels at presentation according to admission hs-cTnI status and final diagnosis

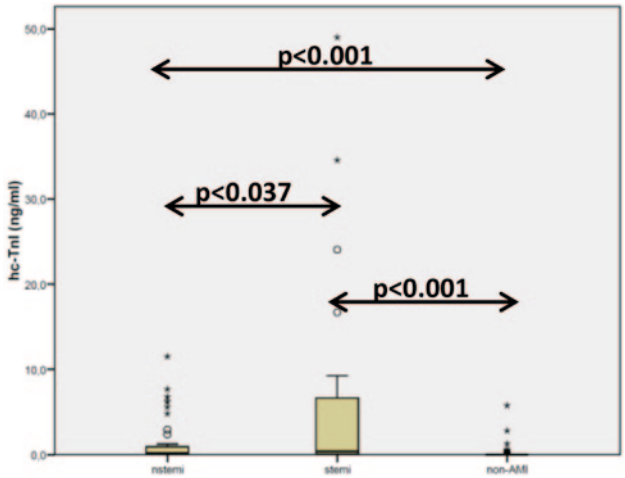

Fig. 3 Hs-cTnI levels at presentation to ED in all patients according to final diagnosis

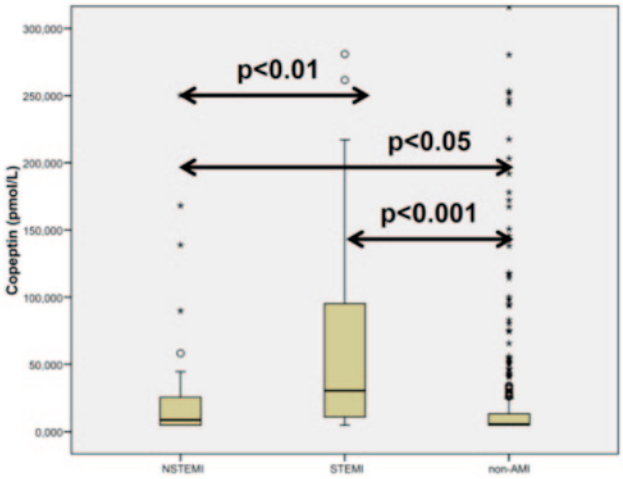

Fig. 4 Copeptin levels at presentation to ED in all patients according to final diagnosis

I-10

Akute Koronarsyndrome bei Migranten versus Nicht-Migranten: Ergebnisse einer prospektiven Pilotstudie

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Einleitung: Bei Akut-Koronarangiographien ist eine Häufung junger Patienten mit Migrationshintergrund aufgefallen, wobei es keine Unterschiede in der Häufigkeit klassischer Risikofaktoren zwischen Migranten und Nicht-Migranten gab. Aus diesem Grund wurden prospektiv auch soziodemographische Faktoren dieser Patienten erfasst. Methode: Eingeschlossen wurden konsekutive Patienten, die seit September 2011 an unserer Abteilung wegen eines akuten Koronarsyndroms (ACS) koronarangiographiert wurden. Während des Krankenhausaufenthaltes wurden Alter, Geschlecht, Koronarangiographie-Befund, klassische Risikofaktoren, sozioökonomische Faktoren sowie die ethnische Herkunft erhoben. Als „Migranten" wurden Patienten definiert, deren Geburtsort außerhalb Österreichs gelegen war.

Ergebnis: 79 Patienten (28 % weiblich) mit einem mittleren Alter von 56 Jahren wurden eingeschlossen. Die Koronarangiographie zeigte eine Eingefäßerkrankung bei 55 %, eine Zwei- und Mehrgefäßerkrankung bei 41 %, und keine Koronarstenosen bei 4 %. Eine Hypertonie fand sich bei 75 %, Hypercholesterinämie bei 72 %, Nikotinkonsum bei 59 % und Diabetes mellitus bei 23 %. Dreißig Patienten (38 %) waren Migranten: Achtzehn kamen aus dem ehemaligen Jugoslawien, 4 aus Nordosteuropa, je 2 aus Zentraleuropa und der Türkei, einer aus Bangladesh und 3 aus Südamerika. Die Migranten waren tendenziell jünger als Patienten mit österreichischer Herkunft (56 vs 61 Jahre, $p=0{,}3$) und hatten häufiger eine Zwei-oder-Mehrgefäßerkrankung (53 versus 33 %, $p=0{,}09$). Keine Unterschiede gab es bei Hypercholesterinämie (69 versus 77 %), bei Nikotinkonsum (57 versus 63 %), arterieller Hypertonie (73 versus 79 %), und in der Geschlechtsverteilung (Frauenanteil: Migranten 26 % versus Österreicher 30 %). Migranten hatten häufiger Diabetes mellitus (27 versus 14 %, $p<0{,}05$). Laut Bevölkerungsregister betrug im Jahre 2012 der Anteil an Migranten in Wien 21 % der Gesamtbevölkerung. Im Vergleich ist der Anteil an akutkoronarangiographierten Patienten mit Migrationshintergrund mit 38 % überproportional hoch.

Nicht-Migranten gaben häufiger als Migranten an, Sport zu betreiben (83 versus 60 %, $p<0{,}05$). Migranten haben häufiger Berufe mit niedrigem „skill level" als Nicht-Migranten (18 versus 2 %, $p<0{,}05$) und haben häufiger ein monatliches Einkommen unter 1000 € (45 versus 13 %, $p<0{,}05$).

Schlussfolgerung: Migranten mit akutem Koronarsyndrom sind jünger und leiden häufiger unter koronarer Zwei- oder Mehrgefäßerkrankung, unterscheiden sich aber wenig in Hinblick auf klassische Risikofaktoren, von Nicht-Migranten.. Der demoskopisch hohe Anteil an Migranten unter Patienten mit ACS weist auf ein höheres, möglicherweise psychosoziales Risiko von Migranten hin.

Postersitzung II: Basic Science 1

II-1

Endogenous interleukin-33 is protective during obesity development in mice

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Background: Interleukin (IL)-33 is the most recently described member of the IL-1 family of cytokines and it is a ligand of the ST2 receptor. IL-33 and ST2 are expressed in human and murine adipose tissue, and are elevated in adipose tissue of severely obese humans and in diet-induced obese mice. Treatment of genetically obese diabetic mice (ob/ob) with IL-33 as well as ST2 deficiency revealed protective effects of IL-33 in adipose tissue inflammation. The aim of this study was to investigate the development of obesity in IL-33 deficient (IL-33 −/−) mice.

Methods: IL-33 −/− mice and IL-33 +/+ littermates were fed with high fat diet (HFD, 60 kcal % fat) or low fat diet (LFD, 10 kcal % fat) to serve as a lean control for 18 weeks. Body weight was moni-

tored weekly and oral glucose tolerance tests (oGTT) and insulin tolerance tests (ITT) were performed after 16 and 17 weeks on diet, respectively. Plasma insulin was measured by ultra-sensitive ELISA. Epididymal white adipose tissue (eWAT), brown adipose tissue (BAT), inguinal adipose tissue, liver, spleen and pancreas were weighted at the day of sacrifice. The stromal vascular fraction (SVF) was isolated from eWAT and analysed by flow cytometry.

Results: IL-33 −/− mice on both HFD and LFD displayed impaired glucose tolerance compared to IL-33 +/+ mice on the respective diet ($p \leq 0.05$). Interestingly, basal blood glucose concentrations after overnight fasting showed no difference between the groups on the same diet. Baseline plasma insulin levels were equal in all groups on both diets. However, 15 min (min) after challenging mice with glucose, insulin levels were lower ($p \leq 0.05$) in IL-33 −/− mice on HFD compared to wild type controls. During ITT, blood glucose concentrations were higher in IL-33 −/− mice on HFD before and 15, but not 30, 45 or 60 min after intraperitoneal injection of insulin compared to IL-33 +/+ mice on HFD. Body weight did not differ between IL-33 −/− versus IL-33 +/+ mice after 18 weeks on a particular diet (49.4 ± 3.5 vs 50.2 ± 2.9 on a HFD and 34.1 ± 3.0 vs 33.7 ± 3.0 grams (g) on a LFD, respectively). However, IL-33 −/− on a HFD had larger liver as IL-33 +/+ on a HFD (3.6 ± 0.9 vs 3.0 ± 0.8 g). Interestingly, FACS analysis of SVF isolated from eWAT of obese mice (fed HFD) showed that SVF of IL-33 −/− mice contained a higher percentage of M1 macrophages (38 ± 2 % as compared to 11 ± 3 % in IL-33 +/+) and a lower percentage of M2 macrophages (23 ± 2 % as compared to 47 ± 3 % in IL-33 +/+) of the total adipose tissue macrophage population (Cd11b + F4/80 +). Lean mice (fed LFD) in general showed prevalence of M2 over M1 macrophages but macrophages numbers did not differ between IL-33 −/− and IL-33 +/+ mice.

Conclusion: Endogenous IL-33 is protective during obesity development in mice by influencing glucose and insulin tolerance as well as inflammatory cells content in adipose tissue.

II-2

Gain-of-function defect in the ryanodine receptor advances myocardial remodeling in response to experimental-induced pressure overload in mice

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Introduction: Malfunction of the sarcoplasmic reticulum (SR) Ca^{2+} release channel (ryanodine receptor, RyR2) underlies increased diastolic SR Ca^{2+} release associated with arrhythmias and contractile dysfunction in inherited and acquired cardiac diseases, such as catecholaminergic polymorphic ventricular tachycardia (CPVT) and heart failure. However, it remains unknown whether (1) RyR2-mediated spontaneous SR Ca^{2+} release provokes adverse cardiac remodeling in mice carrying a CPVT-associated RyR2R4496C +/− gain-of-function mutation in the setting of pressure overload, and if (2) stress-induced hypertrophy and heart failure increase the vulnerability for arrhythmias in RyR2R4496C +/− mice.

Materials and methods: Minimally invasive aortic constriction (TAC) was performed to induce pressure overload. Echocardiography was used to test in vivo cardiac function. Picrosirius red staining was employed to stain for collagen (fibrosis). Intracellular Ca^{2+} handling of isolated cardiomyocytes in the absence and presence of 300 nM RyR2-stabilizer K201 (at least 1 h pre-incubation) was assessed by confocal microscopy. Protein expression of Ca^{2+} cycling proteins was quantified using immunoblotting. ECG was continuously monitored (24 h) by means of radiotelemetry. In rescue experiments, K201 was applied by mini-osmotic pump infusion (12 mg/kg/day).

Results: At baseline, no differences were observed between WT and RyR2R4496C +/− hearts. In RyR2R4496C +/− hearts, however, TAC rapidly induced eccentric hypertrophy, ventricular dilatation, reduced ejection fraction and increased fibrosis. RyR2R4496C +/−TAC cardiomyocytes showed increased incidence of spontaneous SR Ca^{2+} release events (measured as Ca^{2+} spark frequency), reduced Ca^{2+} transient peak amplitude and SR Ca^{2+} content as well as reduced SR Ca^{2+} -ATPase2a and increased Na^{+}/Ca^{2+}-exchange protein expression. Heart failure phenotype in RyR2R4496C +/−TAC mice was associated with reduced survival due to pump failure in the absence of tachyarrhythmic episodes. K201 significantly reduced Ca^{2+} spark frequency in RyR2R4496C +/−TAC cardiomyocytes and prevented deleterious remodeling resulting in improved survival in RyR2 R4496C +/−TAC mice.

Conclusions: The combination of congenital alterations of SR Ca^{2+} release and pressure overload advances eccentric remodeling and heart failure death in RyR2R4496C +/− mice, and pharmacological RyR2 stabilization prevents this adverse interaction. These findings suggest potential clinical implication for patients with hypertension and acquired and/or inherited gain-of-function of RyR2-mediated SR Ca^{2+} release.

II-3

Early alterations of nucleoplasmic Ca^{2+} signalling in cardiac hypertrophy

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Background: A hallmark of heart failure is impaired cytoplasmic Ca^{2+} handling of cardiomyocytes. It remains unknown though whether specific alterations in nuclear Ca^{2+} handling—via altered excitation-transcription coupling—contribute to the development and progression of heart failure. We thus characterized changes of nuclear Ca^{2+} handling and the activation of Ca^{2+} -dependent transcription factors at the early and late stage of hypertrophy in mouse model of pressure overload and in failing human hearts.

Methods: Ventricular CMs were isolated 1 and 7 weeks after transverse aortic constriction (TAC) in mice as well as from 8 donor and 4 failing human hearts. Subcellular [Ca] transients (CaTs) were recorded in electrically stimulated CMs loaded with Fluo-4/AM. Phosphorylation levels of CaMKII were quantified by Western blots.

Results: During the early remodelling (i.e. 1 week after TAC intervention in mice and in moderately failing human hearts (55 % > EF > 35 %))—in contrast to diastolic $[Ca^{2+}]$ in the cytoplasm—diastolic $[Ca^{2+}]$ in the nucleus was already elevated at very low stimulation rate (0.5 Hz) as compared to the non-failing group, and than overproportionally increased with faster stimulation rates. In failing cardiomyocytes (7 weeks after TAC and severely failing human hearts (EF ≤ 35 %)), the changes in nucleoplasmic vs. cytoplasmic diastolic $[Ca^{2+}]$ were qualitatively comparable, though the increase was more pronounced in the nuclear compartment. High pacing frequency caused significantly higher phosphorylation of CaMKII in CMs from hypertrophic hearts compared to healthy controls.

Discussion: In conclusion, we found that the increased stimulation frequency led to a higher build-up of diastolic $[Ca^{2+}]$, especially in the nucleoplasmic compartment, in CMs from hypertrophic hearts which may be involved in the dysregulation of Ca^{2+}-dependent gene transcription and progression of adverse cardiac remodeling.

II-4

CD4+CD28null cells are an independent predictor of mortality in patients with heart failure

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Purpose: Immune activation and subsequent release of pro-inflammatory cytokines plays a central role in the pathophysiology of chronic heart failure (CHF). Cytotoxic CD4+CD28null cells are rarely found in healthy persons but expand dramatically under inflammatory conditions and therefore are implicated in a variety of pathological processes like atherosclerosis and autoimmune diseases. The study aim was to assess the impact of CD4+CD28null cells on survival in CHF patients.

Methods: Circulating lymphocytes from 107 CHF patients were analyzed for the distribution of CD4 subsets by flow cytometry. After gating on lymphocytes and CD4, CD28 was used to determine the CD4+CD28null subset which is given as percentage of CD4. The presence of CHF was defined by NYHA functional class ≥ II and either left ventricular ejection fraction (LVEF) <40 % or pro-BNP >500 pg/mL. Patients underwent a complete echocardiographic examination. Cox regression models were used to assess the influence of CD4+CD28null T cells on survival. The multivariable model was adjusted for age, gender, CHF etiology, NYHA functional class, diabetes, NT-proBNP and estimated glomerular filtration rate (eGFR). Man-Whitney-U-test was used for comparison between groups. Relations between variables were assessed using Spearman-Rho correlation coefficient. A p-value of 0.05 (2-tailed) was considered to be statistically significant.

Results: During a median follow-up of 23 months, 22 (20 %) persons died including 17 deaths due to cardiovascular causes. CD4+CD28null cells independently predicted all-cause mortality with an adjusted hazard ratio (HR) of 1.88 per 1-standard deviation increase (95 % confidence interval (CI): 1.26–2.79, $p=0.002$) and with a HR of 1.83 for cardiovascular mortality (95 % CI: 1.18–2.86, $p=0.008$), respectively. The 2-year survival rate was 68 % in patients with CD4+CD28null cells >10 % compared to 86 % in the remaining patients ($p=0.046$). The effect of CD4+CD28null cells on mortality was not affected by CHF etiology (for interaction, $p=0.87$). Further, we found significant associations with NT-proBNP ($r=0.23$, $p=0.016$), chronic obstructive pulmonary disease ($p=0.041$) and diabetes ($p=0.024$) as well as an inverse correlation with eGFR ($r=-0.26$, $P=0.007$).

Conclusions: Circulating CD4+CD28null cells are associated with CHF severity and represent a strong and independent predictor of mortality in CHF fostering the implication of the immune system in CHF pathophysiology. The predictive value of CD4+CD28null cells in CHF patients points towards chronic antigenic stimulation with adverse functional consequences for cardiac tissue.

II-5

Impact of levosimendan on cardiac performance due to antioxidative effects?

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Objectives: Due to cardio-pulmonary bypass with ischemia and reperfusion, oxidative stress plays an important role leading to contractile dysfunction, apoptosis and necrosis of myocytes. The inodilator Levosimendan (LS) is a calcium sensitizer showing pleiotropic effects beside to its positive inotropic action. However no inotropic effect could be shown in isolated rat hearts so far in literature.

As LS also preserved contractile performance in human atrial strips exposed to oxidative stress an antioxidative effect was assumed.

Present studies aim was to differ between positive inotropic and antioxidative effects of LS.

Methods: Hearts of male adult Wistar rats were rapidly excised and left ventricular muscle stripes were dissected. Muscle strips were mounted in an organ bath and electrically stimulated. Tissue was superfused with carbongenated Krebs Henseleit solution (KHS) and stretched to the length associated with the maximum twitch force. After an equilibration period LS (10–7 M) and H_2O_2 (10–4 M) were added and twitch force was registered after reaching steady state. Statistical analysis was performed using Mann–Whitney U Test.

Results: In a first series of experiments ($n=8$) no significant change of twitch force compared to baseline was recognizable after administration of LS (98.1 % ± 6.6 %) or LS + H_2O_2 (94.5 ± 6.8 %). In a second series a significant decrease (77.3 ± 2.4 %) was observed after muscle stripes were superfused with H_2O_2. After subsequent superfusion with H_2O_2 + LS a significant increase of twitch force followed (84.6 ± 4.4 %).

Conclusions: Our data suggest, that LS has no inotropic effect on muscle stripes, obtained from male rat hearts. But exposition to oxidative stress revealed an additional effect of LS in preventing contractile dysfunction. This could reveal new therapeutic options of postoperative contractile disorders. Further it opens new strategies in preventing systemic inflammation after extracorporeal circulation.

II-6

Impact of diastolic dysfunction on global contractile capacity on the level of the myofilaments

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Introduction: Diastolic dysfunction (DD) accounts for as many as 40 % of all cases of congestive heart failure (CHF). The prevalence of diastolic heart failure (DHF) in patients with normal systolic function increases with age and is significantly higher in women than in other groups: up to 75 % of patients who have diastolic heart failure are women. In the progression of most cardiac diseases, diastolic dysfunction precedes systolic impairment. Because of lack of data, there are no therapeutic recommendations for treatment. Therefore we performed a study to compare the cardiac capacity of the contractile elements of patients with (Group I) and without diastolic dysfunction (Group II).

Material and methods: Right auricle tissue from eight patients (four patients per group), undergoing aortic and/or mitral valve replacement was obtained prior to right atrial cannulation. Patients in both groups are reported to have normal left ventricular function. The tissue was transported in an oxygenated Krebs-Henseleit-solution and skinned with Triton-X. The fibers were exposed to a gradual increase of calcium concentration (six steps of calcium concentration) and the corresponding force was measured and recorded. We performed three experiments with different fibers in each patient ($n=48$).

Results: (1) Patients with diastolic dysfunction showed statistically significant less force compared to those without diastolic dysfunction ($p=0.0002$). (2) This difference could also be found when focused on gender: female fibers from group II showed significant higher force values than fibers with the dysfunction ($p=0.0001$) (3) Also the male fibers without the diastolic dysfunction developed significant more force than male fibers without the dysfunction ($p=0.01$).

Discussion: Our data shows, that the contribution of diastolic dysfunction to the global cardiac performance is underreported and not imaged by statements about the LVF or EF. We observed a significant less force capacity in patients with diastolic disorder. This significance is even more pronounced in female fibers with and without diastolic dysfunction, but also seen in the male gender. Based on the fact that there is no standardized therapy concept regarding diastolic dysfunction further studies are required to prevent diastolic heart failure and provide patients with the best available therapy.

II-7

GM-CSF and M-CSF expression by human endothelial cells is up-regulated by the IL-1 cytokine family member IL-33

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Background: Although its involvement in various other inflammatory diseases could already be shown, the role of IL-1 cytokine family member interleukin (IL)-33 in atherosclerosis is still controversially discussed. Granulocyte-macrophage colony-stimulating factor (GM-CSF) and macrophage-CSF (M-CSF) are other cytokines involved in atherosclerosis. The aim of this study was to find out whether IL-33 influences GM-CSF and M-CSF production in human coronary artery endothelial cells (HCAEC) and human umbilical vein EC (HUVEC) in vitro.

Methods: HCAEC and HUVEC were incubated with IL-33 at various concentrations for different periods of time. GM-CSF and M-CSF mRNA expression was analysed by qRT-PCR and protein amount by ELISA. Further, HUVEC were infected with adenoviral vectors for overexpression of IκBalpha (AdV-IκBalpha) or a dominant negative form of IκB kinase 2 (dnIKK2, AdV-dnIKK2), or a control adenovirus (AdV-green fluorescent protein (GFP)). IL-1 receptor antagonist (IL-1-RA) was added to HUVEC treated with IL-1β (as a positive control) or IL-33. In additional experiments, cells were incubated with IL-33 with or without addition of recombinant human (rh)ST2 Fc chimera or IgG (as an isotype control).

Results: IL-33 significantly up-regulated GM-CSF and M-CSF mRNA and protein production in HCAEC and HUVEC. GM-CSF mRNA expression was significantly increased between 1 and 24 h of incubation with IL-33 at 100 ng/mL with the maximum after 9 h (up to 1,800-fold in HUVEC and 86-fold in HCAEC). M-CSF mRNA expression was increased after incubation with IL-33 for 9 h up to 13-fold in HUVEC and 26-fold in HCAEC. The effect on GM-CSF and M-CSF protein production was concentration-dependent. As adenoviral overexpression of IκBalpha and dnIKK2 inhibited IL-33-induced GM-CSF and M-CSF mRNA expression, the effects of IL-33 on the production of these cytokines in EC seem to be mediated by NF-κB. Stimulation of GM-CSF production by IL-33 was found to be IL-1-independent as addition of IL-1-RA did not inhibit IL-33-induced GM-CSF mRNA up-regulation in human EC. Addition of rhST2 Fc chimera, but not IgG, to IL-33-treated cells inhibited the effects of IL-33.

Conclusion: IL-33 may contribute to the pathogenesis of atherosclerosis by stimulating the production of GM-CSF and M-CSF by human endothelial cells. This effect appears to be NF-$_{\kappa}$B-mediated, inhibited by soluble ST2 and, at least for GM-CSF, IL-1-independent.

II-8

Arrhythmogenic effects of angiotensin II

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Increased levels of angiotensin II (ATII) are associated with the progression of heart failure and arrhythmias. We investigated the cellular mechanisms of Ca-mediated arrhythmias induced by ATII via the Gq-coupled AT1 receptor pathway. In CM from murine or human non-failing left ventricle, Ca transients (Fluo4-AM, confocal line scans, 1 Hz), SR [Ca] (caffeine), SR Ca leak (spark frequency, SparkF) and arrhythmic action potentials (arrhAP, visualized as synchronized diastolic Ca release) were quantified without and with ATII (100 nM, 20 min). The decay time constant (tau_caff) of caffeine-induced Ca transients was used as a measure of NCX forward mode activity. Pyr3 (10 μM) served as TRPC3-inhibitor. AP duration (APD, current clamp) was recorded in parallel experiments. TRPC3 protein expression (Western blot) and immunocytostaining (CM) was performed in sham and transverse aortic constriction (TAC, 6 weeks)-operated mice and in human myocardium.

In mouse CM ATII increased the [Ca] transient amplitude (F/F0: 4.1±0.3 vs. 2.7±0.2 in CTRL, $P<0.05$). ATII also induced Ca sparks (SparkF (s-1*pL-1): 277±28 vs. 48±20) and arrhAP (0.77±0.12 vs.0.03±0.01*s-1) despite unchanged SR [Ca]. ATII induced significantly more arrhAP than ouabain (0.06±0.02) at similarly increased SparkF (ouabain: 284±44). ATII tended to increase AP duration from 53±6 to 92±34 ms (APD90; $p=0.1$). In CM matched for similar SparkF, Pyr3 abolished ATII-induced arrhAP. ATII was also arrhythmogenic in human non-failing CM (SparkF: 407±93 vs. 90±23 in CTRL; cells with arrhAP: 6/10 vs.2/11; $p<0.05$). Pyr3 also effectively reduced AT-II induced arrhythmogenity in human CM. ATII accelerated tau_caff (1,987±131 vs. 3,164±390 ms in CTRL; $p<0.05$), and this was abolished in presence of PyR3. Following TAC TRPC3 expression levels were increased (TRPC3/GAPDH; 1.3±0.1 vs. 1.0±0.05 in sham; $p<0.05$). TAC TRPC3 expression was also increased in human end-stage HF patients (1.6±0.15 vs. 1.0±0.6 in non-transplantable donor hearts; $p<0.05$). In healthy CM, TRPC3 was distributed in a T-tubular-like pattern. In TAC and in end-stage failing hearts, TRPC3 relocalized towards the outer cell surface.

Conclusion: ATII facilitates Ca-dependent arrhythmias by mechanisms beyond an increase in SR Ca leak in mouse and human CM. In the progression of HF TRPC3 is upregulated and relocalized to the outer membrane in mouse and human myocardium. ATII-induced arrhythmogenity is mediated by increased NCX activity and potentially modulated by TRPC3.

Postersitzung III: Basic Science 2

III-1

Cellular contractile dysfunction in a rat model with compensated renal failure and diastolic dysfunction

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Background: Chronic renal failure is often connected with myocardial dysfunction. The underlying pathomechanism of myocardial dysfunction are currently not fully identified. We investigated whether contractile dysfunction is related to the intrinsic properties of the cardiomyocytes in a rat model with compensated stable renal failure and diastolic dysfunction.

Methods: Fifty-six young male Wistar rats (260–290 g) underwent subtotal nephrectomy (NXT) or sham operation (SOP). After 8 or 24 weeks the hearts were removed and used either for isolation of left ventricular (LV) cardiomyocytes or histological analysis of fibrosis. For the latter, the middle part with two visible papillary muscles of the LV was cut out and stained with picosiriusred for the assessment of the total collagen content. Contractile function (cell shorthening) was studied in isolated single LV cardiomyocytes using epifluorescence ratiometric microscopy and different stimulation frequencies (1–8 Hz and recovery 1 Hz).

Results: After 8 and 24 weeks fractional cell shortening (CS) amplitude was unchanged at 1 Hz stimulation (CS 3.6±0.6 and 3.8±0.5 in NXT vs. 4.2±0.7 and 4.5±0.8 % in Sham; $n \geq 10$ cells/group). Time to peak cell shortening was unchanged in both groups at 8 and 24 weeks at all stimulation frequencies (TTP 70±6 and 87±5 vs. 53±7 and 86±4 ms, 1 Hz, $n \geq 10$). Time for early (50 %) relaxation of cell shortening was significantly prolonged in NXT at 8 and 24 weeks (CS RT50 53±8 and 42±2 vs. 32±5 and 34±1 ms, 1 Hz, $n \geq 10$, $p < 0.05$) with no further increase at higher stimulation frequencies. However time for 90 % relaxation of cell shortening was not significantly changed at 8 and 24 weeks. Fibrosis was significantly more pronounced in NXT vs. Sham after 8 weeks (total collagen area 6.12±0.22 vs. 3.97±0.09 %, $n \geq 10$, $p < 0.01$), with a further significant increase at 24 weeks (total collagen area 7.41±0.12 vs. 4.33±0.05 % in NXT, $n \geq 10$, $p < 0.01$ vs. Sham and 8 weeks).

Conclusion: Early relaxation is impaired in isolated cardiomyocytes in this model of compensated renal failure with diastolic heart failure. Additionally LV tissue samples suggest that increased fibrosis may contribute to the phenotype early in cardiac remodeling.

III-2

Overexpression of GATA-4, TGF3, Mef2c and HIF-1alpha contributes to improvement of infarct size in porcine model of chronic myocardial infarction, treated with percutaneous intramyocardial delivery of secretome of apoptotic white blood cells (APOSEC)

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Background: The high apoptotic rate of the cardiac transplanted cells in the infarcted heart and the negligible differentiation rate toward cardiomyocytes suggest that stem cell transplantation in ischemic heart disease is clinically not enough effective. Transcription factor GATA-4, hypoxia-inducible factor (HIF1)-alpha, transforming growth factor (TGF)-3beta and myocyte-specific enhancer factor (MEF)-2c are considered to be key regulators of angio- and cardiomyogenesis. The aim of the present experimental study was to investigate the association between gene expression of ischemic cardiomyocytes and size of ischemia.

Methods: Under general anaesthesia farm pigs ($n=16$) underwent closed chest reperfused AMI by 90-min percutaneous balloon occlusion of the mid LAD, followed by balloon deflation for reperfusion. At 3-day follow-up (FUP) baseline cardiac magnet resonance imaging (MRI) with late enhancement (LE) was performed. At day 30 post-AMI, the animals were randomized and received either porcine APOSEC (resuspended supernatant of irradiated apoptotic peripheral white blood cells) ($n=8$) or Medium (cell culture medium) ($n=8$) by 3D NOGA percutaneous intramyocardial injections, located in the periinfarction areas (11±2 treatment points). At day 60 (post-AMI (30 days post-treatment), control cardiac MRI + LE was performed. Gene expression of the infarction border zone and the necrotic areas were evaluated by using quantitative real-time polymerase chain reaction (PCR).

Results: Significant ($p<0.05$) overexpression of HIF1alpha, MEF2c and GATA-4 with a trend towards higher level of TGF-3beta gene expression was measured in the border zone of chronic infarction in Aposec-treated animals as compared with the Medium-treated pigs. In contrast, caspase-3 gene was significantly downregulated in the Aposec group. Percutaneous intramyocardial injections of Aposec led to improvement in left ventricular ejection fraction (EF) (45.4±5.9 vs 37.4±8.9 %), and decrease in infarct size (13.9±3.8 vs 21.1±4.7 %) ($p<0.05$). Significant ($p<0.05$) negative linear correlation could be demonstrated between gene expression level of GATA4 and infarct size ($r=-0.668$) and TGF-3beta and size of infarction ($r=-708$). LV EF did not show correlation with any of the gene expression.

Conclusion: Overexpression of transcription factor GATA-4 and TGF-3beta is related to decrease in infarct size in secretome-treated animals. The significant increase in cardiogenic and angiogenic gene-expression 1-month post treatment suggest a long-acting effect of injected paracrine factors in a "cell-less cell therapy".

III-3

Apelin-13 has no effect on left ventricular contractility and compliance in healthy closed-chest pigs

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Background: Apelin is an endogenous small peptide that binds to the APJ-receptor located on endothelial cells and cardiomyocytes. It induces endothelium-dependent vasodilation. Apelin is further involved in cardiac remodeling and impacts on myocardial contractility, however, controversial findings have been reported here. We therefore analysed contractile effects of apelin in a large animal species in vivo.

Methods: Six anaesthetised pigs (58±2 kg) were acutely instrumented (closed-chest) with a left-ventricular (LV) pressure-volume catheter, a Swan-Ganz catheter and an intraaortic balloon catheter. Apelin-13 was administered as a steady-state intravenous infusion of 10 µg/kg/min, followed by bolus infusion of 1 and 3 mg, respectively. Steady-state haemodynamics as well as pressure-volume

relationships at end-systole and end-diastole (ESPVR, EDPVR) were assessed.

Results: At 15 min of apelin-13 infusion, heart rate (87±5 vs 87±4 bpm), cardiac output (6.6±0.2 vs 6.6±0.3 L/min), mean aortic pressure (86±10 vs 88±8 mmHg) and systemic vascular resistance (12.3±1.3 vs 12.7±1.0 mmHg/L/min) were similar compared to baseline (all p = NS). Also LV end-diastolic volume (154±12 vs 147±6 mL), LV end-diastolic pressure (8±2 vs 9±1 mmHg), LV maximum pressure (103±9 vs 105±7 mmHg) and LV dP/dtmax (1,646±69 vs 1,693±79 mmHg/s) were unchanged. The ESPVR and EDPVR were not different vs baseline (see graph). Bolus-injections resulted in a temporary drop of systemic vascular resistance, which returned to baseline at 3 min after bolus-injection.

Conclusion: In healthy pigs in vivo, pressure-volume analysis did not indicate any effect of apelin-13 on LV contractility or compliance. However, potential long-term effects on cardiac function and remodeling remain to be investigated. Species-specific effects of apelin should be considered in such studies.

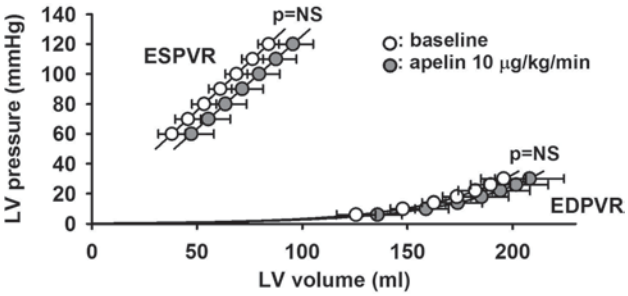

Fig. 1 Apelin-13 did not indicate any effect on LV contractility or compliance

III-4

Loss of regenerative response upon low energy shock waves in toll-like receptor 3 silenced endothelial cells and TLR-3 knock out mice in a hind limb ischemia model

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Introduction: Low energy shock waves (SW) have been shown to induce angiogenesis in ischemic myocardium. The mechanism remains unknown. Toll-like receptor (TLR)-3 is activated by RNA binding. It plays a key role in inflammation and angiogenesis. SW cause cellular cavitation, thus liberating cytoplasmic mRNA that activates TLR-3.

Methods: The effect of SW was tested in human umbilical vein endothelial cells (HUVECs): untreated (control) vs. SW treated (SW group) vs. treated with 200 µg/mL poly I:C (agonist). We measured mRNA expression of TLR-3 and Tie-2 after 2, 4 and 6 h post stimulation. Gene silencing was done with TLR-3 siRNA. Hind limb ischemia was performed in TLR-3 −/− mice. Laser Doppler perfusion imaging and necrosis score were assessed (n=6).

Results: TLR-3 gene silencing in SW treated HUVECs causes loss of response for TLR-3 mRNA (107.0±13.3) as compared to SW group (378.3±14.2 or agonist (1,261±72.1, both p<0.0001).

SW treated TLR-3 −/− mice showed no improvement of perfusion ratio 4 weeks after hind limb ischemia as assessed by laser Doppler perfusion imaging (0.52±0.07 vs. 0.57±0.04 controls, p=0.55) nor in necrosis score (1.6±0.2 vs. 1.7±0.2 controls, p=0.84), whereas wild types regenerate significantly.

Conclusion: Low energy shock waves activate toll-like receptor 3 in endothelial cells as does the specific agonist Poly I:C. Effects are suppressed in TLR-3 silenced cells and in TLR-3 −/− mice. Our data indicate that SW effects may at least in part be mediated via TLR-3.

III-5

CD80 antigene expression is increased during ischemia in human myocardium, but not affected by ß-blockers

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Introduction: Neuroendocrine/inflammatory and endothelial functions have been indicated as crucial for ischemic heart disease patients. The effect of carvedilol on cytokines, asymmetric dimethylarginine and left ventricular ejection fraction at baseline after long-term administration of carvedilol have been investigated by others: Carvedilol, for example, appears to reduce symptoms and the expression of inflammation, oxidative response, myocardial fibrosis and apoptosis, as well as in preserving energy transcription factors and LV function. Cardiac injury activates innate immune mechanisms initiating an inflammatory reaction. Immunological receptor-mediated pathways, the complement cascade and reactive oxygen generation induce nuclear factor (NF)-kappaB activation and upregulate chemokine and cytokine synthesis in the infarcted heart. In an earlier paper, we have shown that interleucin pathway is upregulated by nebivolol, not by atenolol during experimental ischemia.

Methods: Myocardial tissue probes derive from the right auricle of patients undergoing cardiac surgery. A small part of the right auricle is removed when the heart is put on extra-corporal circulation. This sample is then be placed in cooled Tyrode solution and hypoxia is brought about by switching 100 % oxygen to 100 % nitrogen (hypoxia) in one of the two chambers. By doing so, we are able to compare ischemic and non-ischemic tissue of the same patient. Snap frozen samples are stored at – 70 °C until RNA isolation. Quality of isolated RNA is analysed by Agilent's Bioanalyzer 2,100 system. Arrays are scanned with the AB1700 Chemiluminescence Array Reader and images, data are processed by PANTHER software.

Results: Here we specifically look at CD80 expression, because using microarray, we find that CD80 is more than 3× down-regulated in nebivolol under hypoxia (0.23) , but almost 4× up-regulated under normoxia (3.9). CD80 is also up-regulated in atenolol under hypoxia (1.18) as well as in normoxia (1.83). However, using PCR, it can be seen that during experimental ischemia, there is an up-regulation of CD80-expression from 0.09+0.01 to 0.13+0.01. However, a significant regulation under the influence of beta-blockers during myocardial ischemia cannot be verified by PCR control.

Conclusion: We find that during experimental ischemia, there is a significant up-regulation of CD80-expression. Chemokines stimulate the chemotactic recruitment of inflammatory leukocytes into the infarct and cytokines promote adhesive interactions between leukocytes and endothelial cells. They enhance early transmigration of inflammatory cells into the site of injury and, during the early phase of ischemia, additional cell damage. One of the Key molecules in this context, CD80, however, underlies no cardioprotective regulation of ß-blockers.

III-6

Glycoprotein 130 polymorphism predicts soluble glycoprotein 130 levels

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Background: Interleukin-6 (IL-6) is a key cytokine in inflammatory diseases. It exerts its biological function via binding to a homodimer of its signal transducer glycoprotein 130 (gp130). Soluble gp130 (sgp130) is the natural inhibitor of IL-6 trans-signaling and is proposed to act anti-inflammatory. The aim of this study was to test a possible influence of the gp130 genotype on sgp130 serum levels.

Material and methods: In two separate populations, subjects were genotyped for the gp130 polymorphism G148A and sgp130 serum levels were measured. The OSLO population consisted of 546 male subjects at high risk for CAD. The VIENNA population consisted of 299 male subjects with angiographically proven CAD.

Results: In the OSLO population, 124 (22.7 %) subjects were hetero- or homozygote for the rare A allele. Individuals carrying the polymorphism had significantly higher levels of sgp130. In a multivariate linear regression model adjusted for common risk factors, this association remained significant. (adjusted $p=0.001$) In the VIENNA population, 48 (16.1 %) subjects were hetero- or homozygote for the rare A allele. Consistent with the former study, sgp130 levels were significantly higher in carriers of the polymorphism compared to wildtype carriers, independent of common risk factors. (adjusted $p=0.038$) Sgp130 levels were significantly higher in diabetic patients in both populations and in smokers in the OSLO population. ($p<0.05$).

Conclusions: Sgp130 serum levels are significantly higher in subjects carrying the gp130 polymorphism G148A compared to wildtype carriers. This finding proposes a possible genetical influence on sgp130 levels which may alter individual coping mechanisms in inflammatory diseases.

III-7

Myocardial infarct size measurement in a small animal model using geometric angle calculation

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Introduction: In basic science studies utilizing animal models the efficacy of potential treatments for myocardial infarction (MI) is commonly assessed by histological measurement of infarct size. The planimetric measurement of the infarcted area in tissue sections of the left ventricle is a standard approach to determine the extent of MI. This approach has also been used in chronic infarct setting to measure infarct areas several weeks after MI, however, it has been proposed that an infarct length based approach might provide better results in a chronic MI setting. We tested this hypothesis, because wall thinning is known to occur in the chronic setting and an area measurement approach might be less accurate. We compared infarct measurements in tissue sections based on (1) infarct area, (2) epicardial and endocardial infarct lengths, and (3) infarct angles calculated utilizing the centroid of the left ventricle by using a new calculation approach.

Materials and methods: Acute myocardial infarction was induced in adult male Sprague-Dawley rats ($n=30$, weight 300–350 g) by ligating the left anterior descending artery (LAD). Six weeks after induction of myocardial infarction, rats were anaesthetized and transthoracic echocardiography was performed. After examination, hearts were explanted and then sliced at three layers at the level of the largest extension of infarcted area. Tissue samples were stained according to an Elastica van Gieson (EVG) staining protocol. On these specimens infarct size calculations were performed using an area, a length and a newly developed angle based approach. For the latter, angle calculations starting from the centroid were performed in relation to endo-, myo- and epicardial border zones between vital myocardium and scar tissue (see Fig. 1a). Infarct size was calculated as follows: mean of all three angle measurements divided by $360° \times 100$.

Results: Length and angle measurement showed comparable infarct sizes (23.94 %±2.04 SEM vs. 24.76 %±2.13 SEM, $n=30$). However, the infarct size values derived from the area measurement approach were significantly smaller than those from the other two measurement approaches due to scar thinning and ventricular remodelling (14.81 %±1.27 SEM, $p<0.003$ vs. length and $p<0.0001$ vs. angle measurement, see Fig. 1b). Infarct sizes from all three measurement approaches correlated significantly with parameters of cardiac function. However, the infarct size values derived from the angle measurement approach showed the best correlation with parameters of cardiac function (e.g. ejection fraction; $r=0.73$ for angle, $r=0.64$ for length and $r=0.59$ for area measurement).

Conclusions: We concluded that area-, length- and angle based measurements can be used to determine relative infarct size in MI models, although results from area-based measurements are substantially smaller due to wall thinning. Moreover, our proposed new method of infarct angle measurement is a reliable and simple way to calculate infarct size compared with conventional measurement approaches.

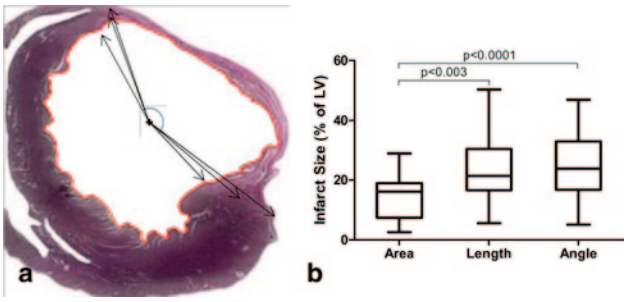

Fig. 1 Infarct angle measurement and infarct size calculation

III-8

Possibility of a feed-back mechanism which regulates dimethylarginine dimethyaminohydrolase expression upon the availability of NO

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Methylation of arginine residues in proteins and subsequent proteolysis results in the liberation of free methylarginines, including asymmetric dimethylaginine (ADMA; R-Me2), an inhibitor of nitric oxide sythetases (NOS). ADMA is metabolised by dimethylarginine dimethyaminohydrolase (DDAH) to citrulline (CIT) and dimethylamine (MA). ADMA is recognised as a plasma marker of increased cardiovascular risk but it is unclear whether it ever accumulates to sufficient levels to affect NO pathways. However, it has been shown by chemical biology and gene deletion techniques that that loss of DDAH function elevates plasma and tissue ADMA levels. On the other hand it is possible that a feedback mechanism exists which regulates DDAH expression upon the availability of NO. In this context, it has to be mentioned that nebivolol can stimulate an increase of endothelial NO, which becomes available at the vascular smooth muscle and induces vaso-relaxation. Nebivolol seems to interact with the endothelial NO pathway in two complementary ways: it increases NOS activity and reduces the NO-scavenging radical superoxide anion, by re-directing deranged NOS activity.

In the microarray preliminary analyses we found that DDAH gene expression is significantly down-regulated by nebivolol compared to atenolol both in O_2-perfused preparations and simulated ischemia/hypoxia (N_2-perfused) preparations. Using real-time PCR, we were able to confirm that DDAH gene expression is significantly down-regulated by nebivolol compared to atenolol in simulated ischemia/hypoxia (N_2-perfused) preparations: It could be shown that, without betablockers, there is no significant regulation of DDAH-expression during myocardial ischemia. There is, however a significant difference between the expression of DDAH during myocardial ischemia in the presence of atenolol (33.2+4.2) and nebivolol (6.7+0.7; + SEM; $P<0.05$).

In the present study we find that the myocardial expression of DDAH is reduced in the presence of nebivolol in both normoxia as well as hypoxia. The measured decrease of DDAH seen under nebivolol but not with atenolol both during normoxia and hypoxia could be a measure for the increased availability of NO brought about by nebivolol as a feed back control. This is of interest since several steps in the pathways of interaction have remained unclear as yet. It is certainly promising to investigate further into this interrelation of NO, DDAH and nebivolol.

Postersitzung IV: Bildgebung 1

IV-1

Structural and functional differences in physiological versus pathological patterns of left atrial remodeling: a speckle tracking strain echocardiography study

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Background: Left atrial (LA) remodeling increases the risk of atrial fibrillation (AF); however, few studies have compared LA deformation in physiological and pathological patterns of LA remodeling. We therefore investigated the relation between LA and LV strains (ε) as a determinant of indexed LA volume (LAVi) in athletes and non-athletes over a wide range of age and diastolic function.

Methods: Total 143 subjects were studied in two groups: 91 healthy volunteers including 77 athletes, and 52 patients with diastolic dysfunction including 27 patients with AF. LAVi was correlated with diastolic function and speckle tracking derived global LAε and LVε.

Results: For patients, LAε and LVε (Figs. 1a and b) independently predicted LAVi ($R^2=0.51$, $P=0.04$ for both). In contrast, volunteers showed higher LAε (40±10 vs. 23±12%, $P<0.01$) despite similar LAVi ($P=0.21$). LAε showed diagnostic value in differentiating pathologic and physiologic LA remodeling (Fig. 1c; AUC, 0.84, $P<0.01$).

Conclusions: In patients with diastolic dysfunction, an increase in LA size is accompanied with reduced LA and LV deformation. LA size in athletes, however, is associated with dynamic diastolic flux of blood volume due to enhanced LV lengthening mechanics. This relationship may be useful for distinguishing patients with pathological and physiological pattern of LA remodeling.

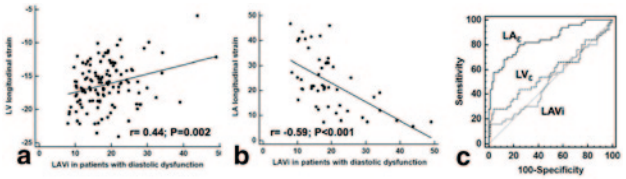

Fig. 1 Increase in LA size is accompanied with reduced LA and LV deformation

IV-2

Cardiac index after acute ST-segment elevation myocardial infarction measured with phase-contrast cardiac magnetic resonance imaging

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Introduction: Cine cardiac magnetic resonance (CMR) represents the gold-standard in the non-invasive determination of left-ventricular function, but might overestimate cardiac output in different pathophysiological conditions. Phase-contrast CMR might provide a fast and robust alternative. We therefore investigated the use of phase-contrast CMR to assess cardiac index in patients early after acute ST-segment elevation myocardial infarction (STEMI).

Methods: We included $n=90$ patients with first STEMI (mean age: 59±11 years) who underwent CMR within 7 days after primary angioplasty for the index event. Cine sequences in the left-ventricular short-axis and phase-contrast CMR on the level of the ascending aorta were applied. The phase-contrast protocol was validated against cine CMR in 15 healthy volunteers. Inter- and intraobserver agreement was determined in volunteers as well as in $n=16$ STEMI patients. The correlations of clinical variables (age, gender, ejection

fraction, NT-pro-brain natriuretic peptide [NT-proBNP]) with cardiac index in STEMI patients were calculated.

Results: There was a strong agreement of cine CMR with phase-contrast CMR in healthy volunteers (r: 0.818, mean difference: −0.13 L/min/m², error ±18%). Agreement was lower in STEMI patients (r: 0.611, mean difference: −0.17 L/min/m², error ±32%). In STEMI patients cardiac index measured with phase-contrast CMR was 2.7 L/min/m² and showed lower intraobserver (1.4 vs. 8.8%) and interobserver variability (8.5 vs. 11.6%) than cine CMR. Cardiac index decreased by 16 mL/min/m² per year (r=0.356, p=0.001) in STEMI patients. Furthermore, cardiac index was correlated with patients ejection fraction (r=0.256, p<0.02) and inversely correlated to NT-proBNP values (r=−0.220, p<0.05).

Discussion: Phase-contrast CMR is a valid and robust method for the measurement of cardiac index. With the use of phase-contrast CMR we observed a decrease in cardiac index with age and ejection fraction in patients after acute STEMI. Observed differences in STEMI patients might be due to presence of subclinical mitral regurgitation, which occurs in up to 50% of STEMI patients and prompts further investigation. Because of the low agreement with cine CMR, measures should not be used interchangeably in patients after acute STEMI.

IV-3

Comparison of NOGA guided infarct parameters with MRI infarct size in porcine myocardial infarction model

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Background: Magnetic resonance imaging is the gold standard for the assessment of infarct size and left ventricular function. The NOGA electroanatomical mapping system is currently used for online evaluation of myocardial viability (expressed as unipolar voltage values, mV) and segmental wall motion (as local linear shortening, LLS). This 3D navigation system enables percutaneous interventional targeted cardiac stem cell therapy. The aim of this study is to compare the extent of the infarction and wall motion abnormalities of NOGA mapping to similar parameters of cardiac MRI.

Methods: Late gadolinium cardiac MRI and 3D NOGA-guided electroanatomical mapping was performed in porcine closed-chest reperfused acute myocardial infarction (AMI) before cardiac cell-based therapy in 14 domestic pigs. The follow up (FUP) cardiac MRI and NOGA investigations were accomplished 30 days after the AMI. Using the NOGA system's bull's eye maps we determined the area of viability (relative size of the AMI and borderzone of the unipolar voltage map) and the extent of hypokinetic areas (local linear shortening map).

Results: The mean values of the NOGA and MRI parameters at baseline and FUP were expressed as mean ± standard deviation (Table 1).

Weak, but significant negative correlation was found between the FUP ejection fraction and the entire ischemic area with reduced viability (R=−0.525; p<0.05) whereas no correlation was found between the other MRI and NOGA parameters.

Discussion: The discrepancy between the two 3D images might be the consequence of the currently used 2D sizing of infarction in the NOGA maps. A construction of 3D hybrid imaging of 3D NOGA and 3D MRI is now on-going, which might ensure a better correlation between the different 3D imaging modalities.

Table 1. Mean values of the NOGA and MRI parameters at baseline and FUP

	Baseline	FUP
MRI		
Infarct size (%) of LV	18.6 ± 7.6	17.8 ± 5.7
Ejection fraction (%)	41.4 ± 7.7	41.5 ± 8.3
3D NOGA		
Viability map		
Infarct size (%) of LV	13.9 ± 10.2	11.6 ± 11.4
Border zone (%) of LV	25.7 ± 7.3	20.2 ± 5.4
Entire ischemic area (%) of LV	39.7 ± 13.7	31.7 ± 15.1
LLS map		
Size of akinetic areas (%) of LV	22.5 ± 9.3	18.9 ± 7.2
Size of hypokinetic area (%) of LV	11.6 ± 4.9	10.1 ± 2.2
Entire size of decreased local wall motion (%) of LV	34.1 ± 13	28.9 ± 8.7

IV-4

The association of copeptin with myocardial infarct size and myocardial function after ST-segment elevation myocardial infarction

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Introduction: High copeptin levels are associated with adverse outcome after ST-segment elevation myocardial infarction (STEMI). However, the association between copeptin and myocardial infarct size and function has not been described so far. We therefore investigated the relationship between plasma copeptin concentrations and infarct size, as well as myocardial function at baseline and 4 months after mechanical reperfusion for STEMI.

Methods: STEMI patients (n=54) successfully reperfused by primary angioplasty underwent contrast-enhanced cardiac magnetic resonance imaging within a median of 2 days after the acute event and 4 months thereafter. Infarct size was determined with the use of late gadolinium enhanced images. Left ventricular dimensions and function were measured from cine true-FISP sequences. Adverse remodeling was defined as an increase in end-diastolic volume of ≥20% after 4 months. Blood samples were drawn 2 days after the onset of symptoms. Copeptin and N-terminal pro-B-type natriuretic peptide values were determined by an automated immunofluorescent assay.

Results: Baseline copeptin concentrations (median: 10.4 pmol/L [6.0–14.4]) were associated with early and chronic infarct sizes (r=0.39, p=0.004 at baseline; r=0.39, p=0.011 at follow-up) and inversely related to left ventricular ejection fraction (r=−0.48, p<0.001 at baseline; r=−0.46, p<0.001 at follow-up). Patients with adverse remodeling showed higher baseline copeptin levels compared to patients without remodelling (10.3 pmol/L [6.1– 13.2] vs. 19.2 pmol/L [10.4–28.5], p=0.024). Receiver operating characteristic analysis indicated a cut-off value of 16.7 pmol/L to best identify patients with future adverse remodelling (area under the curve = 0.79, 95% CI 0.59–0.98). Compared to copeptin, the area under the curve for N-terminal pro-B-type natriuretic peptide (cut-off: 1,916 ng/L) for prediction of remodeling 4 months after STEMI was slightly lower

(0.75, 95 % CI 0.52–0.98). No patient with both biomarkers below the cut-off values developed adverse remodeling during follow-up.

Discussion: Increased copeptin values at an early stage after STEMI are associated with larger acute and chronic infarct sizes. Moreover, copeptin is a potential predictor of myocardial function and remodeling 4 months after STEMI. These findings strengthen the role of copeptin as a biomarker of adverse outcome after STEMI.

IV-5

Longitudinal systolic left ventricular-right ventricular interaction in pediatric and young adult patients with TOF: a magnetic resonance imaging and M-mode echocardiography study

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Aim was to evaluate the longitudinal systolic left ventricular (LV)—right ventricular (RV) interaction in 146 operated tetralogy of Fallot (TOF) patients. Biventricular measures of indexed ventricular end-diastolic volume (EDVi), ejection fraction (EF), and LV longitudinal function parameters determined by magnetic resonance imaging (MRI) were investigated and compared to established normal z-score values.

We found a good correlation between mitral annular plane systolic excursion (MAPSE) and LVEF values in our patients ($r=0.788$; $p<0.001$). Correlations between MRI derived MAPSE and M-mode guided MAPSE ($r=0.879$, $p<0.001$), and between MRI derived TAPSE and M-mode guided TAPSE were significant ($r=0.780$, $p<0.001$). While LVEF was normal in patients with normal RVEF, the LVEF was decreased in patients with significantly reduced RVEF. Patients with RVEDVi ≤ 150 mL/m^2 had a mean MAPSE of 1.43 ± 0.20 cm, and patients with RVEDVi > 150 mL/m^2 a mean MAPSE of 1.30 ± 0.26 cm, the latter significantly reduced when compared to normal MAPSE z-score values. LV longitudinal function is decreased below the -2 SD of normal MAPSE z-score values after 22 postoperative years in our TOF population. Our data confirm progressive adverse RV-LV interaction in the long-term postoperative follow-up of TOF. We show that simple M-mode measurement of the systolic LV function (i.e. MAPSE) is a sufficient surrogate for the LVEF. Therefore, in case of poor sonographic windows MAPSE measurement is helpful for LV systolic function investigations.

IV-6

Tricuspid annular peak systolic velocity (S') in children and young adults with pulmonary artery hypertension secondary to congenital heart diseases and tetralogy of Fallot: echocardiography and MRI data

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Background: The tricuspid annular peak systolic velocity (S'), as echocardiographic index to assess right ventricular (RV) systolic function, has not been investigated thoroughly in children and young adults with tetralogy of Fallot (TOF) and pulmonary artery hypertension secondary to congenital heart disease (PAH-CHD).

Methods: S' values of patients with TOF ($n=183$) and PAH-CHD ($n=55$) were compared to normal subjects. S' values were compared to RVEF and RVEDVi determined by MRI.

Results: S' values become significantly reduced after an age of 10.4 years in PAH patients, and after an age of 13.6 years in TOF patients when compared to the lower bound of the ± 2 SD interval of normal subjects (Fig. 1). A significant positive correlation between S' with RVEF was seen in both, TOF ($r=0.66$, $p<0.001$) and PAH-CHD ($r=0.82$, $p<0.001$) patients (Fig. 2). A significant negative correlation between S' with RVEDVi was also seen in TOF ($r=-0.29$, $p=0.002$) as well as in PAH-CHD patients ($r=-0.59$, $p<0.001$).

Conclusions: Although initially preserved, in our prospective study we found impaired S' values with increasing age in patients with TOF and PAH-CHD. We suggest that persistent pressure overload in PAH-CHD patients as well as volume overload in TOF patients might be able to lead to a systolic RV function impairment and increased RVEDVi. The validity of S' data could be confirmed by MRI data (RVEDVi and RVEF).

IV-7

Assessment of principal strain by 3D echocardiography

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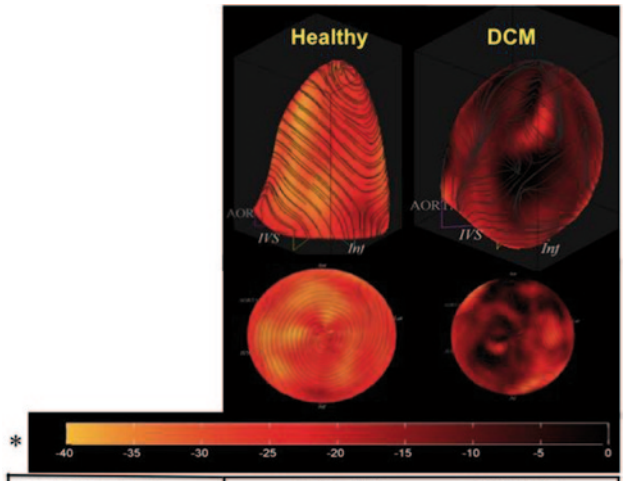
Background: Novel 3D speckle tracking echocardiography is able to track myocardial motion irrespective of directionality, potentially providing an integrated measure of myocardial deformation.

Methods: Nine healthy volunteers and eight patients with dilated cardiomyopathy (DCM) underwent 3D echocardiograph and were analyzed to evaluate the tissue motion in the sub-endocardium (4D LV-analysis TOMTEC). Longitudinal and circumferential strain were extracted and integrated to obtain the principal strain vector, which incorporates direction and magnitude. Spatial variability was calculated as the normalized standard deviation of principal strain representing spatial disuniformity of contraction. Secondary strain represents the deformation perpendicular to the principal direction. The ratio of secondary to principal strain indicates the relative contribution of transverse strain to myocardial deformation.

Results: Compared to healthy volunteers (mean age 33 ± 11 years, 11 % female, LVEF 61.8 ± 2.9 %), patients with DCM (mean age 55 ± 17 years, 37.5 % female, LVEF 25.3 ± 5.2 %) were characterized by significantly lower principal strain ($p<0.001$), higher spatial variability ($p<0.001$) and a lower secondary to principal strain ratio ($p<0.001$).

Conclusion: Principal strain analysis, facilitated by novel 3D speckle tracking software, may offer an integrated assessment of LV deformation. These preliminary findings suggest that this technique may be useful for better phenotyping myocardial function.



Principal strain, %	-0.32 ± 0.04	-0.12 ± 0.03
Spatial variability, %	0.35 ± 0.05	0.53 ± 0.07
Ratio secondary to principal strain	0.24 ± 0.07	-0.27 ± 0.26

Fig. 1 Principal strain direction is represented by strain lines. *Principal strain magnitude is reflected by color

Postersitzung V: Chirurgie 1

V-1

Erste klinische Erfahrungen mit der Symetis Acurate TA transapikalen Aortenklappenprothese

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Hintergrund: Die Symetis Acurate TA ist eine interventionelle Aortenklappenprothese der 2. Generation, welche transapikal über eine Minithorakotomie links implantiert wird. Diese porcine Prothese ist aufgrund ihres Nitinolstents selbstexpandierend, und ermöglicht eine exakte Positionierung im Aortenannulus durch die Fixierung des Nitinolstents (upper crown) an den verkalkten Klappensegel. Zusätzlich ist die Klappenbasis mit einem speziellen Kunstoff überzogen (PET-Skirt), welcher die Abdichtung am nativen Aortenannulus fördert, und dadurch die Inzidenz von paravalvulären Leaks reduziert. Die einfache Handhabung mit „taktile-feedback" und die kurze Implantationszeit in minimal-invasiver Technik sind Vorteile, die für Patienten mit hohem Operationsrisiko ausschlaggebend sind.

Methodik: Zwischen Dezember 2012 und Februar 2013 wurden 7 Patienten (6 w, 1 m), zwischen 68 und 89 Jahren (mittel: 77a) mit dieser transapikalen Aortenklappenprothese auf Grund einer hochgradigen Aortenklappenstenose, behandelt. Der EURO Score lag zwischen 14 und 48 %, mean 32 %. Die Indikation für einen interventionellen Aortenklappenersatz war neben einem sehr hohen Risikoscore (3 Patienten) eine COPD Gold IV (2 Patienten) sowie eine Porzellanaorta bei weiteren 2 Patient.

Ergebnisse: Die Erfolgsrate der Implantation der transapikalen Aortenklappenprothese lag bei 100 % und die Sterblichkeitsrate bei 0 %. 6 Patienten wurden noch am OP Tag extubiert und einen Tag später auf die Überwachungsstation transferiert Eine Patientin mit höchstgradig reduzierter LV Funktion (18 %) mußte tracheotomiert und über 4 Wochen vom Respirator entwöhnt werden. Kein Patient erlitt einen Schlaganfall. Die postoperative Echokardiographie zeigte nur triviale paravalvuläre Leaks.

Conclusio: Die Vorteile der Symetis Acurate TA transapikalen Aortenklappenprothese sind der selbstexpandierende Nitinolstent, der aufgrund seines „taktile-feedback" bei der Expansion im Aortenannulus eine exakte Positionierung ermöglicht und die spezielle Ummantelung der Klappenbasis, die das Auftreten von paravalvulären Leaks minimiert.

V-2

The new polarizing St Thomas' Hospital cardioplegia: improved efficacy of myocardial protection in pigs on CPB

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Objective: The gold standard for myocardial protection for over 30 years has been hyperkalemic cardioplegia, inducing depolarized arrest. However, depolarized arrest can lead to ionic imbalance, enhanced energy utilization and ischemia (I)-reperfusion (R) injury. An alternative is to use 'polarized' arrest. In this study, the efficacy of the new clinically relevant polarizing cardioplegia (the St Thomas' Hospital Polarized solution [STHPol], comprising esmolol, adenosine and magnesium in Ringers solution) was compared to conventional hyperkalemic St Thomas' Hospital solution (STH2) in pigs subjected to cardiopulmonary bypass (CPB) and global IR.

Methods: Thirteen Austrian Landrace pigs (47±4 kg) were anesthetized and monitored (heart rate [HR], mean aortic pressure [MAP]). After sternotomy, pigs were heparinized (300 IU/kg) and put on normothermic CPB. Additional monitoring was: Swan Ganz catheter for PAP and cardiac output (CO); ultrasound flow probe for central LAD flow; a Millar tip catheter for LVP; a coronary sinus catheter to sample coronary effluent. After baseline hemodynamic measurements, CPB was started, the aorta cross-clamped and hearts were arrested via antegrade, warm (35 °C) STHPol (treatment group; $n=7$) or STH2 (control group, $n=6$); in both groups, a total of 1,000 mL was infused (~500 mL for initial arrest and a further 500 mL after 25–30mins). The experimental protocol was: 60 min I followed by 60 min on-pump R, then hearts were weaned from CPB for another 120 min before sacrifice and determination of myocardial high-energy phosphate (HEP) concentrations and ultrastructural changes (electron microscopy). Data are presented as percentage of baseline (mean ± SEM).

Results: Baseline hemodynamic values were comparable in both groups. After 180 min R, recovery of MAP and HR were similar. In contrast, recovery of LVPsys (133±8 vs 97±5 %, $p<0.01$) and external heart work (145±16 vs 88±10 %, $p<0.01$) were significantly higher in STHPol hearts. Coronary flow/heart weight (Fig. 1) was higher throughout the entire experiment and reached significance during early (430±59 vs 211±59 %, $p<0.05$) and late R (269±43 vs 90±16 %, $p<0.01$) in STHPol compared to STH2 pigs. Total CK release was lower throughout reperfusion in STHPol hearts and was significantly lower during early R (2,016±262 vs 1,232±199 U/L, $p<0.05$).

Conclusion: Polarized cardiac arrest, using the new STHPol cardioplegia, was shown to be effective in large hearts, which makes

it useful clinically. It was associated with improved myocardial protection and reduced ischemic damage. In increasingly sicker patients requiring more complex operations, STHPol cardioplegia may provide better cardioprotection and improved clinical outcome. However, clinical studies are required to further evaluate this concept.

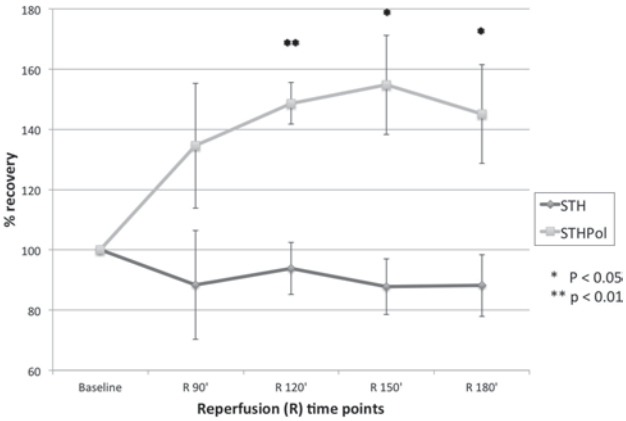

Fig. 1 Recovery of external heart work (rEHW)

V-3

Preoperative patient optimization with veno-arterial ECMO as bridge to permanent ventricular assist device implantation improves outcome of patients with therapy refractory shock

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Background: Patients with refractory cardiogenic shock (RCS) have a dismal prognosis. Implantation of permanent ventricular assist devices (VAD) is an effective therapy in selected patients with RCS. However, the early mortality of this approach is high as patients in shock and multiorgan failure are exposed to a significant surgical trauma. We hypothesized that a two-step approach with initial extracorporeal membrane oxygenation (ECMO) implantation and deferral of VAD implantation to recovery of end organ function will reduce overall mortality.

Methods: We retrospectively reviewed 41 patients (mean age 50±12; 78% male; 46.3% ICMP) receiving a VAD for refractory cardiogenic shock between 07/2003 and 02/2013. A bridge-to-bridge concept with ECMO implantation prior to VAD implantation was pursued in 22 (53.6%) patients. Study endpoints were end organ recovery during ECMO support and survival.

Results: Patients with and without ECMO were comparable with regard to patient characteristics. ECMO support significantly improved renal (creatinine 1.86±0.91 mg/dl vs. 1.32±0.52 mg/dl, $p=0.021$), hepatic (GOT 1,426±2,176 U/L vs. 277±259 U/L, $p=0.041$; GPT 982±1,466 U/L vs. 357±447 U/L, $p=0.037$) and pulmonary function (FiO_2 52±18% vs. 26±23%, $p<0.001$; PEEP 7±3 vs. 5±4 mbar, $p=0.015$) over a period of 7.7±7.2 days. Hence, renal (creatinine 1.33±0.52 vs. 1.61±1.10 mg/dl, $p=0.303$) and hepatic function (GOT 310±459 vs. 465±1,066 U/L, $p=0.571$; GPT 357±447 vs. 490±1,112 U/L, $p=0.610$) were better in the ECMO group at the time of VAD implantation. This led to a strong trend towards an improved 30-day (4.5 vs. 21.1%, $p=0.107$) and in-hospital (9.1 vs. 31.6%, $p=0.070$) mortality in patients pretreated with ECMO support.

Conclusion: Preoperative patient optimization with ECMO support prior to permanent VAD implantation improves end organ function and reduces overall mortality.

V-4

Initial single-center experience of aortic root reconstruction using the Yacoub procedure modified by implantation of an extraaortic ring

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Introduction: Valve sparing aortic root reconstruction (ARR) is an alternative for a selected group of patients suffering from aortic root dilatation and subsequent aortic insufficiency (AI) in order to avoid prosthetic valve replacement. We report our center's initial experience with ARR using the Yacoub procedure modified by implantation of an extraaortic ring.

Methods: Six patients with significant AI underwent aortic root reconstruction at our institution. Five of those patients suffered from aortic root aneurysm, one patient had an acute type-A aortic dissection. A Yacoub procedure was performed in all but one patient. In five patients additional valve reconstruction was done. In three of those cases an extraaortic ring was additionally implanted, however in one patient the ring had to be removed again because of aortic narrowing. In one case the Yacoub procedure was done in conventional fashion without implantation of an extraaortic ring and in one patient interoperative decision was made to perform supracoronary replacement of the ascending aorta and isolated leaflet repair instead of aortic root replacement. In one patient implantation of a prosthetic aortic valve became necessary due to unsuccessful aortic valve reconstruction following aortic root reconstruction using the Yacoub operation.

Results: All patients were free of postoperative complications. Results of postoperative echocardiography showed no ($n=3$) or trivial ($n=2$) aortic valve insufficiency in patients without prosthetic valve implantation at the 3 months-follow up.

Discussion: Our center's initial experience with valve-sparing aortic root reconstruction using the Yacoub procedure with/without leaflet repair and ± implantation of an extraaortic ring showed the feasibility of this combined procedure. However, the efficacy of this technique especially in younger patients will be shown solely by the results of longterm follow-up.

V-5

Minimal invasive LVAD implantation via bilateral thoracotomy

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Objective: Median sternotomy is the standard incision for left ventricular assist device (LVAD) implantation. There are some theoretical advantages of avoiding a median sternotomy in LVAD patients including better right ventricular protection, improved pulmonary function and faster recovery. The present study was

designed to evaluate a novel, minimally invasive sternotomy sparing technique for LVAD implantation.

Methods: From February 2012 to March 2013 Twenty-five patients (mean age 59.0±8.4 yrs., 84 % male, ischemic heart disease 60 %, prior cardiac surgery 16 %) with terminal heart failure (Intermacs level 1: 32 % , level 2: 20 %, level 3: 36 %, level 4: 7 12 %) underwent minimally invasive isolated sternotomy sparing LVAD implantation (Heartware® HVAD $n=19$, Thoratec® Heartmate II $n=6$). Surgical access was established by a left minithoracotomy directly over the apex, the outflow graft was tunneled to the aorta intrapericardially in all but redo cases. The aortic outflow anastomosis was performed via a right minithoracotomy in the 2nd intercostal space. Circulatory support for LVAD implantation was performed using CPB (36 %), ECMO (52 %) or Off-Pump (12 %).

Results: Sternotomy sparing LVAD implantation was feasible in all patients with no need for conversions. Thirty-day mortality was 4 % and in-hospital mortality was 12 %. Overall in-hospital stay was 32.6±26.5 days. One patient (4 %) died during follow-up from pump thrombus formation. One patient underwent surgical revision for postoperative bleeding (retroperitoneal haematoma). We observed no permanent neurological deficits postoperatively but one patient developed subarachnoidal haemorrhage after head trauma on rehabilitation.

Conclusion: Minimally invasive sternotomy sparing left ventricular assist device implantation is feasible and safe. The very encouraging results obtained in this initial series justify a broad application of this technique.

V-6

Ulcerated aortic wall aneurysm following chemotherapy with bevacizumab and local hyperthermia in a 69 year-old patient with non-small cell lung cancer. A case report

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Introduction: The majority of patients suffering from non-small cell lung cancer (NSCLC) already present with advanced stage of disease at timepoint of diagnosis. However, different therapies are established for metastatic or inoperable lung cancer. Bevacizumab is a recombinant humanized anti-vascular endothelial growth factor monoclonal antibody. Its main function is to inhibit angiogenesis and it is used as a first line therapy in different types of cancer. Beside antibody and chemotherapy studies have shown that additional local hyperthermia may increase the efficacy of chemotherapy and radiation.

Our case: A 69 year-old male patient with metastatic NSCLC (cT2b, N2, M1b) and aortic wall ulceration was presented to our department. Diagnose of NSCLC was first done in June 2012. At that time PET-CT showed an ascending aorta with an diameter of 3.8 cm. Following four cycles of chemotherapy (Vinorelbine/Cisplatin) combined with bevacizumab and local hyperthermia he underwent re-CT-staging 3 months later. The CT showed an aneurysm of the ascending aorta with a diameter of 5 cm and an ulceration of aortic wall with a diameter of 2 cm localized at the convexity proximal to the brachiocephalic trunk. After being transferred to our department, the patient underwent a Bentall-procedure with replacement of the ascending Aorta by a Dacron graft during deep hypothermic arrest. The postoperative course was uneventful.

Disscusion: As we know from several studies arterial hypertention is a common negative side effect of Avastin. Several cases of aortic or arterial aneurysm after bevacizumab therapy have already been reported. We highly suppose that the combination of bevacizumab and local hyperthermia may increase the risk for these complications.

V-7

Subclavian artery cannulation for circulatory support following cardiac surgery

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Background: Myocardial dysfunction following cardiac surgery is a rare but life-threatening complication and is generally managed by temporary circulatory ECMO support via femoral arterial and venous cannulation. Subclavian arterial cannulation is currently not performed as clinical routine, but may have beneficial effects in these patients.

Methods: A retrospective data analysis of patients requiring perioperative ECMO support between 09/2011 and 02/2013 was performed. A total of 14 patients required veno-arterial ECMO support at our institution. In 11 patients (mean EUROSCORE II: 17.6) subclavian cannulation was performed via an 8 mm Dacron graft that was anastomosed end to side to the right ($n=9$) or left ($n=2$) subclavian artery. In three patients conventional cannulation was performed via the femoral artery (mean EUROSCORE II: 3.2).

Results: Mean ECMO support times were 174.2 (±116.7) for subclavian and 118.5 (±89.6) hours for femoral arterial cannulation ($p>0.05$). Maximum flow rates were 4.4 (±0.6) and 4.8 (±0.2) L/min, respectively ($p>0.05$). Cannulation-related complications that required reintervention were bleeding ($n=1$) and prosthesis infection ($n=1$) in the subclavian group and limb ischemia ($n=1$) that required switch to subclavian cannulation for the femoral group. Thirty day-survival was 91 % for patients with subclavian and 67 % for femoral cannulation ($p>0.05$).

Conclusion: Subclavian artery cannulation for postoperative ECMO provided sufficient circulatory support in this small cohort of patients. The low complication rate and antegrade body perfusion may enhance myocardial recovery and thus improve overall outcome as compared to patients with femoral arterial ECMO support.

Postersitzung VI: Diverses

VI-1

Transient hypoxia increases serum levels of heat shock protein-27, -70 and caspase-cleaved cytokeratin 18

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Introduction: Myocardial infarction (MI) and chronic obstructive pulmonary disease (COPD) are a worldwide burden and a major cause of death. These disease conditions are accompanied by tissue hypoxia and increased cellular turnover. We and other groups have previously shown that elevated levels of heat shock protein-27 (HSP27), -70 (HSP70) and caspase-cleaved cytokeratin 18 (ccCK-18) were found in serum of MI and COPD patients correlating with disease severity. In this study we hypothesized that transient hypoxia triggers the release of HSPs and ccCK-18.

Materials and methods: Fourteen healthy volunteers were subjected to transient normobaric hypoxia in an air-conditioned hypoxia chamber simulating an oxygen concentration of an altitude of up to 5,500 meters. Serial venous blood samples were drawn after a period of 8 h and serum was stored at – 80 °C. The collected serum samples were evaluated for HSP27, -70 and ccCK-18 using commercially available ELISA assay kits. Significances were calculated using the Wilcoxon matched pairs test, a p-value of <0.05 was considered statistically significant.

Results: During the experiment oxygen concentration was adjusted to an altitude equivalent to a height of 5,500 meters to achieve hypoxic conditions with a peripheral O_2 saturation of around 75 %. Baseline concentrations for HSP-27 were 2,760 pg/mL (±517 SEM), for HSP-70 49 pg/mL (±22 SEM) and for ccCK-18 226 U/L (±20 SEM). During the first hours of the experiment simulating an altitude equivalent of 2,000 and 4,000 m no significant differences were found. After 8 h and a height equivalent of 5,500 meters a significant increase was recorded depicted by serum levels of 3,737 pg/mL (±571 SEM) for HSP-27, of 202 pg/mL (±81 SEM) for HSP-70 and 244 U/L (±20 SEM) for ccCK-18 ($p<0.05$). After reestablishment of normoxia a decline of serum levels was found indicated by a mean concentration of 1,470 pg/mL (±164 SEM) for HSP-27, of 8 pg/mL (±8 SEM) for HSP-70 and of 178 U/L (±13 SEM for ccCK-18 ($p<0.01$).

Conclusions: These experimental results provide explanation for the elevated serum levels of HSP-27, HSP-70 and ccCK-18 found in MI and COPD patients, indicating that hypoxic conditions can trigger the release of the aforementioned factors in healthy volunteers. Cellular stress reactions caused by transient hypoxia seem to be causative for the systemic release of apoptosis-specific proteins and could serve as markers for disease severity.

VI-2

Mutations and polymorphisms of the alpha-galactosidase A gene in patients with hypertrophic cardiomyopathy

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Background: Anderson-Fabry disease (AFD) is a rare cause of hypertrophic cardiomyopathies (HCM). Clinical signs alone do not allow distinguishing a cardiac manifestation of AFD from sarcomeric forms of HCM. Enzyme activity analysis and genetic testing of the α-galactosidase A (α-GAL) gene (GLA) are therefore important for diagnosis and verification of disease causing mutations.

Methods: We enrolled 108 adults (76 males, 32 females) with a referral diagnosis of HCM with a left ventricular wall thickness of ≥15 mm on echocardiography. Laboratory analyses included the measurement of α-GAL activity in leukocytes and sequencing of the GLA gene in all patients. Symptoms were evaluated using a specified questionnaire.

Results: Mutation analyses confirmed AFD in two patients (p.G35R and g.5092A>G; 1.9 %). One female patient (0.98 %) had a rare polymorphism (p.D313Y) previously described as disease causing for AFD. In 31 patients (28.7 %) various combinations of polymorphisms were detected. The g.1170C>T polymorphism was found in nine patients (seven males) and was associated with a significantly decreased α-GAL activity in leukocytes among male subjects compared to the wild type GLA gene ($p=0.003$). Clinically these patients showed higher frequencies of non-sustained ventricular tachycardias (nsVTs, $p=0.009$).

Conclusion: Specific testing of the GLA gene in patients with HCM confirmed AFD in two patients and revealed various polymorphisms in almost one third of patients. The g.1170C>T polymorphism was found in 8 % and is associated with a reduced α-GAL activity and a higher incidence of nsVTs in males.

VI-3

Efficacy, safety and physiologic aspects of the siliciumdioxide inert-coated AXETIS and bare metal stent: a pre-clinical randomized study evaluating short, mid and long-term outcome

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Background: The aim of our randomized pre-clinical study was to assess the short, mid and long-term outcome of the Axetis silicon dioxide (SiO_2, abrading the micropores) inert coated stent implantation regarding safety, efficacy and vascular physiology.

Methods: Domestic pigs were randomized to receive either Axetis or BMS (same design) coronary artery stents undergoing a 1, 3 and 6-month follow-up (FUP), controlled by coronary angiography, optical coherence tomography (OCT), intravascular ultrasound (IVUS) and histology ($n=32$). Time-dependent vasomotor reaction of coronary arteries to the stent implantation was measured using modified myography ($n=12$). Complete endothelialization of Axetis stent was confirmed by OCT, IVUS and histology at 1-month FUP.

Results: During the 6-month FUP of both stent types, the pre- and post-stenting QCA and IVUS revealed a trend towards higher MLD and lower % DS, with smaller intimal volumen and volume obstruction in AXETIS stent group compared with the BMS. OCT image showed complete stent strut coverage in Axetis stents, with some uncovered struts of the BMS. Histology confirmed the complete endothelialization of Axetis stent. The histopathology showed continuous healing of the vessel wall, with a gradual reduction of inflammation and fibrin score, with no difference between the groups. No necrosis around the stent struts was observed. In Axetis stents, a significantly smaller neointimal area and %area stenosis was measured as compared with BMS at each FUP time point. Vascular reactivity measurements revealed a significantly better endothelium-dependent vasodilation of stented arteries with Axetis implantation, while no change in endothelium-independent (media muscular layer-dependent) vasodilation was observed during the FUP.

Discussion: Implantation of Axetis SiO_2-coated stent resulted in a significant better safety, efficacy and vessel physiology profile compared to BMS with the same design. Inert coating did not

worsen the pathophysiological response of the coronary arteries subjected to PCI, the inert coating led to a faster recovery of the endothelium-dependent vasodilation capacity of the PCI-instrumented arteries.

VI-4

Early immediate release of CD31+ cells precedes the mobilization of CD34+ stem cells from bone marrow during experimental profound ischemia and reperfusion

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Background: Acute myocardial infarction (AMI) induces mobilization of the bone marrow (BM) cells for cardiac repair. The aim of our study was to investigate the timely release of BM-origin stem and progenitor cells, and the possible correlation between increase in number of mobilized stem (CD34+), progenitors (CD34+CD31+) and endothelial cells (CD31+) and the functional characteristics of the heart following AMI.

Materials and methods: Closed chest reperfused AMI was induced in 24 pigs by percutaneous occlusion of the mid left anterior descending coronary artery (LAD). Three days later, cardiac magnetic resonance imaging (MRI) was performed to assess left ventricular (LV) end-diastolic, and end-systolic volumes, global LV ejection fraction (EF) and infarct size. Blood samples were collected at baseline (pre-AMI), 1 h post-reperfusion and at 3 days post-AMI. The absolute value of circulating mononuclear cells (MNc) was calculated by counting of mononuclear cells of smears and the circulating white blood cells (WBC). The presence of circulating CD34+, CD31+, and CD34+31+ cell-populations was measured by fluorescence-activated cell sorting (FACS).

Results: AMI induced an immediate increase in an average WBC-number from (pre-AMI) $18.1\pm3.6\times10^6$/uL to (post-reperfusion) $20.9\pm4.7\times10^6$/uL ($p<0.05$), which decreased at 3-day follow-up (FUP) to $19.3\pm3.7\times10^6$/uL, respectively. Interestingly, the absolute numbers of CD34+ (from 314±253 to 288±239/uL) and CD34+31+ (from 474±231 to 194±167/uL) decreased immediately post-reperfusion, with dramatic increase of CD34+ cells at the 3-day FUP (913±638/uL, $p<0.05$) with no change of number of CD34+31+ cells (294±240/uL). The number of circulating CD31+cells increased significantly immediately post-reperfusion (from 219±206 to 438±170/uL, $p<0.05$) with further elevation at 3-day (1,034±584/uL, $p<0.05$). The mean LV EF was 36.0±6.5 % and the infarct size 23.5±3.8 %. Weak, but significant positive correlation was found between increase in number of WBC and EF ($r=0.49$, $p<0.05$). Larger infarct size was associated with higher number of mobilized CD34+ cells ($r=0.59$, $p<0.01$) at 3-days post-AMI.

Conclusions: Profound myocardial ischemia and reperfusion induces differential and time-dependent mobilization of stem, progenitor and mature endothelial cells. Acute ischemia and reperfusion triggers an immediate release of angiogenic CD31+ cells, while the developing infarction provokes delayed but impressive release of CD34+ cells for cardiac repair.

VI-5

Successful re-do of renal sympathic denervation

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Interventional management of resistant hypertension has received growing attention recently. Percutaneous renal sympathic denervation (PRDN) as a therapeutic option for such patients has shown mean reductions in blood pressure of about 30/15 mmHg within a period of 6 months. Data published so far reiterate this technique as a feasible, effective, well-tolerated, interventional, groundbreaking method for the management of resistant hypertension.

However, cases in which PRDN was less successful have been described time and again. A recent paper published in Catheter Cardiovascular Intervention in Nov. 2012 has described a case of re-do of PRDN in a patient with re-current, resistant hypertension after primary treatment success. Here, we report a case of a 48 year old woman with metabolic syndrome and resistant hypertension. Under concomitant therapy with ARBs, amlodipine, hydrochlorothiazide, carvedilol, spironolactone and moxonidine the patient still showed 220/120 mmHg. Thus, renal denervation (Simplicity, Medtronic) was performed in June 2011 (five noches left, six noches right). In early September of the same year, mean 24 h-bloodpressure was 149/104 mmHg. By the end of the same month, blood pressure again rose to 225/125 mmHg and a re-do of renal denervation has been performed (five noches left, four noches right). Control measurements 3 months later in December 2011 showed a mean 24 h-blood pressure of 143/99. Subsequent self-measurements thereafter never revealed values above 175 mmHg. Oral anti-hypertensive treatment, however, could neither be discontinued nor reduced after PDRN.

Our observation indicates that re-do of RDT may well be considered in severe cases of resistant hypertension when alternatives fail.

VI-6

Long-term mortality in patients with chronic obstructive pulmonary disease following extracorporeal membrane oxygenation for cardiac assist after cardiovascular surgery

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Background: Information on predisposing risk factors influencing long-term survival after extracorporeal membrane oxygenation (ECMO) support remains scarce. In critically ill patients chronic obstructive pulmonary disease (COPD) is an independent risk factor for mortality and morbidity. We assessed the influence of COPD on cardiovascular and all-cause mortality in patients undergoing ECMO therapy.

Methods: We prospectively included 191 patients undergoing veno-arterial ECMO therapy following cardiovascular surgery at a university-affiliated tertiary care center into our registry.

Results: The median follow-up time was 51 months (IQR 34–71 months) for corresponding to 4,197 overall months of follow-up. One hundred and twenty-five patients (65 %) died, 88 % of deaths were due to cardiovascular causes. Long-term survival was decreased in patients with COPD after 1 year (23 vs. 44 %) and after

6 years (14 vs. 35 %) compared to patients without COPD. COPD was independently associated with all-cause mortality with a hazard ratio of 4.82 (95 %CI 1.13–20.50, $p=0.033$) and cardiovascular mortality with a hazard ratio of 6.88 (95 %CI 1.57–30.15, $p=0.011$).

Conclusions: We identified COPD as a strong and independent predictor of long-term all-cause mortality and cardiovascular mortality in patients undergoing ECMO therapy following cardiovascular surgery. The current study presents valuable information for a comprehensive decision-making process prior to ECMO implantation and helps to identify high-risk patients that may benefit from intensified treatment of co-morbidities and close check-ups after hospital discharge.

VI-7

Outcome following interventions by an in-hospital resuscitation team

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Purpose: Organized in-hospital resuscitation teams (IHRT) may improve survival in patients with in-hospital cardiac arrests (IHCA) and in those presenting with other types of in-hospital emergencies (IHE). We evaluated the results of our IHRT regarding the outcome after IHCA and IHE.

Methods: Prospective analysis of 128 IHRT calls documented on a mandatory report form in a general teaching hospital between July 2008 and December 2010.

Results: IHRT calls were activated due to 64 incidents of IHCA and 58 incidents with other types of IHE (e.g., syncope, seizure, severe bleeding, arrhythmia, respiratory distress, anaphylaxis, drug overdose). Three patients had a do-not-resuscitate order and three had a false alarm. Return of spontaneous circulation (ROSC) in patients with IHCA was achieved in 54.7 % with a survival to hospital discharge (SHD) of 31.3 %. Rate of ROSC was significantly higher in patients with a shockable rhythm than those with a non-shockable rhythm (100 vs. 45.3 %, $p<0.001$), associated with a trend for a higher rate of SHD (54.5 vs. 26.4 %, $p=0.067$). There was a significant difference in SHD between patients younger than 65 years and older patients (50.0 vs. 23.9 %, $p=0.043$). An IHRT call due to IHCA during daytime resulted in a numerically higher rate of SHD compared to a call during night-time (41.9 vs. 21.2 %, $p=0.074$). Patients presenting with other types of IHE showed a SHD of 89.7 %.

Conclusions: Outcome after IHCA was rather poor with about one third of patients surviving to hospital discharge in this prospective study. Subgroup analysis revealed that SHD was significantly better in patients of younger age, and a positive trend was observed in patients with a shockable rhythm and in those with an IHRT call during daytime. In contrast, the outcome in other types of IHE was more favourable but not necessarily benign.

VI-8

New oral anticoagulants are inferior to vitamin-K-antagonists for stroke prevention in elderly patients with atrial fibrillation

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Background: The prevalence of atrial fibrillation(AF) and the embolic risk increases with age. Elderly AF-patients are undertreated with vitamin-K-antagonists(VKA). The new oral anticoagulants(NOAC) dabigatran, rivaroxaban and apixaban seem noninferior to VKA for stroke prevention in AF. We summarize the knowledge about primary and secondary stroke prevention by anticoagulation including NOAC in AF patients > 75 years.

Methods: A literature search was carried for "dabigatran", "rivaroxaban", "apixaban", "elderly", "octogenarians", "atrial fibrillation" and "anticoagulation" from 1998 to 2013. Randomized clinical trials, longitudinal studies, case series and case reports were included.

Results: Whereas studies investigating the use of VKA for stroke prevention in the 1990ies were carried out by industry-independent institutions, all NOAC-investigating trials were sponsored by the manufacturers of the respective drugs. Frial elderly people were not represented in NOAC-investigating trials due to various exclusion criteria, and only a third of patients were > 75 years. Subgroup analyses from the NOAC-investigating trials show that elderly patients have a higher risk for bleeding complications with NOAC than with VKA. Further arguments against the use of NOAC in elderly are the high prevalence of renal insufficiency, the risk of drug-drug- and drug-food interactions, the lack of easily available laboratory monitoring tests of anticoagulant activity, the lack of an antidote and high costs for the drugs.

Conclusion: There is no evidence from manufacturer-independent and unbiased studies that NOAC are effective in elderly AF patients with the same efficacy and risk of side effects as VKA.

VI-9

High-sensitivity cardiac troponin T is predictive of adverse outcome after acute ischemic stroke

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Introduction: High-sensitivity cardiac troponin T (hs-cTnT) is used for risk stratification in cardiac diseases. Data on the previous TnT-assay and ischemic stroke so far are conflicting, due to inadequate analytical sensitivity at the low measuring range. Therefore, we sought to investigate hs-cTnT as a predictor for ischemic stroke outcome.

Material and methods: Five hundred and seventeen consecutive Stroke Unit (SU) patients were screened. Data included time of onset, clinical severity scales for stroke on admission and discharge [National Institute of Health Stroke Scale (NIHSS), modified Rankin Scale (mRS), and Barthel Index (BI)], and various clinical and laboratory parameters. At day 90, mRS and BI were assessed by telephone interview. Exclusion criteria were transient ischemic attacks, bleedings, undetermined onset, no hs-cTnT < 24 h, estimated glomerular filtration rate (eGFR) < 15 mL/min, MI during stay or within 4 weeks prior, and missing follow-up. The final sample consisted of 340 patients.

Several definitions for adverse outcome were tested: Death; mRS > 2; BI < 90(= median BI); mRS > 3 and/or BI < 60 combined. hs-cTnT was divided into five groups: undetectable (< 5 ng/L), and quartiles of detectable hsTnT (Q1 5.09–8.0; Q2 8.29–12.6; Q3 12.76–27.62, Q4 27.7–221 ng/L). Group differences vs. outcomes and other parameters were tested. Odds ratios (ORs) for adverse outcomes vs. hs-cTnT groups (< 5 ng/L vs. Q1–Q4) were calculated using multivariate logistic regression and were adjusted for all univariately significant correlations. *P* for trend was calculated from group medians.

Results: Median age was 68 years (range: 18–96); 208 patients were men. One hundred and seventeen (52 %) had hs-cTnT levels <5 ng/L. Median hs-cTnT (Q1–Q4) were 6.70, 10.30, 18.65, and 43.0 ng/L. Patients with higher hs-cTnT were older, more often male, and more severely ill. There was a significant rise of NIHSS and adverse outcomes over quartiles. eGFR, Hb, and CRP were more pathological in higher quartiles, but CK was not. Stroke etiology was more likely cardiac, and heart conditions (atrial fibrillation, coronary heart disease) more prevalent in Q3/Q4. There was a trend for higher hs-cTnT in more severe stroke syndromes. Associations between hs-cTnT and outcomes remained significant after adjustment for heart conditions. hs-cTnT was independently associated with all adverse outcomes (p for trend <0.001). NIHSS and age emerged as only other independent risk predictors.

Discussion: Elevated hs-cTnT is independently predictive of adverse stroke outcomes after 90 days. Associations with all definitions of outcome were robust. Categorization of hs-cTnT into quartiles showed a dose-effect relation, with significantly higher ORs in the more elevated groups. MI patients were excluded, and multivariate adjustment for preexisting cardiac conditions did not alter this significant correlation. Hence, hs-cTnT elevation may indicate cerebral impairment translating into cardiac damage, rather than vice versa. Stress-induced patchy myocytolysis caused by centrally mediated vegetative fluctuations has been implicated.

hs-cTnT is a functionally meaningful surrogate predictor of clinical course; pathophysiological connections, however, still need to be elucidated.

VI-10

Circulating immune cells after splenectomy

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Background: Splenectomy is associated with venous thrombosis in general, and in particular, with non-resolving and recurrent thrombosis. The spleen serves as a blood cell filter and as source of immune cells. We hypothesized that splenectomy alters the composition of circulating immune cells.

Methods: We compared peripheral immune cell counts of patients splenectomized in the course of trauma (S) (n=24) and non-splenectomized matched controls (Co) (n=20).

Results: Mean follow up time between splenectomy and screening was 10.4 years (±9.5 years). One patient had developed deep vein thrombosis 18 years after splenectomy, whereas no control reported any thrombotic event. There were no differences in age (S 50 years, Co 57 years; n.s.), sex (S: 40 % females, Co 60 % females; n.s) or smoking status (S 15 packyears, Co 10 packyears; n.s.) between both groups. Platelet counts (S 370±88×103/µl, Co 245.8±51×103/µl; p<0.01), monocyte counts (S 726±272/µl, Co 474±144/µl; p<0.01), B-lymphocyte counts (S 515±292/µl, Co 239±83/µl; p<0.01), T- helper cell counts (S 1,374±506/µl, Co 965±319/µl; p<0.01), cytotoxic T-cell counts (S 773±478/µl, Co 439±201/µl p<0.01) and natural killer cell counts (S 446±298/µl, Co 249±137/µl; p<0.03) were significantly increased after traumatic splenectomy. Prothrombin time was significantly longer in S (S 99±9 %, Co 90±8 %, p<0.03).

Conclusion: Further studies will be designed to understand how peripheral immune cells may be involved in thrombosis and thrombus resolution.

Postersitzung VII: Herzinsuffizienz 1

VII-1

ESC heart failure guideline conform prescription rates and dosage of heart failure medication varies significantly in patients hospitalized for heart failure compared to outpatient treated

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Purpose: The heart failure (HF) guidelines of the European Society of Cardiology (ESC) give specific recommendations on HF medication including target dosages for patients (pts) with chronic systolic HF. However, underprescription is often seen in practice. The aim of this study was to evaluate prescription rates (PR) of medications in pts hospitalized for congestive HF and pts treated at a HF outpatient clinic.

Methods: Over a period of 9 months pts who were either hospitalized for congestive HF or seen at the outpatient clinic, were asked to join the prospective observational study. Demographic data, co-morbidities and medical prescription information among others were collected.

Results: The study recruited 90 pts (mean age 63.4 SD ±14.0) 32 % hospitalized and 68 % outpatients. PR of HF medications and treatments not recommended by the ESC are reported in the table. The main reasons for not receiving a recommended HF medication was severe renal dysfunction (8.9 %) and symptomatic hypotension (7.8 %). These results remain similar when stratifying for aetiology of HF, sex or age.

Conclusions: PR of the recommended HF medications are low in pts hospitalized for congestive HF. In contrast, pts treated at a HF outpatient clinic have significantly higher PR and receive more often the target dose of the HF medication. Not recommended and potentially harmful treatments are significantly less likely in pts followed in an outpatient clinic. Therefore, all HF pts should be seen regularly in a special HF clinic.

Table 1. Prescription rates (PR) of medications in pts hospitalized for congestive HF and pts treated at a HF outpatient clinic

Medication	PR of patients hospitalized for HF (%)	PR of patients in HF outpatient clinic (%)	*P*	Patients hospitalized receiving target dosage (%)	Patients at HF outpatient clinic receiving target dosage (%)	*P*
Angiotensin-converting enzyme-inhibitors (ACE-I) or angiotensin receptor blockers (ARB)	73	98	<0.01	11	31	<0.05
Beta-blocker	81	95	0.04	7	24	<0.05
Mineralocorticoid receptor antagonists (MRA)	44	75	<0.01	22	33	0.31
Digitalis	28	25	0.78			
Diuretics	32	74	<0.01			
Ivabradine	0	8	<0.05			
Treatments not recommended for HF patients						
Glitazones	0	0	n.d.			
NSAIDs and COX-2 inhibitors	10	2	<0.01			
Calcium-channel blockers	7	2	<0.01			
Combination of ACE-I, ARB and MRA	2	0	<0.05			

VII-2

Abnormalities of left ventricular systolic function in heart failure with preserved ejection fraction

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Background: While diastolic dysfunction is widely considered a key pathophysiologic mediator of heart failure with preserved ejection fraction (HFpEF), concomitant systolic dysfunction despite preserved EF may play a role.

Methods: We assessed myocardial systolic and diastolic function in a contemporary HFpEF clinical trial, PARAMOUNT, which enrolled patients with heart failure, NYHA class II-IV symptoms, an EF ≥ 45 % and NT pro-BNP levels > 400 pg/mL [median 894 (IQR 526, 1,457)]. Longitudinal and circumferential systolic deformation was assessed in 219 PARAMOUNT patients and compared to 50 healthy controls free of cardiovascular disease (mean age 69 ± 78; 68 % female) using a vendor-independent 2D speckle tracking software (TOMTEC). The frequency and severity of impaired deformation was assessed across the spectrum of EF in HFpEF and was correlated with standard measures of diastolic function including E' and E/E' and with NT-pro BNP.

Results: Mean age was 71 ± 9 years, 61 % were female, 83 % white, 92 % hypertensive and 51 % had a history of heart failure hospitalization. Mean EF was 59 ± 8 E/E' was 16 ± 7 and 95 % had diastolic dysfunction ≥ grade I. Compared to healthy controls, HFpEF patients enrolled in PARAMOUNT demonstrated significantly lower longitudinal and circumferential strain across the spectrum of EF although these measures of strain were worse in patients with lower EF (Fig. 1). Neither longitudinal nor circumferential strain were related to standard echocardiographic measures of diastolic function (E' or E/E'). However, worse longitudinal strain was significantly, though modestly, associated with higher NT-pro BNP levels, even after adjustment for 10 baseline covariates including EF ($p = 0.001$).

Conclusion: In this contemporary clinical trial, in addition to diastolic dysfunction, HFpEF was characterized by impaired systolic deformation which was associated with higher NT-pro BNP.

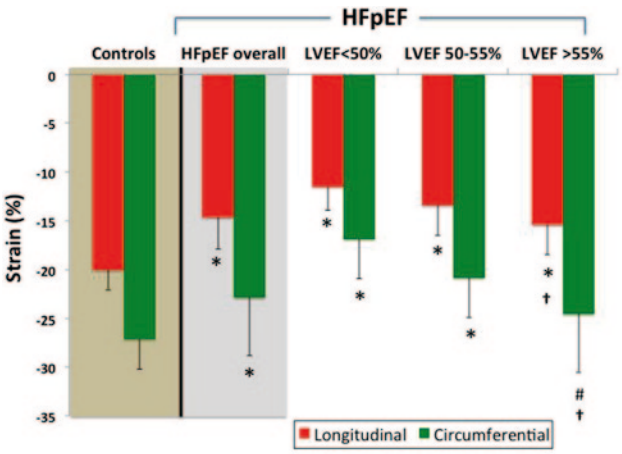

Fig. 1 Heart failure with preserved ejection fraction (HFpEF) characterized by impaired systolic deformation

VII-3

Novel echocardiographic parameters during exercise improve detection of impaired systolic and diastolic function in stage B heart failure with preserved ejection fraction

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Background: Factors that govern the transition from asymptomatic hypertensive hearts disease (HHD) to heart failure with preserved ejection fraction (HFPEF) are largely unknown. We hypothesized that conventional and novel echocardiographic imaging parameters during exercise may improve detection of systolic and diastolic abnormalities in asymptomatic HHD (Stage B HFPEF).

Methods: We recruited 11 controls subjects without risk factors for HFPEF and 15 patients with asymptomatic HHD. We obtained detailed echocardiography at rest and during multistage supine bicycle exercise. Tissue Doppler imaging (E/é) as estimate of left ventricular filling pressure and global left ventricular longitudinal strain (GLS) and early diastolic strain rate (eSR) were determined.

Results: There were significant differences in the response of systolic and diastolic function parameters between controls (mean age 41±13, EF 67±3%) and HHD (mean age 60±9, EF 67±7%) (see Table 1). During exercise the increase of E/é was significantly higher in HHD as compared to controls. GLS increased in controls, but decreased in HHD. EDSR improved during exercise in controls, but to a lesser extent in HHD.

Conclusion: In asymptomatic HHD, alterations of systolic and diastolic function were observed. Bicycle exercise augmented systolic and diastolic dysfunction in HHD, thereby largely improving the accuracy of traditional and novel imaging parameters for detecting subtle abnormalities of the ventricle. These preliminary data suggest that the diastolic stress test in combination with novel imaging technologies may be useful for better risk stratification and diagnosis of patient with diastolic dysfunction or suspected HFPEF.

Table 1. Tissue Doppler imaging (E/é) for better risk stratification

Echo	Controls	HHD
E/é_r	7.5±1.6	10.1±3.2
E/é_s	9.1±2.1	13.0±2.2**
GLS_r	−18.0±1.3	−18.5±3.8
GLS_s	−22.0±3.8	−17.6±2.4
eDSR_r	1.1±0.3	1.0±0.2
eDSR_s	1.9±0.7*	1.5±0.3*

E/é_r, s E/é at rest (r) or stress (s), *GLS_r, s* global longitudinal strain at rest (r) or stress (s), *eDSR_r, s* early diastolic strain rate at rest (r) or stress (s)
*$p < 0.05$ vs. rest ; **$p < 0.001$ vs. rest

VII-4

Können Empfehlungen zur Therapie der chronischen Herzinsuffizienz umgesetzt werden?

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Einleitung: Die Verordnung vieler Medikamente ist gerade bei der Herzinsuffizienz mit ihren vielen Substanzklassen ein großes Problem, das die Umsetzung der Therapieempfehlungen oft erschwert. Mittels der 1-Jahres-Daten der EuroHeart Failure Survey (EHFS) der ESC sollten die Therapieänderungen innerhalb eines Jahres und das Outcome von Patienten mit chronischer Herzinsuffizienz aufgezeigt werden.

Methoden: Die an der Kardiologie der Medizinischen Universität Graz in das EHFS inkludierten Patienten mit chronischer Herzinsuffizienz wurden anhand ihrer Medikation bei der Basisuntersuchung sowie nach 12±2 Monaten analysiert. Es wurde erhoben welche Substanzklassen am häufigsten verordnet wurden und ob die empfohlenen Zieldosen erreicht werden konnten. Als Basis dienten die Empfehlungen der ESC aus dem Jahr 2008. Die Daten wurden entweder im Rahmen einer Routinekontrolle oder durch telefonische Kontaktaufnahme erhoben.

Ergebnisse: Von 61 Patienten (50 m, 11 w; mittleres Alter 57±12 Jahre) wurden bislang 30 nachuntersucht. 66% der Patienten hatten eine nicht-ischämische, 31% eine ischämische Herzinsuffizienz, 2% hatten eine andere kardiale Grunderkrankung. Der systolische Blutdruckwert sank von 131±23 mmHg auf 124±20 mmHg (p=0,23), der Puls änderte sich kaum (von 72±13 auf 71±12). Das NYHA-Stadium zu Beginn verteilte sich auf die Klassen I/II/III/IV mit 8%/61%/31%/0% Patienten, beim Follow-up war die Verteilung 11%/67%/22%/0%. Die LV-EF stieg von 31±8 auf 36±9% (p=0,31), das mediane NT-proBNP sank von 1087 auf 789 pg/mL (p=0,03).

Der Prozentsatz von Patienten mit ACE-Hemmertherapie stieg von 77 auf 81%, jener von Mineralokortikoidrezepterantagonisten (MRA) stieg von 72 auf 78%. Hingegen sank der Prozentsatz bei der Betablockertherapie von 93 auf 89% und bei Angiotensin-Rezeptor-Blockern (ARB) von 23 auf 22%. Der Anteil der Deviceträger stieg von 45 auf 57%.

Die von der ESC empfohlene Zieldosis wurde nur selten erreicht, am häufigsten bei den Betablockern (27%) sowie bei den MRA (19%) und den ACE-Hemmern (15%). Bei den ARB's erreichte kein Patient die in den Guidelines empfohlene Zieldosis.

Die häufigsten Gründe einer Dosisreduktionen waren symptomatische Hypotonie und Hyperkaliämie. Insgesamt verstarben 10% an ihrer Grunderkrankung.

Diskussion: Überraschenderweise werden am ehesten Betablocker innerhalb eines Jahres bis zur Zieldosis titriert, obgleich dies insgesamt dennoch selten passiert. Zugleich muss diese Medikamentengruppe aber auch am häufigsten abgesetzt werden. Für die gesamte Herzinsuffizienztherapie gibt es weiterhin ausreichend Spielraum für Optimierungen.

VII-5

Amino acid status and risk of heart failure death

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Introduction: Amino acids participate in a variety of key biochemical and physiological activities within the cardiovascular system. In particular, amino acids are suggested to modulate the contractile performance of the myocardium and are suggested to influence protein synthetic efficiency of cardiomyocytes by regulating gene expression and neurohormonal activity.

Methods: This study in a large cohort of patients sought to evaluate the association between circulating amino acid status and (1) the cross-sectional relationship to parameters reflecting systolic heart failure and (2) the risk of death from heart failure after a long-term follow-up of almost 10 years.

Serum amino acids concentrations (histidine, alanine, isoleucine, arginine, leucine, asparagine, lysine, aspartic acid, methionine, cysteine, phenylalanine, glutamic acid, threonine, glutamine, tryptophan, glycine, valine, ornithine, proline, serine and tyrosine)

were chromatographically determined in 2,236 patients (mean age: 62.5±10.8 years; 29.9% women) referred to coronary angiography and recruited within the LUdwigshafen RIsk and Cardiovascular Health (LURIC) study.

Results: Using Pearson correlation, left ventricular ejection fraction (LVEF) correlated with histidine ($r=0.209$; $p<0.001$), arginine ($r=0{,}169$, $p<0.001$), methionine ($r=0.154$, $p<0.001$), tryptophan ($r=0.124$; $p=0.001$) and inversely with glutamic acid ($r=0.140$; $p<0.001$) and ornithine ($r=-0.138$; $p<0.001$). Correlation analyses further revealed significant correlations between NT-pBNP and ornithine ($r=0.203$; $p<0.001$), tryptophan ($r=-0.190$; $p<0.001$), histidine ($r=-0.174$; $p<0.001$) and citrulline ($r=0.169$; $p<0.001$).

After a median follow-up of 9.9 years, 95 participants (4.2%) with amino acid measurement at baseline had died due to heart failure. Multivariable-adjusted Cox proportional hazard (backward elimination) analysis showed that for each standard deviation increase in log-tryptophan there was a 22% (HR: 0.78, 95% CI 0.67–0.90; $p=0.001$) decrease in risk death due to heart failure. Furthermore, for each standard deviation increase in log-ornithine a 20% (HR: 0.80, 95% CI 0.66–0.98; $p=0.031$) decrease in risk of heart failure death was seen.

After consideration of both amino acid in one statistical model only tryptophan emerged as significant predictor of heart failure death: multivariable-adjusted Cox analysis revealed that when compared with participants in the highest tryptophan quartile, those in the lowest quartile were at increased risk of heart failure mortality (HR: 2.17, 95% CI 1.18–3.98; $p=0.012$).

Kaplan-Meier analysis showed an increased probability of heart failure death during follow-up with decreasing quartiles of tryptophan (Fig. 1). Patients with low tryptophan levels continued to be separated throughout the follow-up period of almost 10 years (log-rank: $p=0.026$).

Discussion: Among essential and non-essential amino acids only tryptophan is consistently related to NT-pBNP, LVEF and heart failure mortality. These findings underline the need of further clinical and basic research on amino acid biochemistry and nutrition to discover novel diagnostic and therapeutic knowledge of heart failure biology.

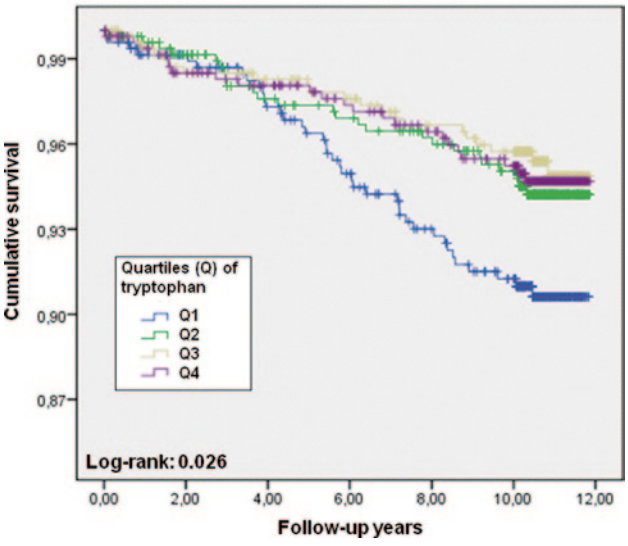

Fig. 1 Survival functions

VII-6

Schlafapnoe bei fortgeschrittener chronisch stabiler systolischer Herzinsuffizienz ist nicht mit exzessiver Tagesmüdigkeit assoziiert

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Hintergrund: Schlafbezogene Atemstörungen (SA) beeinflussen die chronisch stabile systolische Herzinsuffizienz (1–3). Während die obstruktive Schlafapnoe (OSA) einen unabhängigen Risikofaktor für Herzkreislauferkrankungen darstellt und das Fortschreiten der Herzinsuffizienz begünstigen kann, ist die zentrale Schlafapnoe (ZSA) ein Symptom der fortgeschrittenen Herzinsuffizienz.

Wir untersuchten ob bei diesem Patientenkollektiv die Epworth Sleepiness Skala (ESS) geeignet ist, eine klinisch relevante SA vorherzusagen. Die ESS ist ein einfacher Fragebogen zur Bestimmung der Tagesmüdigkeit bei Herzgesunden. Ein Score über 11 Punkte wurde als Cutoff für exzessive Tagesmüdigkeit definiert.

Methoden: Wir untersuchten 176 konsekutive Patienten unserer Herzinsuffizienz Ambulanz der Medizinischen Universität Wien, die unter optimierter medikamentöser Therapie standen. Die Patienten hatten eine mediane linksventrikuläre Auswurfleistung von 25,0% (Bandbreite 7– 35%) und ein medianes NT-pro BNP von 3 413,0 pg/mL (Bandbreite 305,1–35.000,0 pg/mL). Patienten wurden prospektiv mittels ambulanter nächtlicher Polygraphie (sechs Kanal Embletta X10 ® Gerät) untersucht.

Ergebnisse: 50% der Patienten litten an einer zumindest moderaten Form von SA (Apnoe Hypopnoe Index (AHI) ≥15/h). Nur 15 Patienten (17,1%) mit einem AHI ≥15/h hatten einen ESS Score >11. Die medianen ESS Scores und Bandbreiten für Patienten mit einem AHI <15/h, OSA und CSA waren 6,5 (0–24), 8,0 (0–19), 6 (0–17) ohne statistische Signifikanz zwischen den drei Gruppen ($p=0{,}249$; $p=0{,}523$; $p=0{,}249$).

Konklusion: Chronsich stabile Herzinsuffizienzpatienten mit zumindest moderater SA leiden nicht unter exzessiver Tagesmüdigkeit. Daher kann in dieser Population die SA nicht mit dem ESS Fragebogen ausgeschlossen werden.

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VII-7

Erfassen von Beinödemveränderungen bei kardial dekompensierten Patienten mittels 3D Kamera

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Einleitung: Herzinsuffizienz (HI) führt häufig zu stationären Aufenthalten wegen kardialer Dekompensation. In vorangegangenen Studien konnte gezeigt werden, dass durch Telemonitoring und insbesondere durch regelmäßiges Messen des Körpergewichts solche Entgleisungen teilweise verhindert werden können. Um die Anzahl an kardialen Dekompensationen jedoch noch weiter zu senken, sind neue Verfahren zur Früherkennung nötig. Wenn etwa Beinödeme frühzeitig erkannt werden könnten, würde das für die PatientInnen hilfreich sein. Um dies zu bewerkstelligen, soll in der gegenständlichen Studie geprüft werden, ob mittels 3D-Bildgebung Beinödeme mit ausreichender Genauigkeit quantifiziert werden können.

Material und Methode: In einer Pilotstudie an der Kardiologie der Medizinischen Universität Graz wurden kardial dekompensierte PatientInnen mit massiven Beinödemen während ihres stationären Aufenthaltes analysiert. Es wurden täglich die Beine vermessen, um den durch die Rekompensationstherapie bedingten Rückgang der Ödem zu erfassen.

Mittels 3D Kamera (Microsoft Kinect ®), einer Körperwaage (A&D Medical, UC-321PBT) und Maßband wurden die Beinödeme quantifiziert. Aus dem 3D Bild wurden 2 Parameter mit einem halbautomatischen Fotobearbeitungsprogramm extrahiert: a) die Höhe des rechten Fußrückens (gemessen von einer horizontalen Ebene 1,5 cm oberhalb der Bodengrundfläche zur Mitte des Spanns) und b) die Krümmung vor dem Schienbein (1, 9 sowie 17 cm über dem Innenknöchel). Als Referenzwerte wurden am rechten Unterschenkel vier horizontale Umfänge (am Innenknöchel, sowie 1, 9 und 17 cm darüber) und am linken Fuß ein frontaler Umfang (siehe Abb.; im Übergang zwischen Fußwurzeln und Mittelfußknochen) vermessen und das Körpergewicht erfasst.

Für jede/n PatientenIn wurde die Korrelation zwischen Spann, Beinkrümmung, mittlerem Beinumfang und Körpergewicht errechnet.

Ergebnisse: Im Zeitraum von Oktober 2012 bis Februar 2013 wurden 12 PatientInnen (6 m, 6 w; mittleres Alter 76±18 Jahre) vermessen. Die mittlere Untersuchungsdauer betrug 3,9±2,1 Tage mit 1 Messung/Tag.

Die mittlere Gewichtsreduktion als Erfolg der Ödemausschwemmung betrug 3,1±2,7 kg.

Die höchste Korrelation wurde festgestellt zwischen Spann-Höhe und Körpergewicht und bewegte sich zwischen 0,60 und 1,00 (mit einem Ausreißer mit $r=0{,}21$) was sogar höher korreliert als die beiden Referenzwerte: mittlerer Beinumfang und Körpergewicht (r variierte zwischen 0,40 und 0,94 mit einem Ausreißer $r=0{,}04$).

Diskussion: Die 3D-Erfassung von Beinödemen ist als zusätzliches Instrument zur Quantifizierung der Ödemveränderung der unteren Gliedmaßen bei stationären PatientInnen geeignet. Weitere Studien sind erforderlich, um zu untersuchen, ob dieses Instrument zur Früherkennung von Beinödemen geeignet ist (z. B. Home-Monitoring).

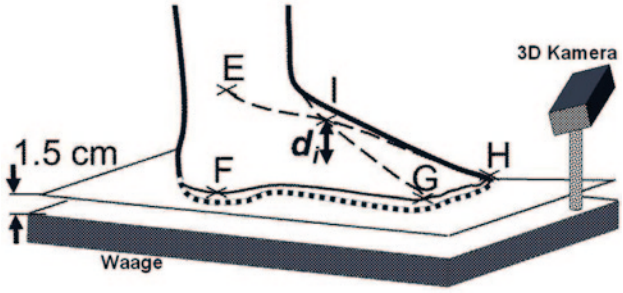

Abb. 1 Die 3D-Erfassung von Beinödemen

Postersitzung VIII: Interventionelle Kardiologie 1

VIII-1

Sicherheit bei Koronarangiographie mit femoralem Zugang durch semiautomatischen Deviceverschluss und Management beim Auftreten einer etwaigen Leistenkomplikation

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Einleitung: Die Verwendung von semiautomatischen Gefäßverschlusssystemen nach femoralem Zugang bei Koronarangiographie bieten eine größere Sicherheit als die rein manuelle Kompression. Sollte trotzdem ein Aneurysma spurium entstehen, stellt dies eine relevante Komplikation dar, die oft einer prolongierten neuerlichen Kompression oder sogar einer chirurgischen Sanierung bedarf.

Methodik: Seit 2008 wurde an unserer Abteilung nach Koronarangiographien ein spezielles Schema zur Vermeidung von unerwünschten Leistenproblemen verfolgt (siehe Flow Chart). Sowohl nach diagnostischer (Cordis 5F Schleuse) als auch interventioneller (Cordis 6F+7F Schleuse) Koronarangiographie via A. femoralis wurde routinemäßig ein Verschluss mit einem semiautomatischen Device (StarClose Vascular Closure oder Femoseal, St. Jude Medical), sofern technisch möglich, angestrebt. Zusätzlich erfolgte eine milde Leistenkompression mit einem Druckverband für ~3,5 h. Nach Abnahme des Druckverbandes erfolgte zwingend eine klinische und auskultatorische Kontrolle der Punktionsstelle. Bei auffälligem Strömungsgeräusch, palpablem Tumor oder ausgedehntem Hämatom erfolgte eine umgehende sonographische Evaluierung (linearer Schallkopf L12–4, Philips IU 33). Bei banalem Hämatom erfolgte ein konservatives Procedere mit klinischem Follow up (FU). Bei Nachweis eines Aneurysma spuriums erfolgte nach lokaler Desinfektion die ultraschallgezielte Thrombininjektion (500 I.E. humanes Thrombin/1 mL aus Tissel oder Tissucol Duo S, Fa. Baxter). 4–12 h nach erfolgreicher Sanierung erfolgte eine abschließende Kontrolle mittels Ultraschall. Bei erfolgreicher Prozedur und Nachweis einer Thrombosierung der Aneurysmahöhle konnte der Patient wieder mobilisiert werden und die Entlassung war möglich. Bei Persistenz des Aneurysma spuriums wurde ein 2ter Versuch mit Thrombininjektion unternommen und falls frustran eine gefäßchirurgische Sanierung durchgeführt.

Resultate: Wir haben von Jänner 2008 bis incl. Dezember 2012 insgesamt 10.069 diagnostische und 3209 interventionelle Koronarangiographien (davon 631 Akutintervention) über einen femoralen Punktionszugang durchgeführt. Insgesamt wurden dabei mit Sonographie bei 122 Patienten ein Aneurysma spurium (1,03 %) identifi-

ziert. Dabei war bei 10 (8,2 %) der 122 Patienten nur eine Kompression mit nachfolgendem Druckverband erfolgt und 61,5 % hatten eine 5F Schleuse. Insgesamt konnten 121/122 aller Aneurysma spurii mittels Thrombininjektion erfolgreich behandelt werden. Bei insgesamt 12 Patienten (9,8 %) war die Gabe von Erythrozytenkonzentraten notwendig. Bei 1 Patienten (0,8 %) gelang keine erfolgreiche Sanierung mit Thrombininjektion, sodass eine Operation angeschlossen wurde.

Zusammenfassung: Die routinemäßige Anwendung eines semiautomatischen Verschlusssystems führt zu einer niedrigen Komplikationsrate im Bereich der Leistenpunktionsstelle nach Koronarangiographie. Die konsequente klinische Kontrolle der Punktionsstelle und wenn notwendig sonographische Evaluierung mit etwaiger Thrombininjektion bei Nachweis eines Aneurysma spuriums konnte in nahezu allen Fällen die chirurgische Sanierung verhindern.

VIII-2

Single center experience with the mitraclip system in patients with severe mitral regurgitation and congestive heart failure

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Introduction: Mitral regurgitation (MR) is the second most common valvular disease and symptomatic patients should undergo valve surgery. A part of these patients were refused by cardiac surgeons because of impaired LV-function, older age or multiple co-morbidities. Edge-to-edge repair using the MitraClip system was introduced as an alternative treatment option in this group of patients.

Methods and results: From August 2009 to February 2013 we treated 39 patients with a percutaneous catheter-based mitral valve repair with the MitraClip system. All patients had significant MR ≥ grade 3+ and were severly symptomatic. 38/39 patients were refused by cardiac surgeons, 1 had failed surgical mitral repair. Twenty-eight patients (71.8 %) presented with functional MR, 5 patients (12.8 %) with degenerative disease and 6 patients (15.4 %) had a mixed pathology. Patients median age was 73 years (IQR; 64–80) and 56.4 % were male. Twenty-nine (74 %) of all patients had a LVEF ≤35 % and 11(28.2 %) of them even ≤25 %. The Euroscore of the total group was 23.06±13.04 %. A single clip was succsessfully implanted in 25 patients (64.1 %), 12 patients (30.8 %) received two clips and 1 patient (2.6 %) received three clips. In one patient no clip could be positioned succesfully and in another patient we had a single leaflet detachment of the second clip. One patient had to be operated due to functional stenosis within 1 week. The mean device implantation time was 118±57 min Only one patient developed cardiac tamponade treated succesfully by conservative means, all the other procedures were uncomplicated. In-hospital and 30 days mortality was zero. The 12 months mortality of the successful treated patients was only 15.1 %. ICU median duration was 2 days and total hospitalitzation was median 8 days (IQR; 7–11 days). In all patients with a 12 month follow up the NTproBNP levels could significantly be reduced from median 3,969 pg/mL (IQR; 1,558–9,486) to 1,691 pg/mL (IQR; 843–5,742) and the 6 min walk-test increased from median 190.5 m.(IQR; 62–307) to 385 m.(IQR; 281–502).

Conclusion: Mitral valve repair using the MitraClip system was shown to be feasible with high success rate in patients with significant mitral regurgitation and severe congestive heart failure. Despite distinct impaired LV-function in combination with multiple co-morbidities, the periinterventional risk was low and the 1 year mortality was acceptable. Nevertheless each case has to be selected very carefully in this sick group of patients.

VIII-3

Einfluss der Atheroskleroselast auf das Ausmaß der Blutdrucksenkung nach perkutaner renaler Denervierung

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Einleitung: Die perkutane renale Denervierung (PRD) ist eine neue Behandlungsoption für Patienten mit therapieresistenter arterieller Hypertonie unter medikamentöser Mehrfachtherapie. Allerdings sprechen nicht alle Patienten auf diese interventionelle partielle Sympathektomie gleich gut an. Wir untersuchten den Zusammenhang zwischen Atheroskleroselast und blutdrucksenkender Wirkung der PRD. Eine erhöhte Gefäßsteifigkeit im Rahmen der Atherosklerose könnte ein geringeres Ansprechen auf die PRD bewirken, da der Sympathikus die Gefäßmotorik bei fortgeschrittener Atherosklerose nicht mehr wesentlich beeinflussen kann. Des weiteren könnte die Energieabgabe während der Prozedur bei Atherosklerose der Nierenarterien selbst weniger effektiv sein.

Patienten und Methoden: Bei allen 132 Patienten (Pat.), die an unserer Abteilung eine PRD bis Juni 2012 erhalten hatten, wurde retrospektiv der Atherosklerose-Status erhoben. Pat. wurden bei

1. Vorliegen einer 1-, 2- oder 3-Gefäßerkrankung im Koronarangiogramm
2. oder dem Vorliegen signifikanter Stenosen der Carotiden in der Doppler-So nographie oder in einem CT-/MR-Angiogramm
3. oder ischämischem Schlaganfall, peripherer arterieller Verschlusskrankheit, abdominellem Aortenaneurysma oder koronarer Herzkrankheit (KHK) in der Anamnese

als „Atherosklerose positiv" bewertet, bei Abwesenheit dieser Faktoren als „Atherosklerose negativ". Als Responder nach 6 Monaten wurden Patienten definiert, die bei der Blutdruckmessung in der Ambulanz einen mindestens um 10 mmHg niedrigeren systolischen (syst.) Blutdruck aufwiesen als vor dem Eingriff oder in der ambulanten 24-Stunden Blutdruckmessung im Tagesschnitt einen mindestens 5 mmHg niedrigeren syst. Blutdruck hatten oder mindestens 1 Medikament absetzen konnten. Die Häufigkeit der Responder der einzelnen Gruppen wurden mittels Chi-Quadrat-Test verglichen, die Blutdruckwerte zwischen den Gruppen mittels U-Test.

Ergebnisse: Der Blutdruck vor der PRD war 160/87± 20/13 mmHg (Office Messung). Die Pat. waren 62±12 Jahre alt, 38 % waren Frauen. Nach 6 Monaten konnte bei 122 Pat. (92 %) der Responder Status nach unseren oben genannten Kriterien bestimmt werden (109 Responder, 89 %, 13 Non-Responder, 11 %). Der mittlere Office Blutduck der Non-Responder vs. Responder war 165/92±24/17 vs. 152/86±23/18 mmHg (p=0,03 für syst. bzw. p=0,29 für diast. Werte). Bei 95 (72 %) aller Pat. war ein Koronarangiographie-Befund verfügbar. Bei 106 der 132 Pat. (80 %) waren sowohl Atherosklerose-Status als auch Blutdruckwerte nach 6 Monaten erhebbar (12 % Non-Responder, 49 % Atherosklerose positiv). Zwischen der Atherosklerose positiven und negativen Gruppe konnte kein signifikanter Unterschied hinsichtlich des Ansprechens auf die PRD festgestellt werden (p=0,16). Da bei Vorliegen eines Koronarangiogrammes das Vorhandensein einer KHK mit hoher Validität bestimmt werden konnte, wurden die KHK-Patienten auch isoliert betrachtet. Es konnte kein statistisch signifikanter Unterschied zwischen der KHK positiven und KHK negativen Patientengruppe (p=0,47) bzw. zwischen den Pat. mit einer 1-, 2- oder 3-Gefäßerkrankung (p=0,34) hinsichtlich des PRD-Erfolges festgestellt werden.

Diskussion: In Anbetracht unserer Daten besteht derzeit kein Hinweis, dass das Vorliegen einer systemischen Atherosklerose oder einer isolierten koronaren Herzkrankheit den Erfolg der PRD Prozedur beeinflusst. Da unsere Fallzahl allerdings limitiert war, sind größere Studien notwendig, um endgültige Schlüsse ziehen zu können.

VIII-4

Redo der perkutanen renalen Denervation bei fehlendem Ansprechen auf die Erstprozedur – erste Erfahrungen

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Einleitung: Seit wenigen Jahren steht mit der perkutanen renalen Denervation (PRD) in der Behandlung der therapieresistenten arteriellen Hypertonie eine interventionelle Behandlungsform mit viel versprechenden Ergebnissen zur Verfügung.

Nach bisherigen Erfahrungen kommt es bei gut zwei Dritteln der Patienten (P) innerhalb von 6 Monaten zu einem Therapieerfolg.

Ob P, die auf die Erstprozedur nicht ansprechen, von einem Zweiteingriff profitieren ist bislang ungeklärt.

Material und Methode: Seit Juni 2010 wurde an unserer Abteilung bei 157 P mit therapieresistenter arterieller Hypertonie (Ambulanzblutdruck >160 mmHg systolisch unter mind. 3 antihypertensiven Medikamenten inklusive Diuretikum) eine PRD unter Verwendung des Symplicity-Katethers (Fa. Medtronic) durchgeführt. Nach 6 Monaten erfolgte eine Evaluierung des Therapieerfolges anhand der Ambulanz- (Therapieerfolg: Blutdruckreduktion >10 mmHg systolisch) und 24-Stunden-Blutdruckwerte (Therapieerfolg: Blutdruckreduktion >5 mmHg systolisch). P mit fehlendem Therapierfolg wurden über die Möglichkeit einer Re-Intervention im Rahmen eines prospektiven Registers aufgeklärt. Hierfür wurde unter neuerlicher Verwendung eines Symplicity-Katheters dasselbe Protokoll (6 Ablationspunkte/Nierenarterie, jeweils 8W für max. 120 s) wie bei der Erstprozedur verwendet. Vor dem Redo wurde eine Angiographie beider Nierenarterien durchgeführt. Unter Heranziehen der dokumentierten Applikationspunkte der Erstprozedur wurde beim Redo versucht, noch nicht behandelte Gefäßabschnitte zu abladieren.

Nach 3 Monaten erfolgte sowohl eine Kontrolle des ambulant gemessenen Blutdrucks als auch eine 24-Stunden-Blutdruckmessung.

Ergebnisse: Gemäß oben genannten Kriterien kam es bei 95 der 141 P (67,4 %), die bereits die 6-Monatskontrolle erreichten, zu einem Therapieerfolg. Von den 46 P ohne Therapieerfolg entschlossen sich 8 (17,4 %) zu einem Redo. Bei diesen P lag trotz Einnahme von 4±1 antihypertensiven Medikamenten ein mittlerer systolischer Ambulanzblutdruck von 166±20 mmHg und systolischer 24-Stunden-Blutdruck von 154±19 mmHg vor.

Der Redo wurde im Mittel 17±6 Monate nach der Erstprozedur durchgeführt. Bei allen P wurde angiographisch das Vorliegen von Nierenarterienstenosen als Folge der Erstprozedur ausgeschlossen. Der Redo konnte bei allen 8 P (100 %) komplikationslos und gemäß Protokoll durchgeführt werden. Drei Monate nach dem Redo zeigte sich bei 5 P (62,5 %) ein Therapieerfolg im systolischen Ambulanz-Blutdruck (−8±16 mmHg) und 24-Stunden-Blutdruck (−12±13 mmHg), während die Senkung des systolischen Blutdrucks bei den übrigen 3 P die Kriterien für einen Therapieerfolg nicht erfüllte.

Diskussion: In dieser ersten Serie von P konnte ein PRD-Redo mindestens 10 Monate nach der Erstprozedur komplikationslos durchgeführt werden. Mit einer präliminären Erfolgsrate von 62,5 % nach 3 Monaten könnte ein PRD-Redo eine mögliche Behandlungsoption bei P mit primärem Therapieversagen darstellen.

VIII-5

Prädiktoren für Schrittmacherimplantation aufgrund von atrioventrikulären Reizleitungsstörungen nach transfemoralem Aortenklappenersatz mit dem CoreValve® System

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Einleitung: An unserer Abteilung erfolgt routinemäßig beim Auftreten von AV-Überleitungsstörungen (AV-ÜS = Linksschenkelblock mit AV-Block I° bzw. AV-Block II° oder III°) während der ersten 48 h nach transfemoralem Aortenklappenersatz (TAVI; CoreValve® Medtronic) die Implantation eines permanenten Schrittmachers (PSM) mit einem integrierten Algorithmus zur Förderung der AV-Eigenüberleitung sowie der Detektion und Speicherung intermittierender AV-Blockierungen (Symphony®, Sorin). Ziel unserer Studie war es, Prädiktoren für das Auftreten oben genannter AV-ÜS und damit einer Schrittmacherindikation nach TAVI zu identifizieren.

Patienten und Methodik: In einer retrospektiven Analyse wurde nach einem Zusammenhang zwischen PSM-Implantation nach TAVI gemäß oben genannten Kriterien und potentiell zu AV-ÜS prädisponierenden Faktoren gesucht (Alter, Geschlecht, EuroScore, Gradient über der Aortenklappe vor TAVI, Auswurffraktion, Durchmesser des linksventrikulären Ausflußtraktes LVOT, TAVI-Durchmesser, Flächen-Ratio TAVI-Fläche/LVOT-Fläche, Implantationstiefe). Die Implantationstiefe wurde aus Herz-CT-Bildern vermessen, welche routinemäßig 3 Monate nach TAVI angefertigt wurden. Sie wurde als Abstand zwischen nativem Klappenring und Unterrand der CoreValve® im LVOT definiert. Die statistische Analyse erfolgte mittels logistischer Regression. Zur Evaluierung einer tatsächlichen intermittierenden oder permanenten PSM-Abhängigkeit wurden im Rahmen der 3-Monats-PSM-Kontrollen alle AV-Block-Episoden II° und III° abgefragt.

Ergebnisse: Zwischen November 2008 und Dezember 2012 erhielten 69 Patienten eine CoreValve®-Klappe (mittleres Alter 82±5 Jahre, 57 % Frauen, EuroScore 21±11, Gradient 90/62±19/15 mmHg, EF 57±12 %). Bei einem mittleren Follow-up von 14±11 Monaten betrug die 30-Tages-Mortalität 5.8 % (4 Patienten) und die 6-Monats-Mortalität 11.6 % (8 Patienten). 7 Patienten hatten bereits vor der TAVI einen PSM und wurden von der Analyse ausgeschlossen. Von den verbleibenden 62 Patienten erhielten 32 (52 %) einen PSM nach TAVI (20 aufgrund eines AV-Blocks II°/III°, 12 aufgrund eines neu aufgetretenen Linksschenkelblockes mit AV-Block I°). Unter den möglichen Prädiktoren für das Auftreten einer AV-ÜS konnte lediglich für die Implantationstiefe der Klappe, die zwischen 3,7 und 18,0 mm variierte, ein statistisch signifikanter Zusammenhang gefunden werden. Hierbei war eine tiefere Implantation der TAVI in den LVOT mit dem häufigeren Auftreten von AV-ÜS assoziiert (OR: 1,44; 95 % CI: 1,01–2,03; $p=0,04$). Das Patientenalter ($p=0,98$), Geschlecht ($p=0,83$), der EuroScore ($p=0,24$), der Spitzen- und mittlere Gradient über der Aortenklappe vor TAVI ($p=0,43$ bzw. $p=0,71$), die Auswurffraktion ($p=0,93$), der LVOT-Durchmesser ($p=0,32$), die TAVI-Klappengröße ($p=0,54$) und die Flächen-Ratio ($p=0,21$) waren nicht mit dem Auftreten von AV-ÜS assoziiert. Für 20 PSM-Patienten waren Abfrageprotokolle des Schrittmachers verfügbar: lediglich 2 (10 %) dieser Patienten waren ohne AV-Block-Episoden im Ereignisspeicher.

Diskussion: In unserer Population war die Implantationstiefe der CoreValve®-Klappe als einzig statistisch signifikanter Parameter mit dem Auftreten postinterventioneller AV-ÜS und konsekutiver PSM-Implantation assoziiert. Die hohe Rate (90 %) an detektierten AV-Blockierungen im Ereignisspeicher der PSM rechtfertigt aus unserer Sicht eine hohe PSM-Implantationsrate und könnte mit ein Grund für die geringe postinterventionelle Mortalität in unserer Kohorte sein.

VIII-6

Herzschrittmacherimplantation – Lernkurven bei 1- und 2-Kammersystemen

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Fragestellung: Medizinisches Handwerk muss erlernt und geübt werden. Übungsmangel durch zu seltene Anwendung bestimmter Techniken und Prozeduren muss eine Verlängerung des Eingriffs und im Falle der Schrittmacherimplantation eine Zunahme der Strahlenexposition annehmen lassen – oder ist einmal gelernt, immer gekonnt?

Methodik: Nach 4-jähriger Operationspause wurden vom Operateur A die Mitarbeiter B, C und D mittels mindestens 50–80 gemeinsamen Schrittmacherimplantationen trainiert bei ca. 160 Neuimplantationen pro Jahr in der Abteilung. Ausgewertet wurden Op-Dauer und Durchleuchtungszeit (DLZ) selbständig durchgeführter Implantationen von 1- und 2-Kammer-Systemen von 2003 bis 2011.

Ergebnisse: Bei deutlich mehr als 50 Operationen pro Jahr lässt sich ein deutlicher Trainingseffekt in Bezug auf signifikante Senkung der Op- und Durchleuchtungsdauer um 20–30 % erkennen. Sinkt die Zahl der Schrittmacherimplantationen eines Operateurs wieder unter 50 pro Jahr, nehmen die Zeiten wieder zu. Die Häufigkeit der Komplikationen Sondendislokation oder Infektion änderte sich nicht.

Fazit: Die Problematik der Mindestmengen wird von Medizinern, Funktionären und Gesundheitsökonomen aus unterschiedlicher Motivation kontrovers diskutiert. Intensiviertes Training lässt kürzere OP-Zeiten messen, während „Trainingsmangel" die erarbeitete Schnelligkeit wieder verlieren lässt. Dieses Ergebnis unterstützt die Forderung nach Mindestmengen bei handwerklich anspruchsvolleren Prozeduren.

Tab 1. Op-Dauer (Op-Z; Schnitt-Naht-Zeit) und Durchleuchtungszeit (DLZ ± Standartabweichung) in Minuten für die Implantation von 1-Kammersystemen (obere Tab.- Hälfte) und 2-Kammersystemen (untere Tab.-Hälfte) der Operateure A, B, C und D mit der Anzahl selbständig durchgeführter Operationen in den Jahren 2003–2011

Jahr	2003	2004	2005	2006	2007	2008	2009	2010	2011
A	33	29	39	25	20	26	15	9	11
Op-Z	44,2±20,6	35,3±9,6	37,8±9,8	33,0±9,6	30,0±6,1	32,1±7,8	33,0±9,0	27,2±6,2	34,5±6,9
DLZ		2,4±2,5	2,6±1,9	2,0±1,2	2,2±1,3	1,6±0,9	1,9±1,2	1,7±0,7	2,5±1,2
B	33	28	35	6	3	2	5		
Op-Z	47,4±20,2	37,9±10,4	38,6±13,8	44,2±8,6	43,3	40,0	47,0±13,0		
DLZ		3,2±2,6	3,0±2,2	4,0±1,9	2,4	2,6	5,1±3,0		
C				21	20	13	8	5	4
Op-Z				49,8±12,8	42,3±14,8	39,2±17,9	41,0±11,9	42,0±11,5	41,3±14,9
DLZ				5,6±4,2	2,6±2,3	2,4±2,8	2,4±0,9	3,0±1,9	1,4±1,0
D								26	16
Op-Z								47,5±11,9	45,3±15,5
DLZ								3,6±2,9	3,0±2,6
A	32	43	24	42	49	39	21	41	22
Op-Z	60,8±13,2	57,4±11,1	57,5±10,6	50,8±11,5	47,4±9,5	45,6±9,4	48,6±9,4	46,5±10,7	50,0±16,7
DLZ		5,6±3,1	4,7±2,2	4,4±2,3	3,7±1,6	3,1±1,6	3,7±1,6	3,2±1,8	3,9±2,1
B	26	48	42	6	7	10	7		
Op-Z	72,3±19,5	60,5±17,7	60,2±18,4	57,2±9,6	65,7±7,3	52,0±9,2	56,4±9,9		
DLZ		7,0±4,4	6,9±5,7	7,4±6,5	8,2±3,9	5,5±2,5	5,2±2,4		
C				27	29	28	16	19	13
Op-Z				64,6±13,6	57,6±14,7	52,0±10,4	52,8±8,8	55,0±12,1	58,5±11,4
DLZ				7,7±4,1	5,1±3,8	3,3±2,3	3,8±2,3	4,2±2,6	5.8±2,8
D								48	63
Op-Z								59,3±16,4	58,0±12,0
DLZ								5,1±3,0	4,9±3,2

VIII-7

Percutaneous coil embolization of a huge coronary artery aneurysm with 16 coils: a case report

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Introduction: Coronary artery aneurysms are defined as a localized dilation of the coronary artery with a diameter ≥1.5 times that of an adjacent coronary segment. The incidence is described as up to 5%. The majority are atherosclerotic in origin. Other causes include tissue disorders, vasculitis, congenital aneurysms, and coronary trauma as percutaneous coronary intervention. The primary complication is myocardial ischemia or infarction due to thrombosis and subsequent distal embolism. Other possibilities are spasms, dissections, and rupture. Treatment options include anticoagulation, covered stents, and surgery. Few reports describe coil embolization.

Case description: A 75 year-old male presented with progressive onset of exercise related shortness of breath with a medical history of coronary artery disease with a NSTEMI 8 years ago and a 6×6 mm big coronary artery aneurysm of a marginal branch of the LCx.

A coronary angiogram revealed a diffuse coronary artery disease with a 60% stenosis of the RCA but a progress of size of the aneurysm of the marginal branch with thrombus formation. A distal flow was not detected, leading to the hypothesis of occlusion of the distal artery due to thrombus formation in the aneurysm. The aneurysm now appeared pedunculated with a short shaft to the LCx. Measuring the aneurysm at the luminography revealed only 10×10 mm. A cardiac-CT revealed a size of 30×33×29 mm.

An attempt was performed to implant a covered stent (Jostent graft master 4×19 mm) into the LCx in order to seal the origin of the aneurysm. Unfortunately the Jostent was too rigid due to its structure (PTFE graft material wrapped between the two stents) to pass an extreme kinking of the LCx. A second attempt with a much more flexible covered stent (aneugraft Dx 4×13 mm) failed again to pass the kinking. Due to the favourable anatomy of the aneurysm with a shaft, we decided to perform coil embolization using a microcatheter and a coil pusher. Sixteen coils were necessary to fill the complete aneurismal lumen. At the next day the patient was discharged in a stable condition.

Conclusion: Hereby we report a case of a huge coronary artery aneurysm which was treated by coil embolization.16 coils were necessary to occlude the aneurysm. In conclusion, besides of surgery and covered stent implantation, coil embolization is one possible method to treat coronary artery aneurysms.

VIII-8

Evaluierung der frühen antihypertensiven Wirkung der perkutanen renalen Denervierung mittels Cold Pressure Test

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Hintergrund: Die perkutane renale Denervierung (PRD) ist eine neue Methode zur Blutdrucksenkung bei therapieresistenter arterieller Hypertonie. Durch interventionelle intraluminale Verödung im Bereich beider Nierenarterien kommt es durch Narbenbildung binnen Wochen zu einer partiellen Sympathektomie. Über die klinischen Sofortwirkungen durch die Verödung in den ersten 24 h nach der PRD, in denen die Narbenbildung noch nicht abgeschlossen ist, ist bis jetzt noch wenig bekannt.

Methodik: Zur Evaluierung der frühen blutdrucksenkenden Wirkung wurde bei 10 konsekutiven Patienten, die eine PRD an unserer Abteilung erhielten, einen Tag vor und einen Tag nach der PRD ein Kaltwassertest (cold pressure test – CPT) durchgeführt. Hierbei wurde nach 15 min Bettruhe und Messen des Ruheblutdruckes die rechte Hand des Patienten bis zum Rist über 5 min in 3±1 °C kaltes Wasser getaucht und der Blutdruckanstieg durch den Kältereiz minütlich mit einer Blutdruckmanschette am linken Arm gemessen. Der mittlere arterielle Blutdruck (MAP) wurde nach der Formel MAP = diastolischer Blutdruck +1/3×(systolischer – diastolischer Blutdruck) berechnet. Die Blutdruckwerte der 10 Patienten sowie das Alter wurden als Mittelwert mit ± Standardabweichung angegeben, die Mittelwerte zwischen den Gruppen wurden mittels Wilcoxon-U-Test verglichen.

Ergebnisse: Die 10 Patienten (Alter 61.8±9.9 Jahre, 2 weiblich) hatten einen mittleren Ruheblutdruck von 170/90±18/14 (MAP 117±12). Vor der PRD war der Blutdruck beim CPT sofort nach Eintauchen ins Eiswasser sowie nach Minute 1, 2, 3, 4 und 5 (mean ± SD, mmHg): 175/99±16/15 (MAP 124±9), 186/104±18/13 (MAP 131±7), 189/105±17/17 (MAP 133±11), 193/106±17/12 (MAP 135±8), 190/105±18/13 (MAP 131±10) und 170/90±18/14 (MAP 133±11). Die korrespondierenden Werte nach der PRD waren für den Blutdruck Ruhe (p-Werte im Vergleich zu Werten vor PRD für systolischen und diastolischen Blutdruck): 160/85±24/16 (p=0,25, p=0,49) und MAP 110±17 (p=0,25). Der Blutdruck nach Eintauchen ins Eiswasser sowie nach Minute 1, 2, 3, 4 und 5 betrug (p-Werte im Vergleich zu Werten vor PRD für systolischen und diastolischen Blutdruck): 169/96±26/15 (p=0,54, p=0,62) – MAP 120±17 (p=0,34), 183/104±21/12 (p=0,87, p=0,97) – MAP 130±12 (p=0,91), 185/102±23/13 (p=0,73, p=0,64) – MAP 130±14 (p=0,62), 184/101±21/15 (p=0,36, p=0,41) – MAP 129±13 (p=0,36), 180/95±21/16 (p=0,25, p=0,19) – MAP 123±13 (p=0,10), 174/95±18/15 (p=0,10, p=0,13) – MAP 121±13 (p=0,06).

Diskussion: Sowohl systolische als auch diastolische Druckwerte waren trendmäßig im Mittel nach der PRD niedriger als vor der PRD. Dies könnte auf eine Sofortwirkung der Methode hinweisen, da am Tag nach der PRD eine Nachwirkung der Sedoanalgetika nicht mehr anzunehmen ist. Die statistische Signifikanz wurde allerdings wahrscheinlich aufgrund der geringen Fallzahl nicht erreicht. Daher ist eine Studie mit einer größeren Fallzahl notwendig, um diesen Effekt valider beurteilen zu können.

VIII-9

Procedural and 6 months clinical outcome in patients treated with the endothelial progenitor cell capturing Genous™ coronary stent

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Background: The endothelial progenitor cell capturing Genous™ stent is covered with CD34+ antibodies that bind circulating endothelial progenitor cells (EPCs) and thereby accelerate endothelialization of stent struts. In our cathlab Genous™ stents are employed as an alternative to bare metal stents in patients with contraindication for long-term dual anti-platelet therapy (DAPT).

Aim: Our study aimed to assess procedural and 6 months clinical outcome after Genous™ stenting in our cathlab.

Method: We included 50 consecutive patients (age: 72.2±10.8, 67% men) treated with EPC capturing Genous™ stents between 08.07.2010 and 23.07.2012. The sample included 40% diabetics; renal insufficiency was present in 44% of the patients. Clinical indication for percutaneus coronary intervention was myocardial infarction in 18%, instable angina in 40% and stable angina in 42%. Long-term DAT was contraindicated because of scheduled surgery (58%), ongoing Cumarin therapy in patients with atrial fibrillation (36%) or recent severe gastric bleeding (6%). The patients received DAPT up to one month following the procedure. Endpoints were procedural success and six months clinical outcome (myocardial infarction, target vessel revascularisation and death) during a 6 months follow-up period.

Results: Angiographic baseline: 58 lesions (AHA/ACC class 3/4: 40.7%; ostial lesions: 25.9% occlusion: 19.0% calcification: 41.3%; RD: 2.8±0.3 mm; length: 17.9±11.5; stenosis: 74.0±13.5%) in 54 vessels (LAD: 37%; RCA: 35.2%; LCX: 22.2%; RD: 3.7%; OM: 1.9%) were treated.

Angiographic success (residual stenosis <20%) was achieved in 98.3%. Periprocedural myocardial infarction was observed in 6% of the patients. No cases of vessel dissection/perforation or acute stent thrombosis (≤24 h) were registered.

During the 6 months follow-up period target vessel revascularisation was reported in 6%, cardiac/noncardiac death in 8%.

Conclusion: Our trial confirms the results of previous trials with regard to high procedural efficacy of the EPC-capturing Genous™ stent. The rate of target vessel revascularisation is also comparable to the findings of previous studies, although this result has to be interpreted with some caution because the statistical power is obviously limited by the relatively small sample size. The same applies to the rate of 6 months mortality, which is considerably higher than in previous studies. However, the interpretation of this finding must take into account that our sample includes a large number of elderly patients (68% older than 65) and high-risk patients suffering from diabetes and/or renal insufficiency.

VIII-10

Radial versus femoral access for acute percutaneous coronary intervention in patients suffering acute myocardial infarction a randomized prospective multicenter trial

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Aim: To objectively evaluate the impact of a radial versus a femoral access for coronary angiography (CAG) and primary percutaneous coronary intervention (PCI) on clinically significant vascular access complications in the setting of acute myocardial infarction (AMI).

Methods: This multicenter study randomly assigned 250 AMI patients with an indication for an urgent CAG, in a 1:1 fashion, to a radial or femoral access in 4 Austrian PCI-centers. The primary endpoint was defined as the occurrence of a hematoma, pseudoaneurysm or local bleeding at the access site with the necessity for manual or ultrasound compression, surgical intervention, thrombin injection, prolongation of the hospital stay or a need for blood transfusion. Secondary endpoints included the components of the primary endpoint as well as the incidence of stroke and death after 30 days. Tertiary endpoints were the radiation exposure to the patient and to the operator.

Results: The median age of the population was 62±12.67 years, 76% were males. The primary endpoint was reached in 5 patients (4 femoral, 1 radial) without a significant difference between groups ($p=0.171$). Hematoma were more frequent in the femoral group (25 vs 8% $p<0.001$). In the femoral group 35.5% of the hematomas were large, definded as palpable swelling >4 cm. In the radial group the surface area of the hematomas was >2≤5 cm in 60% and >10 cm but not above the elbow in 40%.

Time from admission to cathlab until ballon inflation or thrombusaspiration was longer in the radial group (28 versus 32 min $p=0.018$). Radiation exposure to the patient or to the operator was not different between the two groups.

Conclusion: Although the radial access was accompanied by a significantly lower rate of hematomas, we did not find a significant difference in clinically relevant access site complications.

Postersitzung IX: Pulmonale Hypertension 1

IX-1

Intravenous treprostinil delivered by the implantable pump Lenus Pro®: a innovative "surgical" approach to management of PAH

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Introduction: Continuous application of parenteral prostanoids with external pump systems is challenging and associated with frequent side effects such as infusion site pain with subcutaneous (s.c.) and rare but possibly life-threatening catheter related infections with intravenous (i.v.) administration. Lenus Pro® implantable infusion pump was specifically developed to overcome the drawbacks of s.c. administration of Treprostinil. In 2010 we reported the first implantation of a Lenus Pro® pump with a filling interval of 28 days.

Methods and results: Between September 2010 and February 2013 twenty-three patients underwent implantation at our center. All patients had experienced significant clinical benefits with s.c. Treprostinil but reported serious site pain associated with the change of the infusion site. All implantations were performed under general anesthesia by the same surgical team. Preoperatively patients received single-shot antibiotic prophylaxis with Ampicillin/Sulbactam or Clindamycin in case of hypersensitivity to Beta Lactams. After a catheter was placed in the subclavian or cephalic vein according to the decision of the implanting surgeon, the pump pocket was prepared in the abdominal wall. Lenus Pro® pump was filled intraoperatively, placed in the pump pocket and fixed to the fascia. Using a specific device, the catheter was tunneled under the breast tissue and connected with the central venous access by means of a titan connector. To avoid possible overlap effects, s.c. Treprostinil was stopped 1 h after connection. No intraoperative complications occurred;

postoperatively three patients developed mild seroma. One seroma required puncture, two resolved without intervention. During follow-up, no other complications, especially no device related infections were observed. More than 390 refill procedures have been performed without any complications. Control of the reflow volume at every refill procedure revealed accurate and constant flow rate of Lenus Pro® in all patients. Every patient reported a dramatic increase in quality of life due to the absence of infusion site pain.

Conclusions: Parenteral prostanoids are a cornerstone in the treatment of PAH. I.v. Treprostinil administered by Lenus Pro® was safe and effective in our study population, during more than 400 patient-months of treatment there were no pump or catheter related complications, especially no infections. No refill complications were observed. The absence of infusion related side effects is associated with an increase in quality of life, filling intervals of 28 days ensure optimal patient management and compliance. We consider this new treatment option a milestone achievement in prostanoid therapy and management of PAH.

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IX-2

Experimental mild hypothermia potentiates pulmonary vasoconstriction during endotoxemia in pigs

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Introduction: Mild hypothermia (MH) increases systemic vascular resistance and reduces the need for vasopressors in resuscitated patients. Less is known about the effect of MH on pulmonary vascular resistance.

Methods: We retrospectively analyzed data from experimental studies on hemodynamic effects of MH. Anaesthetized pigs (total $n=29$) were instrumented with a Swan–Ganz and a left ventricular (LV) pressure-volume catheter. Animals were cooled from 38 °C (normothermia, NT) to MH (33 °C) by an intravascular device for 6 h after LV myocardial infarction (MI) or for 8 h during endotoxemia. Endotoxemia was initiated by lipopolysaccharide (LPS) infusion, which induces pulmonary vasoconstriction by release of thromboxane A2 (TX-A2) from pulmonary endothelial cells. Total pulmonary vascular resistance (TPVR) was calculated as mean pulmonary pressure (mPAP) divided by cardiac output (CO), and pulmonary vascular resistance (PVR) was estimated as (mPAP minus LV end-diastolic pressure) divided by CO.

Results: In both protocols, mixed venous oxygen saturation was higher in MH vs NT, reflecting improved systemic oxygen supply-demand balance, and no measured systemic hemodynamic parameter indicated further destabilization by MH (data not shown). LV dysfunction after MI increased TPVR and PVR with no additional effect of MH (graph). LPS treatment increased TPVR and PVR, which was potentiated by MH (graph).

Conclusion: When hemodynamic load after LV MI increased pulmonary vascular resistance, MH did not further impact on pulmonary vascular tone. However, MH potentiated pulmonary vasoconstriction after pulmonary endothelial activation by LPS, possibly by higher production or lower clearance of TX-A2. Caution may thus be advised when MH is induced in patients with pre-existing severe pulmonary hypertension.

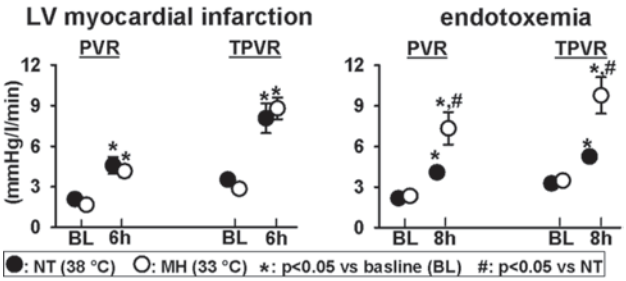

Fig. 1 Effect of MH on pulmonary vascular resistance

IX-3

Abdominal paracentesis to overcome clinical worsening in severe pulmonary arterial hypertension (PAH) patients: first experience in three patients on combination therapy including Treprostinil

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Introduction: Impaired renal function is a prognostic factor for chronic heart failure and for the outcome after hospitalization for acute left heart failure. Recent data show that significant renal dysfunction is also common in PAH patients. An acute decline in renal function is an important marker of in hospital death and short term mortality in right heart failure, which is the primary cause of death in PAH patients. Abdominal paracentesis is an therapeutic option to reduce right ventricular afterload and improve preload. We report our promising experience in three patients with severe PAH with abdominal paracentesis without fluid instillation.

Methods and results: Three male PAH patients deteriorating to functional class (FC) WHO IV developed significant ascites with pathologic creatinin and urea values. Intensified diuretic therapy did not lead to sufficient improvement. Peritoneal paracentesis became an option. Sequential serum creatinine and blood urea nitrogen values reflected the efficacy of the method. The poor status of one patient required hemodialysis for five times before the switch to peritoneal paracentesis as the less burdening intervention. For all three patients advanced combination therapy with PAH-specific drugs including Treprostinil was obligatory as referral to transplant was not possible. By escalation of Treprostinil dosage the PAH targeted therapy was adjusted to the clinical status of the PAH. This integrated treatment algorithm led to significant improvement especially reflected by the change of the WHO FC. One patient outstandingly improved from WHO FC IV to WHO FC II, two patients from WHO FC IV to WHO FC III. The increase in quality of life was tremendous. Paracentesis is performed by the patients relatives at home. The patients are closely monitored. During the observation period of up to 18 months, renal function markedly improved in all the patients. No procedure related side effects were observed.

Conclusion: Worsening of renal function contributes to morbidity and even mortality in severe PAH patients. Besides optimization of diuretic and targeted PAH therapy, peritoneal paracentesis led to clinical and significant improvement of quality of life. Long-term hemodialysis and peritoneal dialysis elevating the rate of cardiac mortality could be avoided. Abdominal parencentesis is a promising option to overcome clinical worsening triggered especially by severe ascites.

Research funding source: None.

Disclosure: No conflicts of interest to disclose.

IX-4

First report on subcutaneous Treprostinil in a PAH patient refusing lung transplantation: a chance for long-term survival

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Introduction: Continuous long-term subcutaneous (s.c.). Treprostinil (Remodulin®) in doses up to 40 ng/kg/min has been shown to improve exercise tolerance and symptoms in patients with PAH and may provide a significant survival benefit. The safety and efficacy of high-dose intravenous Treprostinil has been reported in the literature. We describe the successful re-stabilisation of a patient with severe PAH by triple therapy including dose escalation of s.c. Treprostinil.

Methods and results: A 50-year old male was diagnosed with PAH in another hospital in February 2007. Treatment with Bosentan was initiated. In October 2007 he presented in NYHA functional class IV at our department. Right heart catheterization confirmed the diagnosis of PAH with a mean pulmonary arterial pressure (mPAP) of 65 mm Hg. Six minute walk test (6MWD) was 161 m. Additional s.c. Treprostinil therapy was started, the dose was titrated up to 13.75 ng/kg/min until March 2008. At that time the patient was in class III with a 6MWD of 214 m. In May 2008 the patient reported dyspnea at rest and refused the 6MWD because of general weakness. Increase in Treprostinil dosage restored stabilization until October 2008. However, due to clinical deterioration to class IV we added Sildenafil, in addition the patient refused lung transplantation. Triple therapy with dose increase of Treprostinil up to 29 ng/kg/min stabilized the patient in class III for another year. However in November 2009 he deteriorated again and refused to be listed for transplantation. We increased Treprostinil to 80 ng/kg/min within three months and to a dose of 135 ng/kg/min until September 2010. To keep the patient in stable condition we slowly but constantly increased Treprostinil dose up to 268 ng/kg/min in March 2013 No dose limiting toxicities were observed. During the whole period the patient was monitored closely, including monthly visits.

Conclusion: Subcutaneous Treprostinil is a cornerstone of PAH treatment. In long term treatment doses up to 40 ng/kg/min are effective in most patients. In rare cases, however, increase in dosage is necessary. Our case demonstrates that a triple therapy regime including high-dose s.c. Treprostinil safely allows clinical re-stabilisation even in a patient with reduced compliance. We hypothesize that triple therapy including high-dose s.c. Treprostinil prolongs survival in patients with end-stage PAH.

Research funding source: None.

Disclosure: No conflicts of interest to disclose.

IX-5

Magnetic resonance imaging (MRI) for monitoring of efficacy of advanced PAH-targeted therapy in patients treated with parenteral Treprostinil

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Introduction: Right heart catheterisation (RHC) is the gold standard to prove diagnosis of PAH. As RHC is an invasive method, there is urgent need for reliable noninvase methods to closely monitor these severely ill patients. Functional cardiac MRI variables add important information concerning the clinical status of the treated PAH patients. MR imaging provides the unique opportunity to image the right ventricle in motion without the limitation of echogenicity. Ventricle areas and ratios, delayed enhancement even are seen as prognostic factors. As only parenteral prostanoids provide the opportunity of really tailored therapy during the whole course of this devastating disease, regular noninvasive control of clinical status is obligatory.

Methods: Due to its pharmacological properties we consider Treprostinil the prostanoid of choice. During every control visit an echocardiogram is mandatory at our center. In addition MRI is performed regularly to gain as much information as possible by noninvasive diagnostics. First Prove of echocardiography findings by MRI during the follow up of PAH specific treatment for therapy decisions. Artida (Toshiba) is used for echocardiography and Philips Sonata 1.5 T for MRI.

Results: The therapy of 20 Patients under intravenous Treprostinil therapy administered by the implantable pump LENUSpro® are evaluated with MRI in addition. The improvement of RV function seen by echocardiography (visual examination, ED diameters, TAPSE and RVFAC) correlate to the reduction of ED volumina and ES volumina seen in the MRI. Updated data will be presented at the congress.

Conclusion: Repeated RHCs (e.g. monthly) are not possible for close monitoring of therapy. The tremendous progress in imaging techniques, especially in echocardiography and MRI during the last years gives the opportunity to gain nearly all the information as with RHC, the reliability of the noninvasive methods being high.

Research funding source: None.

Disclosure: No conflicts of interest to disclose.

IX-6

Successful implementation of standard operating procedures (SOPs) for the long-term management of PAH patients treated with intravenous Treprostinil and the implantable pump Lenus Pro®: an interdisciplinary approach

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Introduction: The Lenus Pro® implantable infusion pump was developed to intravenously deliver Treprostinil with a minimized risk of catheter-related infections. In 2010 we reported the first implantation of a Lenus Pro® implantable pump with a filling interval of 28 days. As this novel therapeutic option requires surgical intervention we implemented interdisciplinary SOPs at our center.

Methods: SOP "Preoperative Assessment" defines eligibility criteria for implantation: Patients have to be in stable clinical condition as assessed both by the treating cardiologist and the anesthesist. Uptitration of Treprostinil by continuous subcutaneous infusion is mandatory. Patients who can handle s.c. Treprostinil with only mild to moderate reaction at the infusion site are not eligible for transplantation.

SOPs "Perioperative Management" describe the obligatory anesthetic and surgical protocols from the beginning of anesthe-

sia until discharge of the patient to general ward. Implantations are performed in general anesthesia exclusively by two dedicated surgeons. If none of the dedicated surgeons is available, pump implantation is postponed. Single-shot antibiotic prophylaxis with Ampicillin/Sulbactam or Clindamycin in case of hypersensitivity to Betalactams is obligatory. To avoid possible overlaps s.c. Treprostinil is stopped 60 min after connection of the intravenous catheter. Additionally there is a special SOP for nursing during the hospital stay of the patients.

SOP "Long-term Management" covers refill procedures and control visits. Only specifically trained medical and nursing staff is allowed to perform refill procedures. To ensure adequate care three pysicians were trained. All refill procedures are done exclusively with the specifically developed refill set to avoid damage to the refill septum.

Results: Between September 2010 and February 2013 twenty-three patients underwent implantation at our center. All patients had experienced significant clinical benefits with s.c. Treprostinil but reported serious site pain associated with the change of the infusion site. No intraoperative complications occurred; postoperatively three patients developed mild seroma. One seroma required puncture, two resolved without intervention. Connector dislocation required outpatient surgery in one case. During follow-up, no other complications, especially no device related infections were observed. We performed more than 300 refill procedures without any complication.

Conclusion: Strict adherence to the implemented SOPs for implantation of the Lenus Pro® pump and the refill procedure resulted in the absence of serious device and procedure related complications at our center. We strongly advocate a structured interdisciplinary approach to this innovative way of intravenous application of Treprostinil from the very beginning.

Research funding source: None.

Disclosure: No conflicts of interest to disclose.

IX-7

Hypertrophy of right ventricular septomarginal trabeculation by cardiac magnetic resonance imaging predicts presence and severity of pulmonary hypertension and outcome

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Objective: To prospectively evaluate the predictive value of right ventricular (RV) septomarginal trabeculation (SMT) diameter and area by cardiac magnetic resonance (CMR) imaging in patients with the suspicion of pulmonary hypertension (PH).

Methods: A total of 99 patients (70.1±7.6 years; 59.6% female) with the suspicion of PH prospectively underwent CMR imaging and right heart catheterization within 2 weeks. CMR included assessment of cardiac function and dimensions. SMT maximum diameter and area were also assessed and related to invasive hemodynamics and outcome.

Results: By invasive assessment 63 patients suffered from significant PH (mean PA pressure 31.4±11.1 mmHg). SMT diameters and areas ranged from 1.0–8.9 mm and from 0.1–2.8 cm^2 (mean 3.9±2.1 mm, 0.9±0.7cm2, respectively). SMT diameter and area were significantly correlated with mean PA pressure ($R=0.29$, $p=0.024$ and $R=0.34$; $p=0.007$), pulmonary vascular resistance ($R=0.28$; $p=0.033$), and serum NT-proBNP ($R=0.34$, $p=0.001$ for both).

Patients were followed for 353±212 days. By Kaplan–Meier analysis, event-free survival was significantly worse in patients with SMT diameter and area above the median of 4.75 mm and 1.0 cm^2 (log rank $p=0.014$ and 0.002, respectively).

Conclusion: Right ventricular SMT diameter and area by CMR are easily measureable, noninvasive indicators for the presence and severity of PH, and are related to outcome.

IX-8

Elevated plasma levels of soluble P-selectin predict survival in CTEPH

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Background: The platelet activation marker P-selectin is critically involved in the pathogenesis of venous thromboembolism (VTE). Chronic thromboembolic pulmonary hypertension (CTEPH) is thought to be a late sequelae of venous thrombosis with obstruction of pulmonary arteries by organizing thrombus.

To investigate the role of soluble P-selectin (sP-selectin) as marker and risk predictor for CTEPH, we report on a prospective cohort study of patients (pts) suffering from CTEPH.

Methods: Enzyme-linked immunoassay was used to determine sP-selectin plasma levels in pts with CTEPH at the time of diagnosis. Patients suffering from pulmonary arterial hypertension (PAH), deep venous thrombosis (DVT) and healthy subjects served as control groups. Analysis of overall survival/freedom from double lung transplantation was performed using Kaplan-Meier curves that were stratifed by sP-selectin levels above and below median at baseline.

Results: Soluble P-selectin plasma levels were studied in 182 pts of whom 95 (53.1%) were classified as operable and 84 (46.9%) as non-operable mainly due to an imbalance between hemodynamics and extent of pulmonary arterial obstructions, or comorbidities. Soluble P-selectin plasma levels (sP-selectin, median nanogram per milliliter (range): CTEPH 98.4 (50.7–215)) were significantly higher in CTEPH patients than in the control groups (sP-selectin, median nanogram per milliliter(range): PAH 34.6 (27.1–46.8), DVT 44.3 (36.7–57.6), healthy subjects 35.9 (28.1–45.1); $P<0.001$).

During an observation time of 4.89 years (median; IQR: 2.45–7.67) 83 deaths of any cause occurred and five patients underwent double lung transplantation. Patients with sP-selectin levels ≤98.4 ng/mL survived longer than those with levels >98.4 ng/mL ($P<0.001$).

Conclusion: Soluble P-Selectin is increased in plasma, and predicts survival/freedom from double lung transplantation in CTEPH. The data suggest that platelet activation is involved in venous thrombosis.

IX-9

Circulating markers of inflammation and thrombosis in chronic thromboembolic pulmonary hypertension

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Background: Chronic thromboembolic pulmonary hypertension (CTEPH) results from a failure to resolve acute pulmonary emboli and is surgically curable by pulmonary endarterectomy (PEA). Previous data have suggested that thrombus non-resolution may be triggered by inflammatory conditions. The objective of our prospective cohort study was to investigate circulating markers of inflammation and thrombosis in CTEPH, and how they were affected by treatments.

Patients and methods: Data were collected from CTEPH patients at the time of diagnosis and at least 6 months after the initiation of treatments, off anticoagulation. Patients suffering from pulmonary arterial hypertension (PAH) served as controls. Soluble P-selectin (sP-selectin), soluble CD40 L (sCD40 L), D-dimer, high-sensitive C-reactive protein (hs-CRP), and prothrombin fragment F 1+2 were measured by enzyme-linked immunoassay.

Results: Between March 2006 and January 2011, one hundred and twenty CTEPH patients were consecutively screened. Of those, 53 patients were consented and completed a series of clinical and laboratory follow-ups every 6 months over a period of 3±2 years. At the time of database closure 18 patients had undergone PEA, and 25 remained non-operated. Of those, 18 patients had been randomized in clinical trials for PAH-specific vasodilator treatments, while 17 patients were on optimal medical therapy only.

Levels of sP-selectin ($P<0.001$), hs-CRP ($P<0.001$), and D-dimer ($P=0.036$) were significantly elevated in CTEPH patients compared to PAH patients. No significant differences were found for levels of prothrombin fragment F1+2 and sCD40 L. A significant reduction of sP-selectin ($P=0.005$), hs-CRP ($P=0.035$), D-dimer ($P<0.001$) and prothrombin fragment F1+2 ($P=0.04$) was achieved after PEA. In the non-operated group, elevated levels were sustained at follow-up. Non-operable patients treated with vasodilators had significantly lower levels of sP-selectin ($P=0.007$), hs-CRP ($P<0.001$) and D-dimer ($P=0.02$) than non-operated CTEPH patients who did not receive PAH-targeted treatments. However, the effect of PEA on circulating biomarkers was significantly more robust than the effect of vasodilators (sP-selectin: $P=0.038$, hs-CRP: $P=0.04$, D-dimer: $P=0.018$ and prothrombin fragment F1+2: $P=0.04$).

Conclusion: This prospective cohort study confirmed elevated levels of circulating inflammatory and thrombosis markers in clinically stable patients with CTEPH. Pulmonary endarterectomy and PAH-targeted vasodilator therapies appear to affect the inflammatory and thrombotic activity of CTEPH.

Postersitzung X: Rhythmologie 1

X-1

Combined circular multielectrode catheter and point-by-point ablation is superior to point-by-point ablation alone in eliminating atrial fibrillation

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Background: Besides conventional point-by-point ablation, novel multielectrode catheters emerge for ablation of atrial fibrillation (AF). We sought to evaluate the clinical utility of a pulmonary vein (PV) isolation approach combining the advantages of both technologies.

Methods: Two hundred and forty consecutive AF patients (60±11 years, 68% males, 61.7% paroxysmal) were included. In the combined ablation group ($n=120$), PV isolation was performed with a circular multielectrode catheter (PVAC, Medtronic Ablation Frontiers) and completed by conventional point-by-point ablation (NaviStar ThermoCool Catheter, Lasso/CARTO technology, Biosense Webster). In the point-by-point ablation group ($n=120$), PV isolation was performed with point-by-point ablation alone.

Results: Complete 1-year ablation success (freedom from any atrial arrhythmia after a single procedure off antiarrhytmic drugs) was more frequently observed in the combined ablation group (58.0 versus 43.3%, hazard ratio 1.72, 95% confidence interval 1.19–2.48, $p=0.004$). Also clinical success (≥90% reduction of arrhythmia burden on/off antiarrhythmic drugs) was significantly associated with the combined ablation approach ($p=0.001$). These associations remained significant after multivariable adjustment (both $p\leq0.005$) and were not dependent on the type of AF. The rate of major adverse events (3.3 versus 2.5%) and the procedure time did not differ between groups. The fluoroscopy time, however, was significantly shorter in the combined ablation group ($p<0.001$) reflecting the reduced need for radiation during multielectrode catheter ablation.

Conclusions: A combined PV isolation approach based on multielectrode catheter ablation and complementary point-by-point ablation is superior to point-by-point ablation alone and reveals to be safe. A potential explanation for these findings is the improved stability of ablation lesion after the combined ablation approach.

Table 1. Clinical ablation outcome

Outcome	Combined ablation group		Point-by-point ablation group	
	Paroxysmal AF	Persistent AF	Paroxysmal AF	Persistent AF
	($n=74$)	($n=45$)	($n=74$)	($n=46$)
Complete ablation success	64.9% (48/74)	46.7% (21/45)	50.0% (37/74)	32.6% (15/46)
Recurrence rate of AF	24.3% (18/74)	40.0% (18/45)	40.5% (30/74)	52.2% (24/46)
Recurrence rate of atrial flutter or focal atrial tachycardia	13.5% (10/74)	15.6% (7/45)	18.9% (14/74)	21.7% (10/46)
Clinical ablation success	77.0% (57/74)	60.0% (27/45)	59.5% (44/74)	45.7% (21/46)

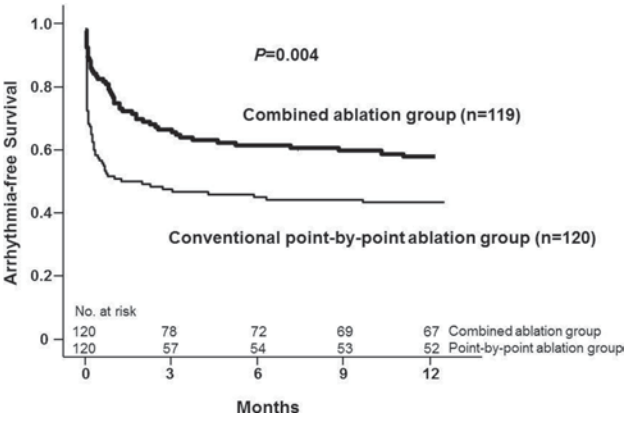

Fig. 1 Kaplan Maier Plot showing the arrhythmia-free survival after the combined ablation approach and after the conventional ablation approach

X-2

Pacemaker dependency after transaortic valve implantation (TAVI)

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Background: Transcatheter aortic valve implantation (TAVI) in high grade aortic stenosis is a feasible treatment in elderly with high comorbidity, possible access routes include the transfemoral, transsubclavian and transapical (TAP-AVI) approach. AV-conduction disturbances requiring permanent pacemaker (PPM) implantation are described in the literature related to the valve type in up to 39 % in contrast to surgical aortic valve replacement with quite lower rates of PPM implantation (9 %). Occurrence of total AV-block after implantation of an self-expandable valve is frequently observed. Preexisting right bundle branch block (RBBB) is a well described risk factor for development of complete AV-block after TAVI.

Methods: Retrospective analysis of a single center population who underwent TAVI due to high grade aortic stenosis. Both the Metronic Corevalve® revalving system (MCRS) and the Edwards Sapien valve (ESV) were used for pts undergoing TAVI via transfemoral route. TAP-AVI was performed by heart surgeons using the Edwards Sapien valve (ESV) with lateral sternotomy. Pts with prior PPM implantation [15 (9 %)] were excluded. The aim was to evaluate the frequency of ventricular pacing at the first follow up 6–8 weeks after implantation as a surrogate parameter for PPM dependency.

Results: A total of 153 pts (age 81 ± 6 years, 63 % female) underwent TAVI, 117 (76 %) pts with MCRS, 27 (18 %) pts with ESV, and 9 (6 %) pts with TAP-AVI. A PPM was implanted in 31 (20 %) pts, 24 (16 %) pts were treated with MCRS, 5 (3 %) with ESV, and 2 (1 %) with TAP-AVI. Complete AV-block was the indication for PPM in 22 (14 %) pts, whereas in 3 (2 %) pts a PPM was inserted for safety reasons because of new LBBB and AV-block I. Preexisting bundle branch block was noted in 9 (6 %) pts, 7 (5 %) of these pts showed a RBBB pattern. All of them developed total AV-bock after TAVI. One patient with a new LBBB received a dual-chamber ICD due to sustained VT. The periprocedural complication rate for PPM implantation was < 1 % (pericardial tamponade in one patient). Independent of programming the percentage of ventricular stimulation (VP) during the short-term observation period was 60 ± 44 % in dual-chamber devices ($N = 18$), and 70 ± 36 % in single-chamber PPM ($N = 5$).

Conclusion: The PPM implantation rate of about 20 % after TAVI is comparable to the literature. Our findings indicate that a small group of pts present temporary AV-conduction disturbances that may recover over time. The device issue is without doubt linked to the procedure which is performed in elderly patients with considerable comorbidity. Calcification of the aortic annulus is frequently found and the conduction system is often vulnerable to mechanical compression. Due to technical reasons a temporary PM is necessary for the TAVI procedure. In case of persistent AV-nodal conduction disturbances PPM implantation should be considered at an early stage to reduce the risk of infection related to the temporary pacing lead.

X-3

Factors influencing the recurrence of atrial fibrillation after electrical cardioversion

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Background: Electrical cardioversion (CV) is used to abolish atrial fibrillation (AF) and to gain a normal sinus rhythm. However, failure of CV or reoccurrence of AF is relatively frequent, requiring repeated CV or aggressive medical treatment. Several biomarkers, such as N-terminal proBNP, have been investigated for the prediction of recurrences of AF with conflicting results. The aim of our study was to investigate the clinical, echocardiographic and laboratory data in relation to (1) success of electric CV; (2) recurrence of paroxysmal AF.

Methods: Consecutive 144 patients (63.9 % male, 67 ± 10 years) with AF and subjected to CV between November 2011 and June 2012 were included into the study and followed for 1 year for reoccurrence. Echocardiographic data, medical treatment, level of NT-proBNP and cardiac risk factors were statistically analyzed.

Results: CV was successful in 93.1 % of patients. During the 1-year follow-up, 29.2 % of patients had relapse of AF of which 80.9 % occurred in the first 3 months. In addition 25 % of the patients had repeated electrical CV because of previous AF. Diabetes mellitus was present in 13.9 % of patients, hypertension in 59.7 %, hyperlipidaemia in 30.6 %, coronary heart disease in 20.1 % and ischemic cardiomyopathy in 11.2 %. The median of NT-proBNP level was 1,431 pg/mL (interquartile range IQR 805–2,686 pg/mL), the mean diameter of the left atrium 60.0 ± 8.2 mm, right atrium 60.4 ± 10.1 mm, left ventricular end-diastolic diameter (EDD) 47.5 ± 9.2 mm. In echocardiography, a mean severity of grade 1 of mitral or tricuspidal regurgitation was measured with a mean pulmonary systolic pressure of 37.5 ± 10.4 mmHg. No correlation was found between failure of CV and prevalence of cardiac risk factors, level of NT-proBNP or echocardiographic parameters (inclusive left and right atrial diameters). Patients with recurrence of AF had similar levels of NT-proBNP (mean difference of −91 pg/mL with 95 % confidence intervals of −742 pg/mL, p = n.s.), diameter of LA, RA and LV EDD. Neither diabetes, nor hypertension or hyperlipidaemia predicted recurrence of AF. Medical treatment did not appear to influence the failure of CV or recurrence of AF. Patients with the highest quartile of NT-proBNP had similar success rate of CV (86.5 vs 81.3 %), or recurrence rate of AF (32.4 vs 28.0 %).

Conclusion: The usual risk factors or echocardiographic or laboratory parameters did not predict reoccurrence of AF or unsuccessful electric CV.

X-4

Isolating pulmonary veins with a single balloon application: efficacy of the novel second-generation cryoballoon

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Introduction: The cryoballoon technology has the potential to isolate a pulmonary vein (PV) with a single energy application.

However, using the first-generation cryoballoon (CB-1G) repeated freezing or additional focal ablation was often necessary. Moreover, visualization of PV isolation (PVI) during freezing was not possible in approximately 50 % of PVs. The novel 28 mm second-generation cryoballoon (CB-2G) features a widened zone of optimal cooling comprising the whole frontal hemisphere as well as an increased refrigerant flow. The aim of this study was to investigate the impact of the novel design on procedural efficacy of cryoballoon PVI (CB-PVI).

Methods and results: Single transseptal CB-PVI using an endoluminal spiral mapping catheter was performed in 60 consecutive patients (CB-1G, 28 mm, 300 s. application time: 30 patients; CB-2G, 28 mm, 240 s. application time: 30 patients). After successful isolation, one "bonus" application was performed per vein. When compared to the CB-1G, using the CB-2G increased single-shot PVI rate from 51–84 % ($p<0.001$); and decreased procedure duration (128±27 vs 98±30 min, $p<0.001$) and fluoroscopy exposure time (19.5±7.4 vs 13.4±5.3 min, $p=0.001$). Effective CB-2G PVI could be performed with increased real-time PVI visualization rate (49 vs 76 %, $p<0.001$). Time to PVI (TPVI) was shorter in the CB-2G group (79±60 vs 52±36 s, $p=0.049$). Procedure-related complications occurred in 2 patients in the CB-1G group and 1 patient in the CB-2G group.

Conclusions: The CB-2G significantly improved procedural efficacy compared to the CB-1G with 84 % of PVs isolated after a single balloon application. Reliable measurement of TPVI may be used to titrate application time individually in future studies.

X-5

Cardiac arrhythmias as first symptom in patients with sarcoidosis

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Background: Sarcoidosis is a multisystemic granulomatous disease of unknown cause, which usually affects lymph nodes, lungs, skin and the hepatic system. Cardiac involvement in pts with sarcoidosis is reported in up to 30 % in autopsy but only 5 % of pts have cardiac symptoms. We report a series of 4 pts in whom cardiac arrhythmias were the first manifestation of sarcoidosis.

Results: Case 1: A 38-year-old female presented with syncope due to paroxysmal high-grade AV block and was implanted with a dual chamber pacemaker (DC-PM). Pulmonary infiltrations were interpreted as pneumonia and later on as tuberculosis. One year later sarcoidosis was diagnosed by bronchoscopy and cardiac involvement with FDG PET-CT. The patient is now PM-dependent and on antiinflammatory therapy.

Case 2: A 46-year-old male was admitted to our hospital with fatigue and dyspnoe. ECG showed junctional rhythm with bradycardia <40 bpm and later on also typical atrial flutter. Bilateral lymphadenopathy on chest X-ray was related to pulmonary sarcoidosis. MRI ensured cardiac involvement. The pt refused permanent PM implantation for about 2 years. After recurrent syncope a DC-PM was implanted.

Case 3: A 59-year-old female demonstrated high-grade AV block following electrical cardioversion of typical atrial flutter. A DC-PM was inserted and cavotricuspid isthmus ablation was performed. After 1 year the patient presented with heart failure. Cardiac sarcoidosis was diagnosed with endomyocardial biopsy. In addition pulmonary involvement was confirmed. The pacemaker was upgraded to a DC-ICD system because of sustained VT.

Case 4: A 36-year-old male with a history of epilepsia developed VF and was successfully resuscitated. Cardiac MRI was indicative for myocarditis. EP study induced multiple VT morphologies and VF. A DC-ICD was implanted and the pt received frequent appropriate ICD shocks despite antiarrhythmic therapy. Due to disease progression endomyocardial biopsy was performed 4 years after the initial diagnosis and revealed cardiac sarcoidosis. No extracardiac manifestation was found. The patient was put on immunosuppressive medication and high dose beta-blocker with satisfactory response.

Conclusion: Our cases demonstrate that a variety of cardiac arrhythmias may be the first clinical presentation of sarcoidosis. In absence of extracardiac signs this systemic disease may be difficult to diagnose as it can mimic different pathologies. Endomyocardial biopsy may be helpful to distinguish between cardiac sarcoidosis and other syndromes (e.g. myocarditis, ARVD). However, the highest sensitivity and specificity is achieved with cardiac MRI, which should be performed at an early stage and best before device implantation. Finally, we emphasize the need for aggressive investigation of high-grade AV conduction disturbances in middle-aged persons irrespective of the decision to implant a pacemaker.

X-6

Safety and efficacy of pharmacological cardioversion of recent onset atrial fibrillation in a major viennese emergency department

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Background and aim: The management of emergency department (ED) patients with presumed recent-onset atrial fibrillation or flutter ≤48 h duration varies widely.

Our aim was to describe the management of patients with recent onset (<48 h) atrial fibrillation or flutter (AF), to determine the safety and efficacy of pharmacological cardioversion at the ED, and to measure the incidence of thromboembolism 30 days after discharge. Furthermore, we were interested to assess the coherence of routine treatment to current guidelines.

Methods: In a prospective observational study at the ED of the Wilhelminen hospital in Vienna, 287 subjects presenting with recent onset AF were enrolled consecutively from January 2011 to January 2013. For between group comparison, univariate and multivariate logistic regression was used. Due to low numbers in the amiodarone group, it was not included in the statistical analysis.

Results: Median age of our population was 68 (62–74) years. As first line therapy, 51.9 % ($n=149$) received ibutilide, 19.5 % ($n=56$) received vernakalant, 17.4 % ($n=50$) received flecainide and 0.7 % ($n=2$) received amiodarone. Successful cardioversion to sinus rhythm was achieved in 75 % ($n=216$) of patients after first line therapy. There was no statistically significant difference between treatment groups, even after adjustment for sex, age, diabetes, hypertension, heart failure, stroke/TIA, vascular disease or CHA2DS2-VASc-score, respectively. Acute side effects were observed in 13 cases as cardiac arrhythmias (non sustained ventricular tachycardia or bradycardia), prolonged QT- interval, broad QRS and paraesthesia. At 1 month follow-up 2 cerebrovascular events were recorded.

In 9.4 % ($n=27$) of patients after initial treatment failure a second or even third anti-arrhythmic drug was administered. The success rate of serial anti-arrhythmic therapy was 70.3 % ($n=19$) and the all-over success rate was 82 % ($n=235$). Combinations were flecainide and ibutilide ($n=7$), vernakalant and ibutilide ($n=17$), vernakalant and flecainide ($n=1$), vernakalant, ibutilide and flecainide ($n=1$) and ibutilide and amiodarone ($n=1$). Two acute side effects were observed in the serial anti-arrhythmic therapy group: one event of reversible hypotension after flecainide therapy and one event of altered taste after vernakalant therapy.

Conclusion: Pharmacological cardioversion with discharge after a short observation time is safe. There was no difference between the substances used in terms of immediate or long-term safety and efficacy. The coherence of the ED to recent guidelines is high regarding first line therapy. In particular, the serial use of up to three anti-arrhythmic drugs to convert AF into sinus rhythm—which is not recommended by the current ESC guidelines—appears safe and successful.

X-7

Luminal esophageal temperature predicts esophageal lesions after second-generation cryoballoon pulmonary vein isolation

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Background: The novel second-generation cryoballoon (CB2) facilitates pulmonary vein isolation (PVI) by improved surface cooling. The impact of this re-design on collateral damage is unknown.

Objective: To investigate the incidence of esophageal lesions after PVI using the CB2 and the role of luminal esophageal temperature (LET) measurement as a predictor of lesion formation.

Methods: Thirty-two consecutive patients underwent PVI using the 28 mm CB2. Target application time was 2×240 s. 92% PVs were isolated after one cryoenergy application. Complete PVI was achieved in all patients. Luminal esophageal temperature with three thermocouples was continuously measured during cryoenergy application. Freezing was only interrupted if weakening/loss of phrenic nerve (PN) function or very low LET (<5 °C) was observed.

Results: The lowest measured LET was—12 °C (despite cryoapplication interruption). Post-procedural gastro-esophagoscopy was performed after 1–3 days in all patients and showed lesions in 6/32 (19%) patients. A minimum LET of ≤12 °C predicted esophageal lesions with 100% sensitivity and 92% specificity (area under the ROC curve 0.97; CI 0.93–1.02, $p=0.001$). Persistent PN palsy occurred in two patients (6%) during ablation at the right inferior PV. Repeat gastro-esophagoscopy confirmed healing of lesions after 16±14 days.

Conclusion: Second-generation 28 mm cryoballoon PVI is associated with significant esophageal cooling resulting in lesion formation in 19% of patients. LET measurement accurately predicts lesion formation and may enhance the safety of the novel device.

Postersitzung XI: Rhythmologie 2

XI-1

Procedural benefit of direct catheter force measurement on ablation of paroxysmal and persistent atrial fibrillation

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Background: Electrode-tissue contact is crucial for adequate lesion formation in radiofrequency catheter ablation (RFCA).

Objective: We assessed the impact of direct catheter force measurement on acute procedural parameters of RFCA for atrial fibrillation (AF).

Methods: Ninety-nine consecutive patients (pts; 72% male) with paroxysmal (63%) or persistent (37%) AF underwent left atrial RFCA using a 3.5 mm open-irrigated tip (OIT) catheter with contact force measurement capabilities (group 1). For comparison of acute procedural parameters a case-matched cohort with standard OIT catheters was used (99 pts; group 2). Case-matching included gender, type of AF, and type of procedure (pulmonary vein isolation, linear ablations, and complex fractionated electrogram ablation).

Results: Procedural data showed a significant decline in radiofrequency ablation time from 52±20 to 44±17 min ($p=0.006$) with a remarkable mean reduction in overall procedure time of 34 min ($p=0.0001$; 225.8±53.1 vs. 191.9±53.3 min). In parallel the total fluoroscopy time could be significantly reduced by 15.9 min ($p=0.0001$).

Periprocedural complications were the same in both groups with 2–3% AV fistula or pseudoaneurysms in the groin and 1–2% pericardial tamponades.

Conclusions: The use of novel contact force sensing technology is able to significantly reduce ablation, procedure, and fluoroscopy times in RFCA of AF in a mixed group of paroxysmal and persistent AF. Energy delivery is substantially reduced by avoiding radiofrequency ablation in positions with insufficient surface contact. Safety and long-term efficacy of this new feature have to be evaluated in larger and randomized cohorts.

XI-2

Procedural and clinical impact of a new open-irrigated radiofrequency catheter with direct force measurement on ablation of paroxysmal atrial fibrillation

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Background: Electrode-tissue contact is crucial for adequate lesion formation in radiofrequency catheter ablation (RFCA).

Objective: We assessed the impact of direct catheter force measurement on acute procedural and clinical parameters as well as on short-term outcome of RFCA for atrial fibrillation (AF).

Methods: Seventy consecutive patients (pts; 48 male) with paroxysmal AF who underwent their first procedure of circumferential pulmonary vein isolation (PVI) were assigned to either RFCA using (1) a standard 3.5 mm open-irrigated tip catheter or (2) a catheter with contact force measurement capabilities. Using the endpoint of PVI with entry and exit block acute procedural parameters were assessed. Outcome data were assessed by clinical recurrences and 24 h Holter monitoring 3 months after the procedure.

Results: Procedural data showed a remarkable decline in radiofrequency ablation time from 50.8±16.1 to 42.1±10.3 min ($p=0.022$) with a mean reduction in overall procedure time of 36.6 min ($p=0.001$; 199.8±37.3 vs. 163.2±43.9 min). In parallel the total fluoroscopy time could be significantly reduced from 35.3±11.4 to 24.7±8.9 ($p=0.0001$). Procedural outcome at 3 months was exactly the same in both groups with an 80% single-procedure success rate.

Conclusions: The use of novel contact force sensing technology is able to significantly reduce ablation, procedure, and fluoroscopy times in PVI. Energy delivery is substantially reduced by avoiding radiofrequency ablation in positions with insufficient surface contact. 3 month outcome data did not differ between both groups. Safety and long-term efficacy of this new feature have to be evaluated in larger cohorts.

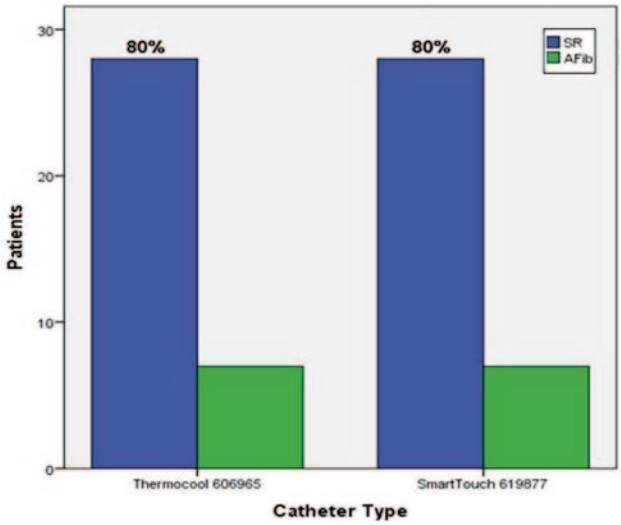

Fig. 1 Single procedural outcome at 3 months

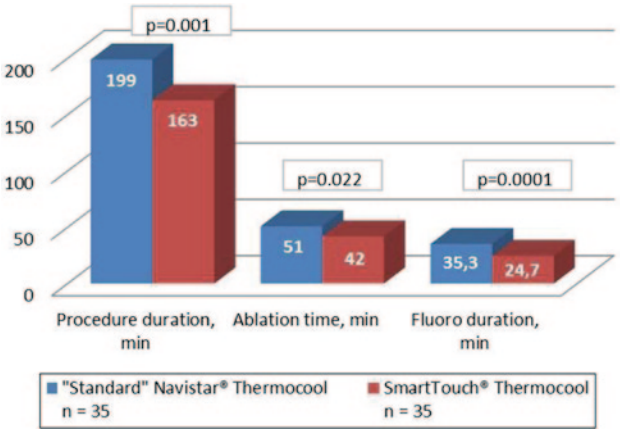

Fig. 2 Contact force sensing technology reduce ablation, procedure and fluoroscopy times in PVI

XI-3

Impact of a new fluoroscopy-integrated catheter positioning system (Mediguide) on procedural data in ablation of atrial fibrillation and inter-operator differences

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Background: Mediguide represents a new catheter positioning system integrated into the C-arm of a conventional fluoroscopic system. The tip of Mediguide-enabled catheters may be superimposed on pre-recorded fluoroscopic loops.

Objective: We assessed the impact of the use of this system on acute procedural parameters in pulmonary vein isolation (PVI) for atrial fibrillation (AF) as well as inter-operator differences.

Methods: Thirty-four consecutive AF patients were included into the analysis using a Mediguide-enabled open-irrigated ablation catheter (group 1). A historical control group with standard ablation was used for comparison (group 2, $n=46$). The endpoint of entry and exit block was used for PVI. Linear ablations were used in persistent cases at operator's decision.

Results: Procedural data showed a remarkable decline in fluoroscopic time from 46.9±18.1 to 22.5±12.9 min ($p=0.0001$) and dose from 12.650±7.657–6.747±4.198 nGy/m² ($p=0.0001$). Average radiofrequency ablation time, overall procedure time, and other procedural parameters were not altered by the use of the positioning system. Acute procedural outcome was the same in both groups with a 100 % acute PVI.

Significant inter-operator differences in fluoroscopy time (11 vs. 22 vs. 33 min; $p=0.001$) were seen in the Mediguide group showing a 21–24 min fluoroscopy reduction in all operators from baseline values (32 vs. 43 vs. 57 min).

Conclusions: The use of the novel Mediguide catheter positioning system is able to significantly reduce fluoroscopic times and dose in PVI with significant inter-operator differences. Acute outcome and other procedural data were not affected by the use of the system.

XI-4

Impact of Heparin-bolus timing on asymptomatic cerebral lesions in pulmonary vein isolation under therapeutic anticoagulation

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Background: Left atrial radiofrequency ablation carries a risk of asymptomatic cerebral lesions. In a study on consecutive patients under continued oral anticoagulation we reported an incidence of 12.2 % of silent cerebral lesions in postprocedural MRI. Parameters showing a significant correlation were age, persistent atrial fibrillation, spontaneous echo contrast in TEE, electrical cardioversion, PVI only, and ablation of complex atrial electrograms (Martinek et al., Europace 2012).

The aim of this study was to assess the impact of Heparin-bolus timing and dosage on the amount of silent cerebral lesions.

Methods: One hundred and thirty-one consecutive patients undergoing catheter ablation for atrial fibrillation (51 persistent, 38.9 %) were included in the study. Pulmonary vein isolation, roofline, mitral isthmus line, and CFAE ablation using 3.5 mm open-irrigated tip catheters were performed, as needed. All patients underwent preprocedural and postprocedural cerebral MRI.

A first Heparin-Bolus of 3.000–5.000 IE was given before and a second Bolus of the same amount was applied directly after transseptal puncture. Thirty minutes after transseptal puncture ACT was checked and a continuous Heparin infusion started.

Results: Time to the first Heparin-Bolus (21.5±12.9 vs. 27.8±15.5 min from groin puncture; $p=0.078$) and time to start of the continuous Heparin infusion (60.0±21.8 vs. 71.1±27.6; $p=0.070$) showed a trend to significance for later application in the cerebral lesion group.

Conclusion: Radiofrequency ablation in patients under continued oral therapeutic anticoagulation is associated with a substantial risk of silent embolism detected by cerebral MRI. Aside other clinical and procedural parameters timing of Heparin administration might have an influence on cerebral lesion creation.

XI-5

Technical evolution of cryoballoon pulmonary vein isolation in patients with paroxysmal atrial fibrillation: first experience with the new artic front advance© cryoballoon

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Purpose: The purpose of this study was to investigate possible differences in procedural parameters and clinical follow-up between the new Arctic Front Advance© Cryoballoon (Medtronic) and the already established Artic Front© Cryoballoon (Medtronic) used for pulmonary vein isolation (PVI) in a paroxysmal atrial fibrillation (PAF) population.

Methods: Between 2010 and 2012, we performed PVI with cryoballoons in 171 patients with PAF (143 with the Arctic Front© and 28 with the new Arctic Front Advance© Cryoballoon, respectively).

Both devices were used according to the recommendations of the manufacturer with a freeze time of 300 s for the Artic Front© and 240 s for the Artic Front Advance©, respectively and a minimum of two freezes for each PV.

In order to eliminate data from the learning curve with a single-shot balloon-catheter, we excluded the first 30 patients ablated with the Arctic Front© from retrospective analysis. In consequence, we compared procedure- and fluoroscopy times, the need for touch-up ablations as well as the incidence of phrenic nerve palsy between 113 Artic Front© – and 28 Artic Front Advance©-patients.

Clinical follow-up consisted of 48 h ECG monitoring at 3, 6, and 12 months after ablation plus additional ECGs recorded during episodes of suspicious symptoms. Freedom from atrial arrhythmias≥30 s was counted as clinical success.

Results: Significant reduction of procedure time (mean 163±27 min for the Arctic Front© vs. mean 108±14 min for the Arctic Front Advance©, $p<0.001$) and fluoroscopy exposure (mean 36±8 min for the Arctic Front© vs. 21±6 min for the Arctic Front Advance©, $p<0.001$) could be observed. The need of touch-up ablations was 7/113 (6%) and 1/28 (4%) for the Artic Front© and the Artic Front Advance©, respectively (p= ns). Phrenic nerve palsy occurred in 4/113 (4%) of the Arctic Front©-patients and in no Arctic Front Advance©-patient (p= ns).

Clinical 3-month efficacy was similar in both groups with freedom from AF: 84/113 patients (74%) in the Arctic Front©-group and 21/28 (75%) patients in the Arctic Front Advance© group, respectively (p= ns).

Conclusions: Compared to the Artic Front© cryoballoon, the new Arctic Front Advance© cryoballoon could significantly reduce the procedure and fluoroscopy times of PVI without a reduction of the safety or efficacy of the intervention. Thus, the positive evolution of this catheter could be a key for increasing the number of treated patients by making the intervention easier and faster.

XI-6

Schrittmachergenerator-Wechsel mit dem neuen Medtronic PEAK PlasmaBlade™ System – erste Erfahrungen im Vergleich zur konventionellen Elektrokaustik

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Einleitung: Beim Schrittmachergenerator-Wechsel wegen Batterieerschöpfung wird an unserer Abteilung bei jedem Patienten zur Reduktion des Infektionsrisikos eine vollständige Taschenexzision angestrebt. Dazu müssen die in die Tasche reichenden proximalen Sondenabschnitte komplett freipräpariert werden. Da ein konventioneller Elektrokauter die Sonden beschädigen könnte, wird dies mit einer Präparartionsschere durchgeführt und ist dementsprechend zeitaufwendig. Seit Ende 2012 verwenden wir bei Generator-Wechsel das neue PEAK PlasmaBlade™ System (Medtronic Inc., USA), das durch niedrigere Temperaturen an der „Klinge“ weniger thermische Schäden verursacht und daher auch zur Sondenpräparation geeignet ist. Die niedrigeren Temperaturen werden hierbei durch gepulste elektrische Entladungen – im Gegensatz zur herkömmlichen, auf kontinuierlicher Radiofrequenz basierenden Elektrokaustik – ermöglicht.

Material und Methode: An unserer Abteilung wird seit November 2012 für Schrittmachergenerator-Wechsel routinemäßig das PEAK PlasmaBlade™ System (PEAK Plasma Blade™ und PULSAR© Generator) verwendet. Zuvor war für die Generatorwechsel mit vollständiger Taschenexzision oben beschriebene Technik mit konventioneller Elektrokaustik und Sondenpräparation mittels Präparationsschere angewandt worden.

Ziel dieser Untersuchung war es, die beiden Techniken in Hinblick auf Machbarkeit, Operationsdauer und prozedurale Komplikationsraten zu vergleichen.

Ergebnisse: Von März 2001 bis Oktober 2012 wurden 405 Schrittmachergenerator-Wechsel mit konventioneller Elektrokaustik und OP-Scheren-Präparation der Sonden durchgeführt, (Gruppe I) während seit November 2012 bei 25 Patienten zum Generatorwechsel das PEAK PlasmaBlade™ System verwendet wurde (Gruppe II).

Gruppe I und II unterschieden sich nicht signifikant bezüglich Geschlecht und mittlerem Alter. Die Verteilung von 1- und 2-Kammer- sowie CRT-Generatoren war in Gruppe I 65% DDD, 28% VVI und 7% CRT, während in Gruppe II 72% DDD-, 8% VVI- und 20% CRT-Generatoren gewechselt wurden.

Alle Generatoren-Wechsel in Gruppe 2 konnten wie geplant alleine mit dem PEAK PlasmaBlade™ System durchgeführt werden. Keine der mit dem PEAK Plasma Blade™ freipräparierten Sonden wurde dabei beschädigt. Die mittlere Operationsdauer war in Gruppe I mit 38±19,1 min im Vergleich zu Gruppe II 25,3±5,4 min signifikant länger (p=0,005). Als einzige prozedurale Komplikation traten Hämatome auf (10/405, 2,4% in Gruppe I vs. 1/25, 4% in Gruppe 2; p= ns).

Diskussion: Die Verwendung des PEAK PlasmaBlade™ Systems ermöglicht, ohne relevante Lernkurve, eine sichere und schnelle Freipräparation von Schrittmachersonden im Rahmen eines Generator-Wechsels mit begleitender Taschenexzision. Ob eine ähnlich niedrige Blutungsrate wie bei der Verwendung von konventioneller Elektrokaustik erzielt werden kann, muss prospektiv evaluiert werden.

XI-7

MediGuide®-basierte Katheterablation bei typischem Vorhofflattern

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Einleitung: Die Hochfrequenz-Katheterablation am cavotrikuspidalen Isthmus (CTI) stellt eine gut etablierte Therapieoption bei typischem („counter clockwise“) Vorhofflattern (VHFL) dar. Zur intraprozeduralen Orientierung werden neben intrakardialen Elek-

trogrammen standardmäßig fluoroskopiebasierte Aufnahmen herangezogen, die je nach Prozedurdauer eine variable Strahlenbelastung für den Patienten und Untersucher darstellen. Seit Mai 2012 ist die MediGuide®-Technologie (Fa. St. Jude Medical, SJM) verfügbar, mittels welcher eine nicht-fluoroskopische, EKG-getriggerte, zeitlich hochauflösende Visualisierung der Katheterspitzen innerhalb vorgefertigter Cineloops (Abb. 1) in Echtzeit möglich ist.

Methodik: Zwischen Juli 2012 und März 2013 wurden im Krankenhaus der Elisabethinen Linz 10 Patienten (2 weiblich, 8 männlich) mit einem durchschnittlichen Alter von 62±8,9 Jahren einer MediGuide®-basierten CTI-Ablation bei typischem VHFL unterzogen und mit 10 Patienten (7 männlich, 3 weiblich; Durchschnittsalter 60,4±7,8 Jahre) verglichen, bei denen im selben Zeitraum eine herkömmliche, fluoroskopiebasierte Ablationsbehandlung durchgeführt wurde. Bei sämtlichen Prozeduren wurden wassergekühlte Ablationskatheter verwendet. Neben dem Vorliegen kardiovaskulärer Begleiterkrankungen (Tab. 1) wurden Prozedurdauer, Ablationszeit, Fluoroskopiedauer und -dosis sowie gesamte und maximale Energieabgabe zwischen beiden Gruppen verglichen.

Resultate: Größe, Gewicht und folglich auch BMI waren in beiden Gruppen vergleichbar (MediGuide®: BMI 29,04±3,96; Vergleichsgruppe: BMI 28,7±4,66), sodass diesbezüglich kein relevanter Einfluss auf das Ergebnis der erreichten Strahlenbelastung angenommen werden musste. Vorbestehende kardiovaskuläre Begleiterkrankungen konnten häufiger in der MediGuide®-Gruppe beobachtet werden (Tab. 1). Bei vergleichbarer Prozedurdauer konnte eine statistisch signifikante Abnahme der Fluoroskopiezeit (um 76,3 %; $p=0{,}001$) und Strahlendosis (um 62,0 %, $p=0{,}038$), sowie ein deutlicher Trend in der Reduktion der reinen Ablationszeit (um 39,5 %, $p=$ ns) und benötigten Energieabgabe (um 39,0 %, $p=$ ns) dokumentiert werden (Abb. 2, Tab. 2).

Schlussfolgerung: Das MediGuide®-System ermöglicht zeitlich hochauflösende, Cineloop-basierte, EKG-getriggerte Katheternavigation in Echtzeit und trägt zu einer signifikanten Reduktion der Fluoroskopiedauer und benötigten Strahlendosis sowie (aufgrund der geringen Patientenzahlen) insignifikanten Reduktion der reinen Ablationszeit und Energie~Gesamtabgabemenge bei gleichbleibender Prozedurdauer bei.

Tab. 1. Studienpopulation, vorbestehende kardiovaskuläre Risikofaktoren und Begleiterkrankungen

Pair	Parameter	Ablation Type	n	%	Mean	Std. dev.
1	Weiblich (n)	Standard	3 von 10	30		
		MediGuide	2 von 10	20		
2	Männlich (n)	Standard	7 von 10	70		
		MediGuide	8 von 10	80		
3	Alter (yrs)	Standard	9		60,44	7,78
		MediGuide	10		62,00	8,94
4	Größe (cm)	Standard	9		172,78	9,45
		MediGuide	9		175,00	8,30
5	Gewicht (kg)	Standard	9		86,55	19,27
		MediGuide	9		89,56	10,57
6	BMI	Standard	9		28,72	4,66
		MediGuide	9		29,04	3,96
7	Arterielle Hypertonie (n)	Standard	7 von 9	77,8		
		MediGuide	9 von 9	100		
8	Diabetes (n)	Standard	0 von 9	0		
		MediGuide	1 von 9	11,1		
9	Periphere arterielle Verschlusskrankheit (n)	Standard	0 von 9	0		
		MediGuide	2 von 9	22,2		
10	Stattgehabter Insult (n)	Standard	0 von 9	0		
		MediGuide	1 von 9	11,1		
11	Dyslipidämie (n)	Standard	4 von 9	44,4		
		MediGuide	6 von 9	66,6		
12	Koronare Herzerkrankung (n)	Standard	0 von 9	0		
		MediGuide	3 von 9	33,3		
13	Herzinsuffizienz (n)	Standard	2 von 9	22,2		
		MediGuide	3 von 9	33,3		

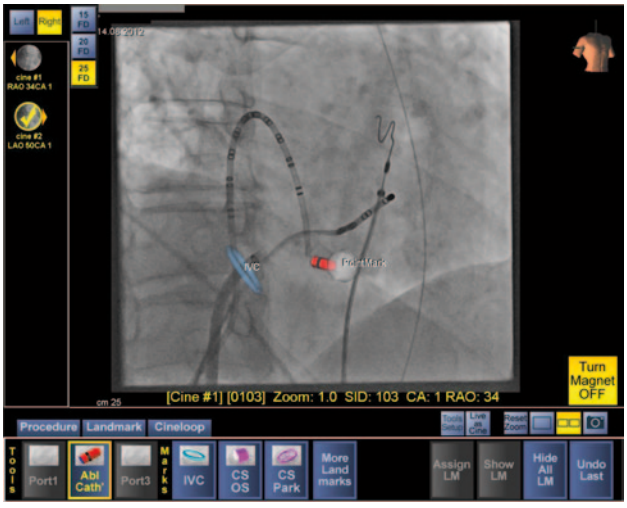

Abb. 1 EKG-getriggerte Echtzeit-Darstellung der Katheterspitze des MediGuide®-Katheters (rot) im zuvor angefertigten Cineloop während der VHFL-Ablationsprozedur. Der blaue Ring stellt die zuvor markierte Vena cava inferior (IVC) dar, der graue Marker („PointMark“) signalisiert den Rand der Trikuspidalklappe.

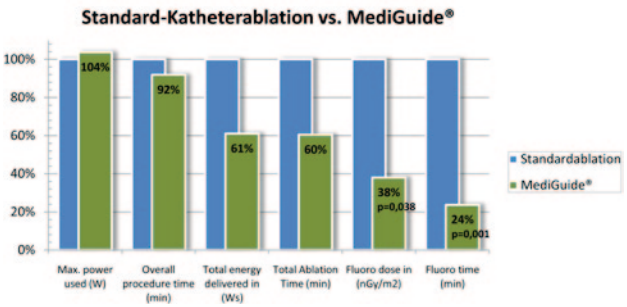

Abb. 2 Vergleich zwischen Standard-Katheterablation (=Referenz, 100%) und Verwendung des MediGuide®-Systems anhand ablationsbezogener Parameter im Rahmen der VHFL-Prozedur

Tab. 2. Vergleich zwischen Standard-Katheterablation und Verwendung des MediGuide®-Systems anhand ablationsbezogener Parameter im Rahmen der VHFL-Prozedur; Signifikante Reduktion der Fluoroskopiedauer

Pair	Parameter	Ablation Type	n	Mean	Std. dev.	Sign. (2-tailed)
1	Overall procedure time (min)	Standard	10	89,50	26,92	$p=0.536$
		MediGuide	9	82,22	23,33	
2	Fluoro time (min)	Standard	10	23,83	12,02	$p=0.001$
		MediGuide	10	5,65	4,65	
3	Fluoro dose in (nGy/m²)	Standard	10	5144	3955	$p=0.038$
		MediGuide	10	1954	1798	
4	Total energy delivered (Ws)	Standard	10	28.240	16.766	$p=0,102$
		MediGuide	9	17.231	9637	
5	Max. power used (W)	Standard	10	35,20	4,59	$p=0,477$
		MediGuide	10	36,50	3,31	
6	Total ablation time (min)	Standard	10	14,85	8,06	$p=0,072$
		MediGuide	9	8,98	4,94	

Postersitzung XII: Risikofaktoren/ Stoffwechsel/Lipide 1

XII-1

Lipoprotein (a), the metabolic syndrome and vascular risk in angiographied coronary patients

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VIVIT, Innere Medizin, Landeskrankenhaus Feldkirch

Introduction: Lipoprotein (a) [Lp(a)] especially in young individuals is an important cardiovascular risk factor. However, data on the vascular risk conferred by Lp(a) in patients with the metabolic syndrome (MetS) are not available.

Materials & Methods: Lp(a) was measured in a cohort of 587 consecutive patients undergoing coronary angiography for the evaluation of stable coronary artery disease. The MetS was diagnosed according to International Diabetes Federation (IDF) criteria. Vascular events were recorded over 8 years.

Results: Median Lp(a) was significantly lower in patients with the MetS ($n=345$) than in subjects who did not have the MetS (12 [interquartile range 0.8–35] vs. 17 [0.8–57] mg/dl; $p=0.004$). Prospectively, 34% of our patients suffered vascular events. Lp(a) proved to be a strong and independent predictor of vascular events in subjects without the MetS (standardized adjusted HR 1.33 [1.01–1.74]; $p=0.029$) but not in patients who had the MetS (HR 1.07 [0.84–1.37]; $p=0.543$). An interaction term MetS × Lp(a) was significant ($p=0.005$), indicating that Lp(a) was a significantly stronger predictor of vascular events in subjects without MetS than in patients with the MetS.

Discussion: We conclude that Lp(a) in patients with MetS is low and is not associated with the incidence of vascular events. The power of Lp(a) as a predictor of cardiovascular events is significantly modulated by the presence of the MetS.

XII-2

HbA1c is a significantly stronger predictor of cardiovascular events in woman than in men among patients undergoing coronary angiography

C. H. Saely, A. Vonbank, P. Rein, D. Zanolin, H. Drexel

VIVIT, Innere Medizin, Landeskrankenhaus Feldkirch

Introduction: The association of HbA1c with future cardiovascular events in the clinically important high-risk population of patients undergoing coronary angiography has not been investigated so far. In the present study we therefore addressed this issue and also tested the hypothesis that gender modulates the impact of HbA1c on cardiovascular event risk.

Materials and methods: We prospectively recorded cardiovascular events over a mean follow-up period of 4.4 years in a large consecutive series of 1,449 patients, including 484 women and 965 men who did not have previously known diabetes and who underwent coronary angiography for the evaluation of stable coronary artery disease.

Results: During follow-up, the incidence of cardiovascular events was 19.5% in women and 25.6% in men, corresponding to annual event rates of 4.4 and 5.8%; $p=0.001$. Among women, HbA1c strongly and significantly predicted cardiovascular events (adjusted OR for a 1% increase in HbA1c = 1.69 [1.16–2.45]; $p=0.006$), whereas the association between HbA1c and cardiovascular events was weaker and statistically non-significant in men (OR = 1.15 [0.95–1.39]; $p=0.147$. An interaction term gender x HbA1c was significant ($p=0.024$), indicating that HbA1c was a significantly stronger predictor of cardiovascular events among women than among men.

Discussion: We conclude that HbA1c is a significantly stronger predictor of cardiovascular events in women than in men among patients undergoing coronary angiography.

XII-3

Eccentric endurance exercise significantly improves both fasting and postchallenge metabolism in overweight and obese individuals

P. Rein, C. H. Saely, A. Vonbank, H. Drexel

VIVIT, Innere Medizin, Landeskrankenhaus Feldkirch

Introduction: Eccentric endurance exercise (e.g. hiking downwards) is less strenuous than concentric exercise (e.g. hiking upwards) but data on its potential to reduce cardiovascular risk are scarce.

Materials and methods: We allocated 68 overweight and obese sedentary individuals to an exercise intervention program, consisting of hiking downwards the same route over two months. For the opposite way, a cable car was used where compliance was recorded electronically. The difference in altitude was 540 m; the distance was covered three to five times a week. A matched group of 12 individuals served as a control group. Fasting and postprandial metabolic profiles were obtained at baseline and after the two months period.

Results: Compared with baseline, eccentric endurance exercise significantly lowered fasting glucose (99±17 vs. 96±13 mg/dl; $p=0.036$) as well as glucose tolerance following the oral intake of 75 g glucose (250±49 vs. 228±54 mg*dl-1 h; $p<0.001$), whereas these parameters remained unchanged in the control group ($p=0.495$ and $p=0.182$, respectively). Furthermore, eccentric endurance exercise significantly improved triglyceride tolerance in

a standardized oral fat challenge test (2,121±1,398 vs. 1,744±1,143 mg*dl-1 h; $p<0.001$), whereas triglyceride tolerance did not change significantly in the control group ($p=0.695$). Body mass index was slightly but significantly lowered in the eccentric endurance exercise group (29.6±3.1 vs. 29.2±3.3 kg/m^2; $p=0.004$) but not in the control group ($p=0.237$).

Discussion: Eccentric endurance exercise is a promising new exercise modality with favorable effects on both fasting and postchallenge metabolism.

XII-4

Lipid parameters in acute coronary syndromes versus stable coronary artery disease in patients with the metabolic syndrome and in subjects who do not have the metabolic syndrome

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VIVIT, Innere Medizin, Landeskrankenhaus Feldkirch

Introduction: Differences in lipid parameters between patients with acute coronary syndromes (ACS) and patients with stable coronary artery disease (CAD) are unclear and are addressed in the present study.

Materials and methods: We enrolled consecutive patients with angiographically proven stable CAD (of whom 37.2% had the MetS according to NCEP-ATPIII criteria and 182 consecutive patients with acute coronary syndromes (of whom 33.9% had the MetS).

Results: When compared to patients with stable CAD, HDL cholesterol and apolipoprotein A1 were significantly lower in patients with ACS than in those with stable CAD both among subjects with the MetS (38±9 vs. 48±13 mg/dl; $p<0.001$ and 139±38 vs.14±25 mg/dl; $p<0.001$, respectively) and among those without the MetS (52±17 vs. 60±15 mg/dl; $p=0.001$ and 147±31 mg/dl vs. 157±26 mg/dl; $p=0.003$, respectively). Analysis of covariance adjusting for age, gender, smoking, BMI, and hypertension confirmed an independent impact of the ACS state on these lipid parameters both among patients with the MetS ($F=5.287$; $p<0.001$) and among subjects who did not have the MetS ($F=6.042$; $p=0.014$). Total cholesterol, LDL cholesterol, apolipoprotein B, and triglycerides neither in patients with the MetS nor among subjects without the MetS differed significantly between ACS and stable CAD patients.

Discussion: We conclude that both among patients with the MetS and among non-MetS individuals, HDL cholesterol and apolipoprotein A1 are lower in the ACS state than with stable CAD.

XII-5

Eccentric endurance exercise significantly lowers liver enzymes in overweight and obese individuals

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VIVIT, Innere Medizin, Landeskrankenhaus Feldkirch

Introduction: Elevated liver enzymes are highly prevalent in overweight and obese patients, reflect the presence of non-alcoholic fatty liver disease, and are associated with an increased risk of diabetes and cardiovascular events. Liver enzymes can be lowered by physical exercise, but many overweight patients are not willing or not able to engage in strenuous exercise regimens. Eccentric endurance exercise (e.g. hiking downwards) is less strenuous than concentric exercise (e.g. hiking upwards) but its effects on liver enzymes are unknown.

Materials and methods: We allocated 42 overweight and obese sedentary individuals to an exercise intervention program, consisting of hiking downwards a pre-defined route in the Austrian Alps over 2 months. For the opposite way, a cable car was used where compliance was recorded electronically. The difference in altitude was 540 m; the distance was covered three to five times a week. A matched group of 12 individuals served as a control group. Metabolic profiles were obtained at baseline and after the 2 months period.

Results: Compared to baseline, 8 weeks of eccentric endurance exercise significantly lowered serum alanine aminotransferase (ALT; 36±23 vs. 31±18 U/L; $p<0.001$), the ALT/aspartate aminotransferase (AST) ratio (1.22±0.41 vs. 1.02±0.33; $p<0.001$), and serum gamma-glutamyl transferase (56±98 vs. 44±65 U/L; $p=0.005$), whereas these parameters did not change significantly in the control group ($p=0.261$, $p=0.272$, and $p=0.644$, respectively). Eccentric endurance exercise was well tolerated and there were no serious adverse events.

Discussion: We conclude that eccentric exercise is a promising new exercise modality which significantly lowers liver enzymes in overweight and obese individuals and therefore is of interest as a therapeutic intervention in non-alcoholic fatty liver disease patients.

XII-6

Aldosterone to renin ratio is associated with 24 h ambulatory blood pressure in essential hypertensives: the Styrian hypertension study

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Introduction: The aldosterone to renin ratio (ARR) is a screening tool for primary aldosteronism (PA). Accumulating evidence suggests that ARR may be significantly associated with blood pressure (BP) even below the threshold for PA. We therefore aimed to evaluate the relationship between the ARR and 24 h ambulatory BP monitoring measurements (ABPM).

Materials and methods: We recruited essential hypertensive patients derived from the outpatient clinic at the department of internal medicine of the local medical university hospital. ABPM measurements were obtained every 15 min during the day (06:00–24:00 o'clock) and every 30 min during the night (00:00–06:00). Plasma aldosterone and plasma renin concentrations were measured by means of a RadioImmunoAssay (RIA).

Results: We examined 172 hypertensive patients (age: 59.6±11.3 years; 51.2% females) with a mean systolic/diastolic 24 h ABPM value of 129/77 mmHg. In linear regression analyses adjusted for age, sex, 24 h urinary sodium and body mass index, ARR was significantly associated with night-time systolic (beta coefficient:0.19; $p=0.017$) and diastolic ABPM (beta coefficient: 0.28; $p<0.001$). In subgroup analyses of patients with ARR below the cut-off for positive PA screening (ARR <3.7—nanogram per deciliter divided by μU/mL) ARR remained significantly associated with diastolic ABPM (beta coefficient:0.26; $p=0.001$) and by trend with systolic ABPM (beta coefficient:0.15; $p=0.056$). These associations remained materially unchanged when additionally adjusted for other possible confounders, e.g. antihypertensive medications, HbA1c or NT-proBNP.

Discussion: In patients with essential hypertension and even in those patients not suggestive for PA, we found a strong relationship between ARR and diastolic night-time BP. In view of the strong relationship between diastolic night-time BP and risk of cardiovascular events further studies are needed to evaluate cardio-protective effects of mineralocorticoid blockade in hypertensive patients without PA.

Postersitzung XIII: Basic Science 3

XIII-1

ProBNP both among patients with type 2 diabetes and among non-diabetic subjects strongly predicts future macrovascular events independently from the baseline coronary artery disease state

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Innere Medizin, Landeskrankenhaus Feldkirch

Introduction: The power of pro-B-type natriuretic peptide (proBNP) to predict cardiovascular events is unclear, in particular in patients with type 2 diabetes (T2DM).

Materials and methods: We therefore aimed at investigating whether proBNP predicts major cardiovascular events in patients with T2DM as well as in subjects without diabetes in a large cohort of patients characterized by coronary angiography at baseline. We prospectively recorded major cardiovascular events in a cohort of 718 consecutive patients undergoing coronary angiography for the evaluation of established or suspected stable CAD over 3.2±1.2 years.

Results: Overall, the incidence of cardiovascular events was higher among patients with T2DM than among subjects who did not have diabetes. Cardiovascular risk increased significantly over tertiles of proBNP both among patients with diabetes (6.3, 24.1, and 32.4%,; $p=0.004$) and among non-diabetic subjects (11.5, 11.4, and 21.1%; $p=0.012$). Also as a continuous variable, baseline proBNP proved strongly predictive of major cardiovascular events both among patients with T2DM and among non-diabetic subjects (standardized adjusted HRs=1.40 [1.12–1.74], $p=0.003$ and 1.19 [1.06–1.33], $p=0.003$, respectively) after adjustment for age, gender, BMI, LDL cholesterol, HDL cholesterol, hypertension, and smoking. Additional adjustment for the angiographically determined baseline presence of CAD did not significantly attenuate these results.

Discussion: We conclude that proBNP both among patients with type 2 diabetes and among non-diabetic subjects strongly predicts future macrovascular events independently from the baseline coronary artery disease state.

XIII-2

Successful implementation of a minimal invasive aortic banding mouse model provides an insight into the influence of tenascin-C during myocardial hypertrophy

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Introduction: The role of the anti-adhesive extracellular matrix protein Tenascin-C (TNC) during ventricular hypertrophy remains unclear. To investigate the hemodynamic influence of TNC, we established a minimal invasive aortic banding model in the mouse to induce left ventricular pressure overload.

Methods: TNC-knockout (TNC-KO) and wildtype (WT) mice were intubated, ventilated and anaesthesia was maintained by 1.0% isoflurane. A partial sternotomy was performed, the thymus was retracted and the aortic arch was identified. A ligature was placed between the innominate and the left common carotid artery and tied around a 27-gauge needle to maintain equal knot tightness. Surgery was performed in TNC-KO ($n=5$) and WT ($n=6$) mice. Sham surgery was performed (TNC-KO-SHAM: $n=5$; WT-SHAM: $n=6$) respectively without tying the suture. After 10 weeks, hearts were assessed by cardiac magnetic resonance imaging. Data are presented as mean ± SEM.

Results: Ejection fraction was significantly decreased only in the WT banding group compared to sham animals as well as compared to the TNC-KO group (WT: 43.36±2.53% vs. TNC-KO-SHAM: 70.93±1.86%, AJ-SHAM: 73.72±3.74%, and TNC-KO: 68.14±3.19% $p<0.01$). Also, stroke volume was significantly reduced in the WT group compared to sham animals (WT: 0.10±0.01 mL/g vs. WT-SHAM: 0.15±0.01 mL/g $p<0.01$), while TNC-KO banding mice showed no significant decrease (TNC-KO: 0.14±0.01 mL/g vs. TNC-KO-SHAM: 0.15±0.01 mL/g n.s.). Interventricular septum thickness was significantly increased in operated WT mice compared to TNC-KO mice and sham mice (WT: 1.62±0.08 mm vs. TNC-KO-SHAM: 1.12±0.06 mm, AJ-SHAM: 1.04±0.05 mm, and TNC-KO: 1.18±0.04 mm $p<0.01$).

Discussion: A standardized minimal invasive aortic banding model to induce left ventricular hypertrophy was successfully established. The hemodynamic function of TNC-null mice remains significantly less affected by ventricular remodeling due to pressure overload. Further histologic investigation is essential to better understand the role of TNC and is currently executed in our laboratory.

XIII-3

The NO-donor S-NO-HSA represses ischemia/reperfusion injury and preserves hemodynamic function in a rat model of ACS

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Introduction: Acute myocardial infarction (AMI) still accounts for high mortality and morbidity. Aim of this study was to tackle ischemia-reperfusion injury (IRI) after reperfused AMI by S-NO-human serum albumin (HSA) therapy—a new direct NO-donor.

Methods: IRI was simulated by LAD ligature for 60', followed by 120' of in vivo reperfusion in 26 male SD-rats. After 15' of ischemia, 12 rats received 0.3 µmol/kg/h S-NO-HSA treatment for 75' intravenously (control: $n=14$; treatment: $n=12$). Blood pressure (BP) was monitored by a tip catheter placed into the right carotid artery in five animals in each group. Afterwards, evans blue and TTC staining was performed in vivo (control: $n=4$, treatment: $n=4$) to determine left ventricular (LV) infarct size (IS%LV) and area at risk (AAR%LV), in the remaining animals hemodynamic evaluation was performed in an erythrocyte perfused isolated working heart for 45' (control: $n=10$, treatment: $n=8$). Blood gas samples and specimens for elec-

tron microscopy (EM) were collected. Data are presented as mean ± SEM.

Results: In vivo monitoring revealed equal BP and heart rate. IS was equal in both groups (control: 39.07±3.20% vs. treatment: 38.08±2.12% n.s.), while AAR was significantly reduced by NO donor therapy (control: 79.36±7.35% vs. treatment: 55.09±3.39% $p \leq 0.05$). Similarly, a significantly better hemodynamic function was observed in the treatment group: cardiac output (control: 22.96±1.37 mL/min vs. treatment: 33.21±2.16 mL/min $p \leq 0.01$), external heart work (control: 4,745±302 mL/min × g vs. treatment: 6,262±548 mL/min × g $p \leq 0.05$). Although coronary flow (control: 1.87±0.15 mL/min vs. treatment: 1.91±0.13 mL/min n.s.) and myocardial oxygen delivery (control: 24.31±1.98 mL/min × g vs. treatment: 28.59±1.49 mL/min × g n.s.) were similar in both groups, myocardial oxygen uptake was significantly higher in the treatment group (control: 5.60±0.21 mL/min × g vs. treatment: 8.21±0.42 mL/min × g $p \leq 0.01$). EM revealed significantly ($p < 0.05$) less ultrastructural damage in the NO donor group.

Discussion: S-NO-HSA seems to be a potent therapeutic option after IRI, which results in less endothelial dysfunction, smaller AAR, and better hemodynamic function. Thus, the NO donor might be an interesting therapeutic option for AMI patients after interventional revascularization.

XIII-4

CD4+CD28null T-cell enrichment at the culprit lesion site in STE-ACS

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Background: ST-elevation acute coronary syndrome (STE-ACS) is among the leading causes of death. Coronary thrombosis is still poorly understood. We hypothesize that circulating leukocytes adhere to rupture-prone plaques and mediate plaque rupture and thrombotic occlusion. It has been shown that circulating CD4+CD28null T-cells are increased in STE-ACS, especially in patients suffering from diabetes and/or recurrent cardiovascular events 1, 2. We aimed to characterize CD4+CD28null cells at the culprit lesion site in STE-ACS patients.

Methods: We studied STE-ACS patients ($n = 109$), who underwent primary percutaneous coronary intervention at the Vienna General Hospital. Culprit site blood and solid thrombus material were aspirated during thrombectomy. In parallel, a blood sample from the femoral arterial sheath was collected. We stained whole blood and solid thrombus homogenate for flow cytometric analyses. Commercial enzyme-linked immunosorbent assays were carried out for plasma protein measurements.

Results: CD4+CD28null T-cells were increased at the culprit lesion site compared to femoral blood. In solid coronary thrombi, CD4+CD28null T-cells represent up to 53% of all CD4+T-cells. Intracellular perforin and granzyme B were decreased in coronary CD4+CD28null T-cells. By contrast, granzyme B concentration was increased in culprit site plasma compared to peripheral plasma and correlated with decreased intracellular levels.

Conclusion: CD4+CD28null T cells accumulate specifically at the culprit lesion site in STE-ACS patients. These cells release high levels of cytolytic proteins. Further experiments will evaluate the impact of this finding on outcome.

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XIII-5

Polymorphonuclear cells release neutrophil extracellular traps in coronary atherothrombosis that are sensitive to DNAse

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Background: Mechanisms of coronary occlusion in ST-elevation acute coronary syndrome (STE-ACS) are poorly understood. We hypothesized that circulating innate immune cells play a key role in thrombotic occlusion. Neutrophil extracellular traps (NETs) represent an efficient effector mechanism of activated neutrophils. We aimed to characterize neutrophils and NETs at the culprit lesion site in STE-ACS.

Methods: We studied 112 STE-ACS patients undergoing primary percutaneous coronary intervention (pPCI), followed by magnetic resonance tomography on day 3±2 after pPCI. Culprit site blood was aspirated with a thrombectomy catheter and particulate thrombus material was separated. In parallel, blood was sampled from the femoral arterial sheath. Flow cytometry was employed to characterize neutrophils at the plaque rupture site. These experiments were complemented by ELISA and immunofluorescence. Efficacy of DNAse as a thrombolytic agent was tested in ex vivo thrombus lysis assays. Endogenous DNAse activity and plasma nucleosome concentration were measured by ELISA.

Results: Coronary thrombus neutrophils are highly activated (carrying large amounts of CD66b, CD11a, CD11b) compared to systemic neutrophils, and aggregate with platelets. Nucleosomes, myeloperoxidase and neutrophil elastase are significantly increased in coronary plasma. NETS act as scaffolds of particulate coronary thrombi. Endogenous extracellular DNAse activity correlated with the concentrations of coronary nucleosomes and with infarct size. Coronary thrombi (ex vivo) were lysed faster with DNAse and t-PA than with t-PA alone ($p < 0.05$).

Conclusion: NET-releasing neutrophils accumulate at the culprit lesion site of patients suffering from STE-ACS. Therapeutic DNAse could be employed as a novel, more effective thrombolytic agent.

XIII-6

Expression of ion handling proteins in the hearts of chronic renal failure model in rats

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Background: Chronic renal failure in patients is associated with higher incidence of cardiac diastolic dysfunction. Subtotal nephrectomy in rats leads to compensated renal failure, increased systolic blood pressure, cardiac left ventricle hypertrophy and diastolic dysfunction. We investigated whether changes in protein expression or phosphorylation of cardiac ion handling proteins like sarcoplasmic reticulum Ca^{2+} ATPase (SERCA) and its regulatory subunit phospholamban (PLB), Calsequestrin (CSQ) and Na^{+}/K^{+} ATPase (NKA), contribute to cardiac diastolic dysfunction in the nephrectomy rat model.

Methods: Chronic renal failure was induced in young male Wistar rats by 5/6 nephrectomy (NXT). Sham operated group (SHAM)

served as the control. Left ventricles taken either 8 or 24 weeks after operation were used for western blotting. The bands intensity was quantified by Quantity One (Bio-Rad) and the expression of proteins was normalized to GAPDH. Average values of NXT were set to 1. The results are presented as number (n) of hearts of NXT/SHAM and as means ± S.E.

Results: In 8 weeks NXT group ($n=4$) expression of NKA α1, NKA α2, CSQ, SERCA2a was not changed when compared to SHAM group ($n=5$). The expression of PLB tended to be increased ($n=3/5$; 1.20 ± 0.07; $p=0.06$). The PLB phosphorylation at Ser16 when normalized to GAPDH showed a significant increase ($n=3/5$; 1.50 ± 0.21; $p=0.04$), whereas at Thr17 was unaltered.

In the 24-weeks NXT group no significant changes were found in protein expression of NKA α2, CSQ, SERCA2a and phosphorylation of Ser16-PLB. However, expression of NKA α1 was significant decreased ($n=4/4$; 0.64 ± 0.02; $p=0.01$).

Conclusion: Subtotal-nephrectomy after 8 weeks led to increased expression and phosphorylation of PLB suggesting deinhibition of SERCA activity. SERCA deinhibition at the level of the cardiomyocytes may be a compensatory mechanism in the presence of diastolic dysfunction.

XIII-7

Introducing a geriatric mouse model of myocardial infarction

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Background: Aging is associated with a higher incidence and mortality of myocardial infarction (MI). The pathomechanisms of MI in elderly are not fully understood. Although the murine model of MI is well-established for analysis in post-MI remodeling, there are only few studies using geriatric mice.

Methods: In male geriatric (age: 18 months; MI: $n=5$; SHAM: $n=6$) and young mice (age: 11 weeks; MI: $n=4$; SHAM $n=9$) MI was induced by permanent LAD ligation. In the SHAM groups the procedure was performed respectively without LAD occlusion. After 4.5 weeks, cardiac magnetic resonance imaging (MRI) was used for hemodynamic evaluation.

Results: MRI examination 4.5 weeks after surgery showed in a 2-way ANOVA significant effects of age ($p<0.001$) and of MI vs. SHAM ($p<0.001$) but no significant interaction between the two effects ($p=0.601$) on ejection fraction (EF). Additionally, similar effects (age: $p=0.003$; MI vs. SHAM: $p=0.006$; interaction: $p=0.438$) were found on stroke volume heart weight ratio (SV/HW). MI had a significant effect on stroke volume (SV; age: $p=0.191$; MI vs. SHAM: $p=0.019$; interaction: $p=0.797$). Moreover, age and MI affected end-systolic (ESV; age: $p=0.012$; MI vs. SHAM: $p<0.001$, interaction: $p=0.460$) and end-diastolic volumes (EDV; age: $p=0.038$; MI vs. SHAM: $p=0.002$, interaction: $p=0.460$) significantly. Nevertheless, heart weight (HW; age: $p=0.032$; MI vs. SHAM: $p=0.729$; interaction: $p=0.879$) was only influenced by age. No significant effects of age and MI vs. SHAM were found on heart rate, cardiac output and cardiac output heart weight ratio.

Conclusion: We have successfully implemented a geriatric mouse model of MI. Confirmed by MRI, we found both between MI and SHAM, and also between geriatric and young mice significant hemodynamic differences in EF and SV/HW. In addition, data showed higher ESV, EDV and HW in geriatric mice. MI-operated mice had increased ESV and EDV and impaired SV. No significant interactions between the effects of age and MI vs. SHAM were found in any parameters. We are currently evaluating post-MI remodeling in geriatric mice histologically.

XIII-8

Isoflurane and ketamine anaesthesia reduce cardiac injury after myocardial infarction in the rat

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Introduction: Heart failure following acute myocardial infarction (AMI) is major cause of morbidity and mortality. Since the 1970s revascularisation therapy is the standard therapy in order to restore coronary blood flow. However, restoration of normal blood flow can led to an "ischemia -reperfusion" injury which augments cell damage. The application of volatile anaesthetics has been shown to protect infracted hearts against ischemia-reperfusion injury.

However, no data exist weather an isoflurane or ketamine anaesthesia in a model of sustained LAD ligation has an effect in myocardial damage. Therefore, we investigated whether isoflurane or ketamine application post infarct protect rat hearts against ischemic injury.

Methods: Myocardial infarction was induced in adult male Sprague-Dawley rats by ligating the LAD artery. 2 h after LAD occlusion rats were assigned randomly to either control group or isoflurane group receiving 10 min 2 % isoflurane in an airtight cage or a ketamine (10 mg 100 g bodyweight) injection. Cardiac function was conducted by echocardiography 6 weeks after myocardial infarction. Animals were killed 6 weeks after experimental infarction. Infarct size was quantified by echocardiography and Elastica von Gieson staining.

Results: Isoflurane and ketamine treated rats showed a significantly reduced infarct size at 6 weeks after intervention: control 17.15 % (±1.49 SEM), ketamine 11.06 % (±2.0 SEM, $p=0.0126$), isoflurane 9.14 % (±1.62 SEM, $p=0.003$) respectively.

Cardiac function measured in echocardiography was significantly better in animal treated with isoflurane in comparison with control animals and ketamine receiving animals. 6 weeks after LAD occlusion the ejection fraction (EF) were determined to be 60.47 % (±3.70 SEM) in sham operated animals, 44.39 % (±3.18 SEM) in control animals, EF 47.09 % (±2.99 SEM) in ketamine group and 55.89 % (±1.44 SEM) in isoflurane group. Ketamine group animals did not show any improvements in echocardiography.

Conclusion: These data indicate that isoflurane as well as ketamine effects infarct size in a rat AMI model even when administrated 2 h after LAD artery occlusion. In studies examining ischemic injury and tissue remodelling the application of post-intervention anaesthesia may introduce uninvited variability in study endpoints and has to be evaluated critically.

Postersitzung XIV: Basic Science 4

XIV-1

Static but not cyclic tensional forces on the heart increase anti-angiogenic sFlt-1 expression in cardiac endothelial cells and inhibit VEGFR-2 activation

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Purpose: The left ventricle (LV) is subject to increased mechanical forces in a variety of diseases that cause chronic increased systolic or diastolic pressures. These are often associated with endothelial dysfunction and/or reduced numbers of capillaries. Further mechanical forces are known to modulate endothelial gene expression. Therefore, we hypothesized, that increase in static tensional forces on capillary endothelial cells of the LV result in up-regulation of soluble VEGF receptor 1 (sFlt-1) and thus leading to an imbalance of pro- and anti-angiogenic stimuli in the heart.

Methods: A rabbit Langendorff heart with retrograde constant pressure perfusion was used as model. As perfusate oxygenated Dulbecco's modified Eagle's medium was used to keep the heart viable as long as possible without deterioration of its function or sings of ischemia. For the tensional force 5 g per g of heart weight was applied to the apex of the beating LV either as static load or every 30 s (cyclic). For a set of experiments cardiac contractions were completely arrested using butanedione monoxime (BDM). Quantitative RT-PCR, immunoblots and co-immunoprecipitation was used to quantify mRNA and proteins of sFlt-1, vascular endothelial growth factor (VEGF) and VEGF receptor-2 (VEGFR-2). Immunohistochemistry was performed for colocalized of proteins.

Results: Increased static tensional force on the LV leads to significant increase in mRNA (3.8 fold, $p<0.05$) and protein expression of sFlt-1 (1.4 fold, $p<0.05$), which can be detected as early as after 30 min and remains increased for the duration of the experiments (up to 6 h). Cyclic tensional forces, however, do not affect sFlt-1 mRNA or protein levels. VEGF levels are unaffected by both static and cycle forces on the beating heart. Complete cardiac arrest without affecting the endothelium by BDM, an ATPase inhibitor of skeletal myosin 2, does not affect sFlt-1 or VEGF expression. Increased sFlt-1 due to increased static force on the LV binds more VEGF, shown by co-immunoprecipitation of sFlt-1 and VEGF, and reduced VEGFR-2 phosphorylation. Endothelial cells of the heart were colocalized by immunohistochemistry as source of sFlt-1 release.

Conclusions: Static, but not cyclic tensional forces on the LV result in increased release of anti-angiogenic sFlt-1 from capillary endothelial cells. While expression levels of VEGF remain unchanged, sFlt-1 binds VEGF and reduces activation of the signalling Receptor VEGFR-2. Thus, chronic increased forces in the LV contribute to the anti-angiogenic setting and reduced capillary density as seen in many heart diseases.

XIV-2

Slower removal of cytosolic Ca^{2+} during relaxation in cardiomyocytes from rats with compensated renal failure and heart failure with preserved ejection fraction

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Background: Heart failure with preserved ejection fraction and renal failure often coincide, especially in elderly people with comorbidities. The underlying cellular pathways of myocardial dysfunction are poorly understood. We investigated whether cytosolic Ca^{2+} transients in isolated cardiomyocytes are altered in a rat model with compensated renal failure and diastolic heart failure.

Methods: Twenty-four young male Wistar rats (260–290 g) underwent subtotal nephrectomy (NXT) or sham operation (SOP). After 8 or 24 weeks the hearts were removed and left ventricular (LV) cardiomyocytes were enzymatically isolated with a Langendorff perfusion setup. Isolated single LV cardiomyocytes were loaded with calcium sensitive fluorescence dye (Fluo 4 AM) for confocal laser scanning microscopy and measurement of Ca^{2+} transients, diastolic sarcoplasmatic reticulum (SR) Ca^{2+} leak (Ca^{2+} sparks), SR Ca^{2+} content and Na^{+}/Ca^{2+} -exchanger activity (time constant of the caffeine-induced Ca^{2+} transient, TAU) at 1 Hz stimulation and 37 °C.

Results: Cytosolic Ca^{2+}transients from isolated single LV cardiomyocytes had similar amplitude at 8 and 24 weeks comparing NXT and SOP (F/FO 3.8±0.1 and 4.2±0.1 vs. 3.8±0.2 and 4.1±0.1, $n\geq20$, p= n.s.). Time to peak of the Ca^{2+} transients was unchanged (33±1 and 27±1 vs. 32±1 and 26±1 ms,$n\geq20$). However time for early (50 %) relaxation of the Ca^{2+} transients was significantly prolonged at 8 and 24 weeks (RT50 31±3 and 42±3 vs. 17±3 and 28±2, $n\geq20$, $p<0.01$). SR Ca^{2+} content was significantly reduced in NXT at 24 weeks (F/F0 5.3±0.2 vs. 6.0±0.2; $n\geq20$;$p<0.01$) while it was unchanged after 8 weeks (F/F0 4.7±0.2 vs. 4.8±0.3; $n\geq10$). Time constant of the caffeine-induced Ca^{2+} transient (TAU) was significantly prolonged in NXT after 8 weeks (1.67±0.08 vs. 1.41±0.06 s; $n\geq10$; $p<0.05$) with a further prolongation after 24 weeks (1.77±0.07 vs. 1.22±0.06 s; $n\geq20$; $p<0.01$). Furthermore diastolic SR Ca^{2+} leak, reflected by the frequency of the Ca^{2+} sparks was significantly increased after 24 weeks in NXT (Ca^{2+} sparks/s/µm^3: 11.5±1.8 vs. 4.3±0.7 in SOP,$n\geq20$; $p<0.01$).

Conclusion: Our results indicate that Ca^{2+} removal from the cytosol is slower in isolated cardiomyocytes from rats with compensated renal failure and heart failure with preserved ejection fraction. Additionally, NCX1 forward mode activity is reduced. Slower Ca^{2+} removal and increased SR Ca^{2+} leak may contribute to the phenotype of diastolic dysfunction in this model.

XIV-3

Reference values of the tricuspid annular peak systolic velocity (TAPSV) in 860 healthy pediatric patients, calculation of z-score values, and comparison to the tricuspid annular plane systolic excursion (TAPSE)

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Objective: The tricuspid annular peak systolic velocity (TAPSV) is an echocardiographic measurement to assess right ventricular (RV) systolic function in children and adults. We determined growth related changes of TAPSV to establish references values for the entire pediatric age group.

Study design: A prospective study was conducted in a group of 860 healthy pediatric patients (age: day 1–18 years), (BSA: 0.14.–2.30 m^2). We determined the effects of age, sex and body surface area (BSA) on the TAPSV values. A stepwise linear multiple regres-

sion was used to estimate TAPSV from age, BSA, and sex. A correlation of normal TAPSV with normal tricuspid annular plane systolic excursion (TAPSE) values was performed.

Results: The TAPSV ranged from a mean of 7.2 cm/s (Z-score±2: 4.8–9.5 cm/s) in the newborn to 14.3 cm/s (Z-score±2: 10.6–18.6 cm/s) in the 18 year old adolescent. The TAPSV values showed a positive correlation with age and BSA with a non-linear course. There was no significant difference in TAPSV values between females or males. A significant correlation was found between TAPSV and TAPSE values ($r=0.260$; $p<0.001$, controlled for age).

Conclusion: Z-scores of TAPSV values were calculated and percentile charts were established to serve as reference data in patients with congenital heart diseases in the future.

XIV-4

Na^+/K^+ ATPase function is enhanced during early stages of heart failure in beta1-adrenergic receptor transgenic mice

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Chronic stimulation of the β1-adrenergic pathway leads to cardiac hypertrophy and heart failure. In mice overexpressing the β1-adrenergic receptor (β1), changes in Ca^{2+} handling precede the development of structural hypertrophy at an early stage of remodeling (8–12 weeks). The relaxation of cardiomyocytes is impaired due to slower Ca^{2+} removal via the Na^+/Ca^{2+} exchanger (NCX) and higher cytosolic Na^+ levels. In this study we investigate whether alterations in Na^+/K^+ ATPase (NKA) expression and/or activity contribute to disturbed Na^+ handling as an early sign of heart failure in β1 mice.

Methods: Single ventricular myocytes were isolated from 8 to 12 weeks old male β1 mice ($N=4$) and wild-type littermates (WT, $N=6$) for whole-cell patch-clamp recordings. Pipette solution for NKA pump current measurements (Ip) contained, in milliMolar: 130 Cs-Asp, 10 Na-Asp, 5 MgATP, 0.5 $MgCl_2$,10 HEPES, 5 EGTA, 20 TEA-Cl (pH = 7.12 with CsOH). To measure maximal Ip, Cs-Asp was replaced with Na-Asp to a final concentration of 100 mM $[Na^+]$pip. Cells were superfused with normal Tyrode solution containing, in mM: 136 NaCl, 5.4 KCl, 1 $CaCl_2$, 1 $MgCl_2$, 10 Hepes, 10 Glucose, 2 $BaCl_2$, 2 $NiCl_2$ (pH = 7.4 with NaOH), at 37 °C. Ip was measured as the difference in outward current, at 0 mV, after rapid solution switch to K^+ -free solution to inhibit Ip, Currents were normalized to cell capacitance. Protein expression levels were determined using Western blotting in whole ventricle homogenates. Protein densities were normalized against GAPDH.

Results: Protein levels of the NKA α1 subunit were unchanged (1.04±0.14 in β1, $n=6$ vs.1.04±0.1 in WT, $n=6$, NS), whereas the α2 subunit was reduced (0.87±0.09 in β1, $n=5$ vs. 1.24±0.08 in WT, $n=4$; $p<0.05$). Phospholemman, an inhibitory subunit of NKA, showed increased phosphorylation (1.3±0.05 in β1, $n=5$ vs. 0.748±0.06 in WT, $n=4$;$p<0.001$), and total amount was reduced in β1 mice (0.71±0.08 in β1, $n=5$ vs. 1.23±0.18 in WT, $n=4$; $p<0.05$). With $[Na^+]$pip = 10 mM, Ip density was significantly increased in β1 myocytes (0.59±0.08 pA/pF in β1, $n=9$ vs. 0.39±0.03 pA/pF in WT, $n=21$, $p<0.05$). Maximal Ip density was unchanged (2.50±0.18 pA/pF in β1, $n=13$ vs. 2.42±0.10 pA/pF in WT, $n=11$; NS).

Conclusion: In β1 mice, reduced expression of NKA α2 subunit had no functional impact on maximal pump activity. The increased NKA current reflects a higher Na affinity of the pump, consistent with less inhibitory PLM. At physiological Na^+ concentrations, this may result in enhanced Na^+ efflux, providing a compensatory mechanism in response to increased Na^+ concentrations during early remodeling in heart failure.

XIV-5

Funktionelle Effekte der Multikinase-Inhibitoren Sorafenib und Sunitinib

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Grundlage: Der Multikinase Inhibitor Sorafenib wird sowohl beim fortgeschrittenen primären Nierenzellkarzinom als auch beim fortgeschrittenen primären Hepatozellulärenkarzinom eingesetzt. Multikinase Inhibitoren hemmen Tumorzell-proliferation und -angiogenese und erhöhen die Apoptoserate. Sorafenib inhibiert die Serin-Threonin-Kinase Raf-1 und B-Raf und die Rezeptor Tyrosin Kinase-Aktivität von VEGFR1, 2, 3 und PDGFR-ß. Wir konnten bei dem ähnlich wirkenden Sunitinib einen neg. inotropen und Kalzium-abhängigen Effekt bei signifikant ansteigenden ROS (reactive oxygen species) nachweisen. Ziel des Projektes war, die kardiotoxischen Effekte von Sorafenib in einem humanen multizellulären Modell, zu untersuchen.

Methoden: Aus 11 humanen Herzohren, von Patienten die sich einer herzchirurgischen Operation unterzogen, wurden atriale Muskelstreifen ($n=36$) isoliert, optimal vorgedehnt, mit einer modifizeriten Tyrodelösung (2,5 mmol Ca^{2+}) bei 37 °C umspült und mit 1 Hz stimuliert. Die Muskelstreifen wurden steigenden Konzentrationen von Sorafenib(1, 3, 10, 30 µM) und Sunitinib (0,1, 1, 10 µg/mL) ausgesetzt. Am Ende des Protokolls wurde ein wash-out mit Tyrode durchgeführt.

Resultate: Die funktionellen Messungen zeigten einen signifikanten dosisabhängigen Abfall der entwickelten Kraft bei 3 µM (74,96±3,99 % vom Ausgangswert), 10 µM (71,35±6,59 % vom Ausgangswert) und 30 µM (57,08±11,94 % vom Ausgangswert) Sorafenib. Die entwickelte Kraft kehrte nach einem 5 min wash-out auf das Ausgangsniveau (96,03±9,31 %) zurück. Sorafenib hatte keinen Einfluss auf Kinetische Parameter wie die RT50 % und die diastolische Spannung. Rhythmusstörungen wurden keine beobachtet. Untersuchungen mit Sunitinib zeigten erhöhte Ca^{2+} Transienten in Einzelzellen und eine unveränderte myofilamentären Ca^{2+} Sensitivität in skinned-fiber Präparationen.

Konklusion: In multizellulären atrialen Muskelstreifen zeigte Sorafenib eine reversible, dosisabhängige negativ inotrope Wirkung, die den Effekten von Sunitinib ähnelt. Somit erscheint für beide Substanzen in der klinischen Anwendung ein Monitoring hinsichtlich der linksventrikulären Funktion indiziert.

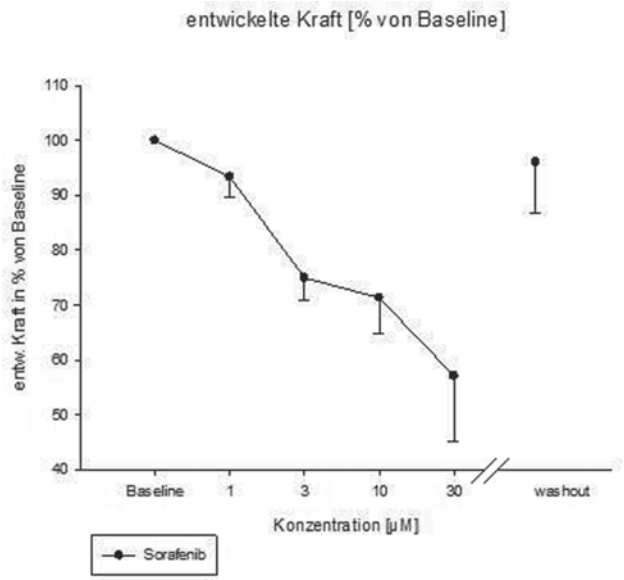

Abb. 1 Entwickelte Kraft [% von Baseline]

XIV-6

Loss of migfilin affects cardiac signaling after myocardial ischemia-reperfusion injury

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Introduction: Myocardial ischemia/reperfusion (m I/R) results in infarction due to intrinsic cardiomyocyte death and damage via excessive immune activation. Migfilin is a recently identified cytoskeleton associated protein interacting with integrins. Moreover, it can translocate into the nucleus in a Ca^{2+}-dependent manner and interacts with the cardiac transcription factor Csx/Nkx2–5. However, the in vivo role of migfilin in cardiac function and signal transduction remains elusive. Ischemia-reperfusion has been shown to activate pro-survival kinase signaling cascades to attenuate reperfusion-induced cell death via various anti-apoptotic mechanisms. Thus, we investigated if loss of migfilin has an effect on the myocardial response following ischemia-reperfusion injury in vivo by modulating the activation of critical signaling pathways.

Material and methods: Migfilin knock-out (KO) and wildtype (WT) mice were subjected to experimental myocardial ischemia (30 min) and reperfusion (1 week). After 1 week, hearts were harvested and the left ventricle was immediately snap-frozen in liquid nitrogen. Proteins were extracted and separated by SDS-PAGE. Immunoblotting was performed with antibodies against: AKT/phospho-AKT (Ser473, Thr308), p44/42 MAPK (ERK1/2)/phospho-p44/42 MAPK (ERK1/2), GSK3ß/phospho-GSK3ß (Ser9), mTOR/phospho-mTOR (Ser2448), p70S6K/phospho-p70S6K (Ser371, Thr389), and S6 Ribosomal Protein (SG10)/phospho-S6 Ribosomal Protein (Ser240/244). An anti-GAPDH antibody was used as a loading control.

Results: Western blot analysis showed reduced phosphorylation of ERK 1/2 and its downstream target p70S6K in hearts of migfilin-deficient mice after 30 min ischemia and 1 week reperfusion. Additionally, we found decreased levels of mTOR and S6 ribosomal protein in migfilin KO hearts. Phosphorylation of AKT was slightly reduced in migfilin-deficient hearts, whereas GSK3ß signaling demonstrated no differences between migfilin KO and control hearts.

Conclusion: So far, our preliminary data indicate that loss of migfilin modulates cardiac signaling and suggest a contribution of migfilin in the myocardial response after ischemia-reperfusion injury.

XIV-7

Limited prediction of incomplete left ventricular relaxation from diastolic time intervals and the isovolumic relaxation constant tau

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Background: Incomplete left ventricular (LV) relaxation can lead to increased LV end-diastolic pressure and contribute to exertional dyspnoe. Mathematical calculations predict that LV relaxation is incomplete when the diastolic duration (tdia) is less than 3.5× the LV isovolumic relaxation constant tau (τ). We tested this widely used assumption in normal pigs in vivo. As the rate of active relaxation depends on temperature, measurements were performed during normothermia and mild hypothermia.

Methods: Seventeen anaesthetized pigs were acutely instrumented with a LV pressure-volume catheter, a Swan-Ganz catheter and a right atrial pacing probe. After baseline measurements, heart rate (HR) was increased to 100, 120, 140, 160 and 180 bpm, if possible. At each HR, steady state haemodynamics and the end-diastolic pressure-volume relationship (EDPVR, aortic occlusion) were assessed. A subgroup of six animals was subsequently cooled to 33 °C and measurements were repeated.

Results: Before cooling, the ratio tdia/τ decreased from 9.1±0.6 at baseline HR (90±2 bpm) to 3.1±0.1 ($p<0.05$) at maximum HR (172±2 bpm). LV end-diastolic volume (LVedV) fell progressively, while LV end-diastolic pressure (LVedP) started to increase at 160 bpm, when tdia/τ was 3.5±0.1. However, a significant leftward shift of the EDPVR occurred already at 140 bpm (see graph), when tdia/τ was 4.3±0.1. At 33 °C, HR was 66±2 bpm and τ was prolonged to 119±16 ms, resulting in a significant leftward shift of the EDPVR, i.e. incomplete relaxation, already at 120 bpm.

Conclusion: A fall of LVedV delays an increase of LVedP at increasing heart rates. Analysis of the EDPVR reveals that incomplete LV relaxation occurs at lower heart rates than predicted from diastolic time intervals and τ. Measurement of LV volumes next to LV pressures and time intervals is thus required to accurately assess incomplete LV relaxation.

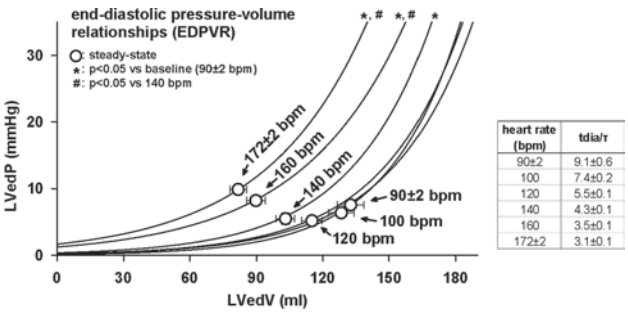

Fig. 1 A fall of LVedV delays an increase of LVedP at increasing heart rates

Postersitzung XV: Bildgebung 2

XV-1

Late gadolinium enhancement in carriers of duchenne muscular dystrophy

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Introduction: Duchenne Muscular Dystrophy (DMD) is an uncurable X-linked recessive disease that manifests in males leading to immobility and death in early adulthood. Female carriers of DMD are generally asymptomatic, but often have elevated CK blood levels and may develop heart failure. We hypothesize that cardiac magnetic resonance (CMR) may detect myocardial fibrosis as an early sign of heart involvement prior to deterioration of left ventricular function or clinical manifestation.

Material and methods: Carriers of DMD as proven by genetic or histological testing were included into our study. Clinical assessment including 6 min walk test (6 MWT), blood sampling, ECG, echocardiography, and CMR were performed. FLASH and PSIR sequences. were performed 10 min after intravenous bolus of 0.2 mmol/kg gadolinium based contrast in order to detect late gadolinium enhancement (LGE).

Results: Fifteen carriers (age 39.64+11.98 years, range 21–62 years) were assessed. Thirteen of the included carriers (86.7%) were clinically asymptomatic, one was in NYHA stage II and III, respectively; one woman had neurological symptoms (weakness of the thigh muscles). Mean walking distance in the 6 MWT was 470.79+103.35 m. Mean CK levels were 462.6+306.7 U/L, proBNP was 118.7+83.79. Mean left ventricular ejection fraction was 61+8%. Seven patients (46.7%) had evidence of a diffuse LGE, which was predominantely distributed in the posterolateral and inferior wall.

Discussion: Myocardial involvement shown as LGE in CMR may occur in a substantial part of DMD carriers in the absence of left ventricular function or clinical symptoms. Careful cardiologic examination and follow-up may be warranted in these cohort.

XV-2

Echocardiographic measurements of cardiac structures: comparison with pathoanatomy

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Background: Systematic comparative trials of echocardiography (Echo) and pathomorphology (Patho) with regard to wall thicknesses and the presence of left ventricular trabeculations have been rarely performed using modern echocardiographic machines.

Methods: Patients who had undergone echo within 2 years before death and were assigned to undergo routine autopsy were included in this trial. Morphologic parameters of the myocardium were measured and registered using a Vivid 7 echo machine with a 1.7/3.4 MHz transducer. The heart was formalin-fixed and primarily cut along the long axis to enable a four-chamber view. Then the heart was assembled again and cut into slices by using the bread-loafing technique. Photographies were taken of all specimens and measurements of the cardiac structures were then carried out using the computer software "ImageJ". Endocardial fibrosis (EF) was assessed by Echo and Patho and quantified as "absent", "moderate" and "extensive". Differences between Echo and Patho measurements were calculated using the mean value ± standard deviations, correlations between the measurements were calculated by the Pearson correlation coefficient (r) considering a tolerance of ±20%.

Results: Eighteen patients were included (seven females) with an age ranging from 61 to 90 years. The mean interval between Echo and autopsy was 22 days. The mean difference of measurements of the thickness of the left ventricular wall between Echo and Patho measurements was 11±8% (r=0.90). The mean difference of measurements of the thickness of the interventricular septum between Echo and measurements of the Patho photographies was 10±9% (r=0.94). Echo and Patho measurements of the thickness of the right ventricular wall showed a mean difference of 14±13% (r=0.85). The difference between Echo and Patho measurements of epicardial fat was 70±121% (r=0.10). Any kind of EF was diagnosed by Patho in 14/18 patients. Echo diagnosed an EF in 13 of those 14 patients, there were no cases of EF only diagnosed by Echo. In six cases the degree of EF was estimated higher by Patho than by Echo, in one case the degree of EF was estimated higher by Echo than by Patho.

At least one left ventricular trabeculation was found echocardiographically in 11/18 patients. At Patho all 18 patients had trabeculations in the left ventricle. A quantification of the trabeculations was not possible at Patho due to morphological heterogeneity. Measurements of the thickness of left ventricular trabeculations showed a difference between Echo and Patho of 34±29% (r=0.63). Nine of the 11 patients (82%) in whom Echo showed left ventricular trabeculations showed EF at Echo as well as at Patho.

Conclusion: There was a good correlation between Echo and Patho measurements of the thicknesses of myocardial walls whereas relevant differences were detected between Echo and Patho when measuring left ventricular trabeculations and epicardial fat. Echo tends to estimate the degree of EF less than Patho. Left ventricular trabeculations appear to be more easily detected by Echo in the presence of EF.

XV-3

Echocardiographic and pathoanatomic relation of left ventricular hypertrabeculation/noncompaction with/without neuromuscular disorders

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Objectives: Left ventricular hypertrabeculation/noncompaction (LVHT) is a cardiac abnormality, frequently associated with neuromuscular disorders (NMD). Aim of this pilot study was to assess pathomorphologic findings (PATHO) in patients with echocardiographically (ECHO) diagnosed LVHT and to compare the trabecular morphology between patients with and without NMD.

Methods: ECHO-criteria for LVHT were: At least four trabeculations, moving synchronously with the compacted myocardium, and forming the noncompacted part of a two-layered myocardium. At autopsy, the hearts were investigated according to the pathologists' preferences. ECHO and PATHO were compared and methodological problems were recorded.

Results: Twelve patients (two females, age 27–81 years, mean 61 years) were included. One patient suffered from Duchenne mus-

cular dystrophy, one patient from mitochondrial myopathy, five patients from NMD of unknown etiology and five patients were not investigated neurologically. The specimens were acquired after explantation during heart transplantation ($n=1$), death due to heart failure ($n=6$), sudden death ($n=2$), death from pneumonia ($n=2$) and death after stroke ($n=1$).

At autopsy, eight hearts were investigated without previous fixation and 4 after formaldehyde fixation. The hearts were opened along the long-axis by performing either the classical "inflow-outflow" method or cutting the heart longitudinally in an anterior and posterior half. In three hearts additional short-axis "breadloafing" cuts were carried out.

At PATHO the left ventricular cavity of all investigated hearts was covered by trabeculae sparing the left ventricular outflow tract. The trabecular meshwork was better visible in the formaldehyde-fixed hearts than in the fresh hearts due to the limp myocardium. The differentiation of trabeculations from papillary muscles and muscle bands was easier on the long-axis cuts, whereas the two-layered structure was better visible on short-axis cuts. Measurement of the layer thickness could be performed better from the short-axis than long-axis cuts. The trabecular pattern was similar in the five patients with NMD and the five patients who did not undergo neurologic investigation. The patient with Duchenne dystrophy had extremely fine trabeculations and the compacted layer was extremely thin. The patient with mitochondrial myopathy had an extremely thickened myocardium where the intertrabecular recesses were only visible as tiny grooves.

Conclusion: Morphology of LVHT at autopsy is not different between patients with and without NMD. Formaldehyde-fixation should be performed when comparing ECHO with PATHO findings in LVHT. Long-axis as well as short-axis cuts should be carried out in order to assess the number of trabeculations and the extent of the two-layered structure.

XV-4

Imaging myocarditis: is it really true?

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Introduction: Myocarditis is one of the most common indications for cardiac magnetic resonance tomography (CMR). However, the findings are not specific and may occur in other cardiac pathologies as well.

Case report: A 42 year old woman presented with fatigue and diminished physical capacity in July 2011. She had been considered to suffer from Burn-Out Syndrome by her family and saw a physician only after 6 months. She reported a respiratory infection five months earlier and a tick bite 3 weeks ago. Cardiac enzymes and inflammatory blood markers including Borrelia serology were normal, but pro-BNP was 827 pg/mL and the echocardiogram showed a moderately decreased left ventricular function (LVF) with a moderate mitral regurgitation due to a prolapse of the anterior cusp in combination with dilatation of the mitral annulus. A 24 h ECG detected paroxysmal atrial fibrillation as well as supraventricular tachycardia and intermittent atrioventricular conduction block Mobitz I. Multislice-computertomography coronary angiography showed regular coronary arteries without any calcification (Agatston Score 0). CMR revealed mild myocardial edema (T2-ratio 2.2) with extensive subepicardial late gadolinium enhancement (LGE) of all apical segments, basal anterior and predominantly midventricular lateral. Thus chronic myocarditis was suspected and neurohumoral medication was established (ACE-Inhibitors, beta-blockers, spironolactone). However, adequate doses could not been achieved due to hypotension and neither myocardial edema nor LGE resolved on CMR. Because of these findings, persisting dyspnea and the further mild decrease of LVF a myocardial biopsy was performed. It showed unspecific inflammatory processes without any virus persistence. For the next twelve months she remained clinically stable at low dose neurohumoral therapy. Then she was admitted to another hospital with a ventricular tachycardia (170 beats/min) which was terminated by intravenous ajmalin. In consequence an AICD was implanted. Since dyspnea persisted a surgical reconstruction of the mitral valve was recommended in early 2013. A CT Scan prior to surgery showed minimal enlargement of the mediastinal lymphatic nodes, and the suspicion of sarcoidosis was reported. The ACE-level was in the high normal range. At mitral annuloplasty one suspicious lymph node was excised and histology revealed granulomatous lymphadenitis with Langhans cells which was negative in Ziehl–Neelsen and real-time PCR for Mucobacterium tuberculosis, so the suspected diagnosis of sarcoidosis was confirmed. Even a revision of the myocardial specimen showed no granulomata, and in retrospective screening of all imaging series from 2011 till today there were no further specific pathologies in the mediastinum or lungs. Treatment with corticosteroids was initiated.

Conclusion: The presented case is peculiar in the fact that no organ manifestation of sarcoidosis was present at the beginning. According to the guidelines, cardiac involvement has to be considered in case of extracardial sarcoidosis in the presence of AV-conduction disturbancies, reduced LVF and/or myocardial fibrosis. Considering the patient's history an inflammatory cause of cardiomyopathy was very likely and matched well with CMR criteria of myocarditis, but the typical feature of subepicardial myocardial fibrosis is also compatible with sarcoidosis as a differential diagnosis.

XV-5

Effektivität der Thrombininjektion bei Aneurysma spurium nach Koronarangiographie über femoralen Zugang

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Kardiologie, KH der Elisabethinen Linz

Einleitung: Nach Koronarangiographie über einen femoralen Punktionszugang stellt die Entwicklung eines Aneurysma spuriums eine relevante Gefäßkomplikation dar, die oft prolongierter neuerlicher Kompressionen oder sogar einer chirurgischen Sanierung bedürfen. Die Verwendung semiautomatischer Gefäßverschlusssysteme bietet hier eine größere Sicherheit als die manuelle Kompression. Sollte trotzdem ein Aneurysma spurium entstehen, stellt die perkutane Injektion von Thrombin in das Aneurysma spurium eine adäquate Möglichkeit zur Sanierung dar.

Methodik: Seit 2008 wurden an unserer Abteilung nach Koronarangiographien ein spezielles Schema zur Vermeidung unerwünschter Leistenprobleme verfolgt (siehe Flow Chart). Nach diagnostischer (Cordis 5F Schleuse) sowie interventioneller (Cordis 6F+7F Schleuse) Koronarangiographie via A.femoralis wurde routinemäßig ein Verschluss mit einem semiautomatischen Device (StarClose Vascular Closure oder Femoseal, St. Jude Medical), sofern technisch möglich, angestrebt. Zusätzlich erfolgte eine milde Leistenkompression mit einem Druckverband für ~3,5 h. Nach Abnahme des Druckverbands erfolgte zwingend eine klinische Kontrolle der Punktionsstelle. Bei auffälligem Strömungsgeräusch, palpablem Tumor oder ausgedehntem Hämatom erfolgte

eine umgehende sonographische Evaluierung (linearer Schallkopf L12–4, Philips IU 33). Bei banalem Hämatom erfolgte ein konservatives Procedere mit klinischem Follow up (FU). Bei Nachweis eines Aneurysma spuriums erfolgte nach lokaler Desinfektion die ultraschallgezielte Thrombininjektion (500 I.E. humanes Thrombin/1 mL aus Tissel oder Tissucol Duo S, Fa. Baxter). 4–12 h nach primärerfolgreicher Sanierung erfolgte eine abschließende Ultraschall Kontrolle. Bei erfolgreicher Prozedur und Nachweis einer Thrombosierung der Aneurysmahöhle wurde der Patient wieder mobilisiert und die Entlassung war möglich. Bei Persistenz des Aneurysma spuriums wurde ein 2ter Versuch mit Thrombininjektion unternommen und falls frustran eine gefäßchirurgische Sanierung durchgeführt.

Resultate: Wir haben von Jänner 2008 bis inkl. Dezember 2012 insgesamt 10.069 diagnostische und 3209 interventionelle Koronarangiographien (davon 631 Akutintervention) über einen femoralen Punktionszugang durchgeführt. Insgesamt wurden dabei mittels Sonographie bei 122 Patienten ein Aneurysma spurium (0,92 %) identifiziert und 121/122 konnten mittels Thrombininjektion erfolgreich behandelt werden. Im Mittel wurden dabei 622,95 ± 335,9 I.E. humanes Thrombin zur Aneurysmathrombosierung verabreicht. Die Thrombininjektion ins Aneurysma spurium führte zu keinen vaskulären Komplikationen. Bei einem Patienten (0,8 %) konnte keine erfolgreiche Sanierung mit Thrombininjektion erzielt werden, sodass eine Operation angeschlossen wurde.

Zusammenfassung: Die Anwendung einer sonographisch gezielten Thrombininjektion zur Behandlung eines Aneurysma spuriums nach Koronarangiographie mit femoralem Zugang ist sicher und zuverlässig und kann in nahezu allen Fällen die chirurgische Sanierung verhindern.

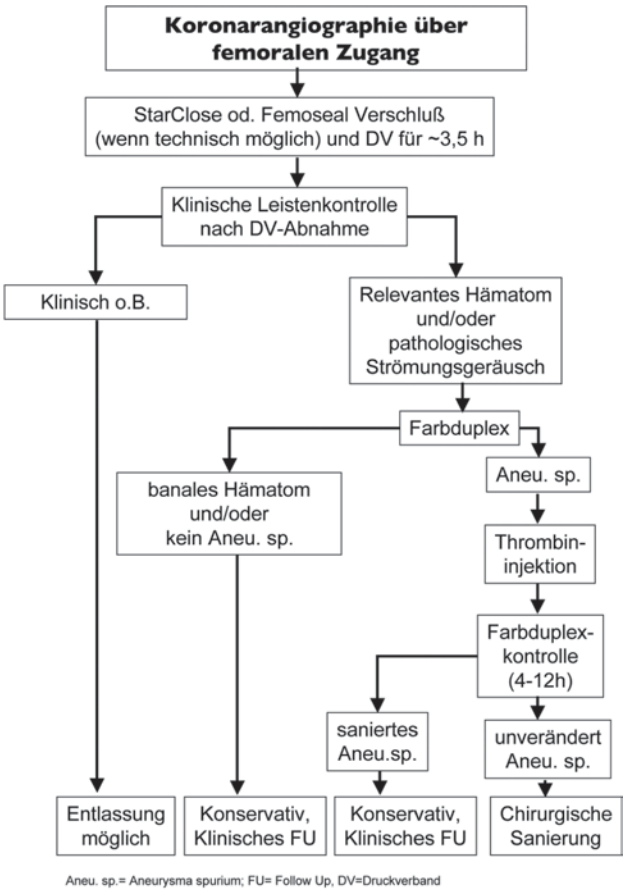

Abb. 1 Schema zur Vermeidung unerwünschter Leistenprobleme

XV-6

Erfahrungsbericht über die Detektion „maligner" Varianten von Koronaranomalien mittels Coronar-CT-Angiographie (64-Zeiler) anhand dreier Fälle

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Einleitung: Die Prävalenz von Koronaranomalien beim Menschen beträgt etwa 1,2 %. Die meisten davon sind asymptomatisch und stellen Zufallsbefunde dar. Einige Koronaranomalien können jedoch eine myokardiale Ischämie oder den plötzlichen Herztod bei jungen Menschen verursachen, hauptsächlich beim Sport. Diese Anomalien werden als „maligne" Koronaranomalien bezeichnet, um sie von den asymptomatischen Varianten abzugrenzen.

Material und methoden: 398 konsekutive Patienten wurden mittels Coronar-CT-Angiographie (CCTA) untersucht (Einschlusskriterien: Thoraxschmerz möglicher koronarer Ursache; Ausschlusskriterien: Akutes Konarsyndrom, eindeutig positiver Stresstest). In einem Zeitraum von 2 Jahren (Jänner 2011–Dezember 2012) wurden drei potentiell maligne Koronaranomalien detektiert, ergänzend wurde jeweils eine selektive Coronarangiographie (CAG) durchgeführt.

Gerät: Philips Brilliance 64-Schicht CT-Scanner; gemeinsame Befundung durch erfahrenen Radiologen und interventionellen Kardiologen.

Ergebnisse: Fall 1: 26-jähriger Mann mit De novo AP – Atypischer Abgang der RCA aus dem linken Sinus Valsalvae mit interarteriellem Verlauf zw. Aorta und Truncus pulmonalis – > maligne Variante: OP-Indikation: „Koronartransfer nach vorne"; [Prävalenz 0,03–0,17 %, SCD bis 30 %]

Fall 2: 72-jährige Frau mit akutem Lungenödem – Koronare Fistel aus der LAD mit Drainage in den Truncus pulmonalis – > CAG, nach Blutgasanalyse kein relevanter Shunt! [Prävalenz 0,1–0,2 %]

Fall 3: 51-jähriger Mann mit rezidivierender Angina pectoris – Aberrant aus der RCA abgehende LAD mit interarteriellem Verlauf zw. Aorta und Truncus pulmonalis – > benigne Variante [Prävalenz 0,13–1,0 %]

52 Patienten mussten wegen hohem Calzium-Score ausgeschlossen werden, in der weiteren Abklärung mittels CAG fanden sich bei diesen Patienten keine Koronaranomalien. In obigen drei Fällen wurden die Ergebnisse der CCTA durch den „Goldstandard" CAG bestätigt. Von den drei potentiell malignen Koronaranomalien war bei Fall 1 eine operative Korrektur indiziert.

Diskussion: Die vorliegende Arbeit zeigt, dass die CCTA als nicht invasive bildgebende Methode, welche die komplexe Anatomie von Koronararterien samt ihren Varianten und angeborenen Anomalien darstellt, sehr gut geeignet ist.

Eine zusätzlich durchgeführte CAG hat in Hinblick auf die Gefäßanatomie keinen weiteren Nutzen. Nur bei hohem Calzium-Score und speziellen hämodynamischen Fragestellungen ist die CAG die Methode der Wahl.

Aufgrund unserer Beobachtung über 2 Jahre, lässt sich eine Prävalenz von 0,25 % für das Vorliegen einer malignen Koronaranomalie ableiten.

Zukünftige Fortschritte bei der Entwicklung von CT-Geräten werden zu weiteren Verbesserungen bei der Qualität von CT-basierter kardialer Bildgebung führen.

XV-7

Regional wall motion score and speckle tracking in patients with NSTEMI

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Background: The European Society of Cardiology recommends immediate echocardiography in all patients with Non-ST-Elevation-Myocardial Infarction (NSTEMI). Nevertheless there is only a small amount of studies, which support this recommendation. Furthermore newer techniques for the evaluation of regional wall motion abnormalities (WMA) were not taken into account. The aim of this study is to outline the value of transthoracic echocardiography (TTE) including two-dimensional and speckle tracking techniques in patients with NSTEMI.

Methods: During a period of 28.5 months, with a gap of 3 month, we retrospectively investigated consecutive patients with NSTEMI, defined as acute chest pain with elevated Troponin level and without ST-elevation. After exclusion of all patients with prior history of coronary heart disease, coronary artery bypass or missing TTE reports and images, 236 remaining patients (74 women, 162 men, age 67 ± 12 a) were included for further analysis. TTE (GE Healthcare) was performed prior to coronary angiography (CA) in all cases and stored digitally. WMA and score index were assessed using the 16 segments model. Speckle tracking analysis was performed by an automatic function imaging software (AFI, EchoPac PC 10.0.), without knowledge of the coronary anatomy. WMA were compared to the regional blood supply of the coronary artery (culprit) lesion.

Results: Obstructive coronary artery disease was excluded in 10 patients. In the remaining 226 patients single vessel disease was found in 78 cases (37 LAD, 22 LCX, 18 RCA, 1 LM) and multivessel disease in 148 cases. Totally occluded coronary vessels were present in 34.5 %. Visual assessment of WMA and speckle tracking were possible in 90.3 and 36.4 % respectively. WMA were found in 148 patients (69.5 %) by visual assessment and in additional 22 patients by speckle tracking analysis. Using the combination of visual assessment and speckle tracking WMA were found in 79.8 %. Excluding the cases poor vision prevented the evaluation, 88.5 % of the NSTEMIs could be identified by WMA in the TTE. In patients with single vessel disease the distribution of detected WMA correlated with segments supplied by the culprit vessel in all cases. Distribution of WMA is shown in Fig. 1. WMA score indexes were 1.25, 1.35 and 1.41 in patients with single vessel disease (34.5 %), multivessel disease (65.5 %)and totally occluded vessels (34.5 %).

Conclusion: The evaluation of the patients' data showed that a large number of NSTEMIs can be detected by echocardiography. The additional use of Speckle Tracking could help to find hidden WMA. Our results confirm the recommendation of the ESC for the reason that the echocardiography appears to be an accurate and sensitive tool for the early detection of NSTEMI.

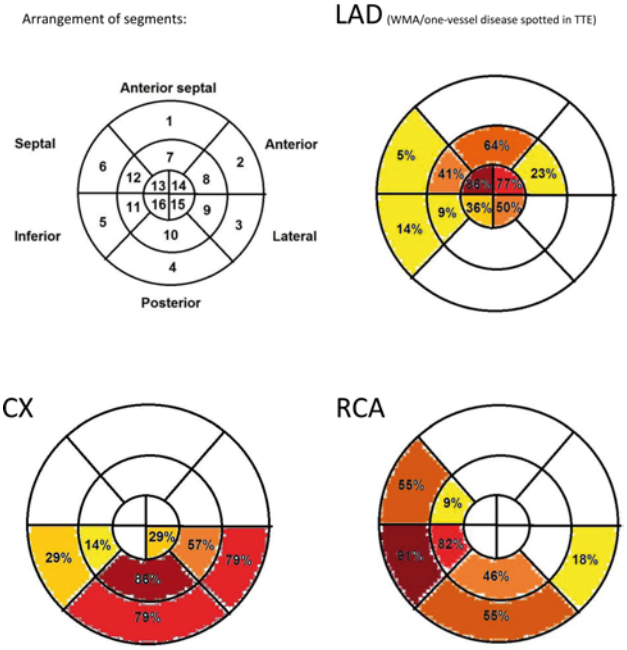

Fig. 1 Distribution of WMA in Bullseye View

Postersitzung XVI: Chirurgie 2 und Vitien

XVI-1

Trace To mild paravalvular regurgitation after transcatheter aortic valve implantation (TAVI): a multivariante analysis

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Objective: Paravalvular regurgitation (PVR) after TAVI appears as a common problem. The aim of this study was to examine the correlation between the symmetry of aortic valve calcification (AVC), the calcium distribution and the prosthesis/annulus-congruence, on the prevalence of PVL.

Methods: Thirty patients referred for TAVI routinely underwent DualScan-CT and TTE preoperatively. The calcium load was analyzed by using "Calcium Scoring" Software. Haemodynamic performance after implantation and the presents and location of PVL was evaluated by echocardiography. The cover index was calculated as a ratio of prosthesis diameter-annulus-size by prosthesis diameter.

Results: Forty-four percent of the selected patients showed asymmetric, 56 % symmetric AVC. Trace to mild PVR was detected in 63 % of patients. Neither symmetry nor the cover index was reliable to predict the prevalence or location of PVL. All patients with a general calcium load higher than 3,000 mm^3 or a calcium load of one cusp above 1,500 mm^3 exhibited PVR. PVLs persisting until 30 day follow up did not seal.

Conclusion: The aortic valve calcium load in general (> 3,000 mm^3) or alternatively of one cusp (> 1,500 mm^3) seems to play a significant role in development of PVLs, independent from

the symmetry of AVC. The detailed genesis of trace or mild PVR remains unknown substantiating the need of further investigations.

XVI-2

Hybrid revascularization with robot and stents: too much of technology or true close chest surgery for multivessel disease?

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Background: Hybrid coronary revascularization combines minimally invasive coronary artery bypass grafting and catheter based intervention. This treatment option represents a viable alternative to open multivessel coronary bypass surgery through sternotomy and to multivessel percutaneous coronary intervention (PCI).The surgical component of hybrid coronary intervention can be offered in a completely endoscopic fashion using robotic technology. We report on one of the largest series to date.

Patients and methods: From 2001 to 2011 Two hundred and twenty-six patients (age 61 (31–90) ,77.0 % male, EuroSCORE 2 (0–13)) underwent hybrid coronary interventions on an intention to treat basis. Robotically assisted procedures were performed using the daVinci TM, daVinci S TM, and daVinci Si TM surgical telemanipulation systems and included 147 single, 72 double, and 7 triple endoscopic coronary bypass grafting procedures. Surgery was carried out first in 160 cases (70.8 %), PCI was carried out first in 38 cases (16.8 %), and 28 patients underwent simultaneous operations in a hybrid OR (12.4 %). Drug eluting stents were used in 69.0 % of the patients.

Results: Hospital mortality was 3/226 (1.3 %), hospital stay was 6 (3–54) days. Patients walked outside 7 (3–97) days postoperatively and performed general household work 14 (7–180) days postoperatively. Full activity was resumed at 42 (7–720) days. Five year survival was 92.9 % and 5 year freedom from major adverse cardiac and cerebral events (MACCE) was 75.2 %. At 5 years 2.7 % of bypass grafts and 14.2 % of PCI targets needed reintervention.

Conclusion: Robotically assisted hybrid coronary intervention enables surgical treatment of multivessel coronary artery disease with minimal trauma. Perioperative results and intermediate term outcome seem to meet the standards of open CABG. Recovery time is short and reintervention rates are acceptable

XVI-3

A case series of Transcatheter Mitral Valve Implantation with the Edwards Sapien XT 29 mm in surgically inoperable patients: open and transapical approach

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Objectives: The number of redo-surgeries for degenerated bioprosthesis is expected to increase, related to the extended life expectancy. The transcatheter mitral valve implantation might offer a promising therapy option for conventional inoperable patients. This case series presents postoperative results of transcatheter mitral valve implantation (TMVI) in high risk patients.

Methods: From April 2011 to December 2012 five patients (73.6 ± 5.8 years), three female, with severe symptomatic mitral valve insufficiency underwent a transcatheter mitral valve implantation. All patients were rejected for conventional mitral valve surgery based on their surgically unmanageable mitral valve pathology as well as their multiple comorbidities, mean Euroscore II 21.3 % (5.5–45.5 %).

Two patients had a Re-Re-Operation after aortic- and mitral-valve-replacement and degenerated bioprosthesis, one mitral valve insufficiency and aortic stenosis, one after failed mitral- and tricuspid-valve-reconstruction, one had a massive calcified native mitral valve annulus, surgical decalcification was unfeasible.

Results: Extracorporeal circulation (123 ± 13 min) was used for three patients, because of concomitant procedures (left atrial thrombectomy, aortic valve replacement, tricuspid valve re-repair) via open approach. The remaining two patients, the TMVIs were performed transapically under rapid pacing. Valve implantation was successful in all patients. Minimal paravalvular insufficiency (PVI) was observed in two patients, mild in one. Two patients did not show any PVI. One patient died 8 days after operation because of multiple organ failure, one patient had a stroke.

Conclusion: Transcatheter heart valve implantation seems to be a promising option for inoperable patients. The transcatheter valve could be placed safely in the annuloplasty ring, as well as in the bioprosthesis or native annulus. Regarding the mitral valve pathology and concomitant procedures the open as well as the transapical approach are feasible.

XVI-4

Five years experience in transapical transcatheter aortic valve implantation with the Edwards Sapien in high risk patients

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Objective: Transcatheter aortic valve implantation (TAVI) is a promising treatment option for frail and very high-risk patients with severe symptomatic aortic stenosis. Many studies show satisfying perioperative and short term results. This study focused on patients mobility after operation, midtermoutcome, as well as durability of the prosthesis.

Methods: Between April 2007 and January 2013, ninety-four patients (81 ± 7 years, 52.1 % male) with severe, symptomatic aortic stenosis and rejected for open heart surgery underwent TAVI. The mean aortic valve area was 06 ± 0.2 cm^2 with a mean aortic gradient of 53 ± 12 mmHg. The estimated perioperative mortality was 35.5 ± 19.8 % by logistic EuroSCORE, EuroSCORE II 17.3 ± 15.1 and 8.7 ± 7 % by STS Score.

89.4 % of patients were classified NYHA III, 37.2 % had impaired left ventricular functions, severe pulmonary hypertension with a systolic PAP of 72 ± 14 mmHg was present in 20 % of the patients.

Results: Valve implantation was successful in 89 patients; the remaining five patients were converted to conventional valve replacement (anatomical reasons in 2 patients and one due to a technical error of the equipment during procedure). The 30 day mortality was 7.6 %; the estimated overall postoperative survival rate using Kaplan–Meier-Analysis was 77.8 % at 1 year, 70.8 % at 2 years, 67.5 % at 3 years, 59.9 % at 4 years and. Postoperatively, 5.3 % of patients required a pacemaker implantation, the stroke rate was 3.2 %. Sixty-two percent of the high risk patients were discharged to

home with a median postoperative hospital stay of 13 days. After 5 year, the majority of patients still live in their private home.

Conclusion: Even in case of frail and very high-risk patients with a high risk for postoperative mortality and morbidity, TAVI is a suitable therapy option with promising results. Further outcome improvement could be achieved by refining the patient evaluation and specific complication management. Further outcome improvement could be achieved by refining the patient evaluation and specific complication management. Major focus at screening process should be put on improvement of quality of life and avoidance of postoperative morbidity, not on surgical or interventional feasibility.

XVI-5

Relative amplitude index: a new tool for prediction of the impact of periprosthetic regurgitation on outcome after transcatheter aortic valve implantation

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Objective: The impact of paravalvular leaks (PL) on hemodynamic performance after transcatheter valve implantation (TAVI) remains disputable. Using common hemodynamic parameters such as the diastolic blood pressure or the blood pressure amplitude after the procedure has not provided reproducible results. The aim of our study was to systematically evaluate changes of hemodynamic parameters by using the relative amplitude index (RAI) and to assess its impact on outcome.

Methods: PL were prospectively evaluated by echocardiography during TAVI and before discharge in 77 patients after TAVI. The RAI was retrospectively calculated according to the formula:

RAI = ((Post TAVI blood pressure amplitude)/(Post TAVI systolic blood pressure) – (Pre TAVI blood pressure amplitude)/(Pre TAVI systolic blood pressure)) × 100 %. Univariate and multivariate analysis for risk factors for perioperative mortality was performed and an ROC analysis for RAI cut-off value was calculated.

Results: The incidence of no PL mild, moderate and severe PL after TAVI was 20, 62, 15 and 3 %, respectively. Evaluation by diastolic pressure or post TAVI amplitude did not correlate to perioperative outcome. RAI increased from 0.7 ± 7 % in the absence of PL to 5.1 ± 8 % in moderate to severe regurgitation ($p = 0.027$). A cutoff value of RAI= 13 % was associated with increased perioperative mortality. Patients with a RAI > 13 had increased perioperative mortality (27 vs 4 %, $p = 0.005$), cardiac (9 vs 0 %, $p < 0.001$), and lung complications (27 vs 4 %, $p < 0.001$) and acute renal injury (20 vs 8 %, $p = 0.002$). Increased periprocedural RAI was associated with higher cardiac (33 vs 15 %, $p = 0.011$), renal (50 vs 8 %, $p = 0.024$) and lung complications (7 vs 0 %, $p = 0.005$) at 1 year. RAI < 13 was an independent predictor of perioperative mortality (RR = 3.4, (CI= 1.8–5.0), $p = 0.017$).

Conclusions: The RAI is useful non-invasive, easy-to-measure tool to predict the effect of paravalvular regurgitation on perioperative and 1-year outcome in patients with PL after TAVI.

XVI-6

Immediate conversion to open heart surgery in case of complications during TAVI: an indispensable safety net

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Objective: The transcatheter aortic valve implantation (TAVI) represents a promising alternative therapy option for frail and high risk-patients with severe symptomatic aortic stenosis. However, if a technical error occurs a conversion to open heart surgery is required. This study presents the immediate and medium-term results of five patients converted to conventional aortic valve replacement after failed TAVI.

Methods: From April 2007 to January 2013 ninety-three patients underwent the TAVI procedure. Five patients with a mean age of 76 years, referred for TAVI were converted to open heart surgery due to procedural errors. TAVI was not suitable in 2 patients because of anatomical reasons, one because of a severe surgical bleeding after preparation of the pericardium and laceration of the right ventricle anterior wall. One patient required a conventional aortic valve replacement after valve malpositioning. The fifth case was related to a technical error of the power injector during procedure. The median predicted perioperative mortality was 19,5 % by EuroScore and the patients suffered from more than 4 additional non cardiac and non EuroScore effective comorbidities.

Results: Aortic valve replacement was successful in all five patients. The mean stay postoperative in hospital stay was 17 days, at ICU 5 days. The 30 day survival was 100 %; One patient died after 33 days, the remaining four patients all passed, 3 years follow-up. One patient developed a VAC requiring wound infection at the right groin (femoral puncture for TAVI), one had a sternal infection, developed a critical illness polyneuropathy and had an embolic event of the right A. retinae. The other patients had an uneventful postoperative stay. No strokes were observed, there was no demand for PM implantation.

Conclusion: TAVI represent a suitable therapy option with promising results for frail and high risk patients. However, we believe that the safety net is inevitable for TAVI procedures. The opportunity of immediate HLM support and conversion to open heart surgery saved the life of those patients, which would be impossible in a catheter lab. In spite of the fact, that all patients underwent an emergency surgery, the postoperative outcome of the converted patients is comparable to elective TAVI patients.

XVI-7

Early recognition and treatment of critical arrhythmias in adults after the atrial switch operation for transposition of the great arteries: remote monitoring vs standard follow-up

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Background: Adults with transposition of the great arteries (TGA) after atrial switch repair have an increased risk for arrhyth-

mias and sudden cardiac death. We analysed whether a remote monitoring (RM) system as part of an implantable cardiac device contributes to timely recognition and improved treatment of critical arrhythmias in this patient population.

Methods: All consecutive TGA patients requiring a pacemaker or cardiac resynchronization therapy with or without implantable cardioverter defibrillator at the Medical University Graz, Austria and the German Pediatric Heart Centre St. Augustin, Germany between 2008 and 2011 were included. RM-detected arrhythmias, abnormalities of the cardiac device integrity and reaction times from event transmission until acknowledgement via email and clinical decision making were analysed and compared to standard follow-up.

Results: In 11 adult patients 17 arrhythmias were detected in 10 (91 %) patients of whom 8 patients (80 %) indicated no symptoms. Mean time interval from transmission to acknowledgement was 2.4 (0–4.5) days. Clinical decision making was advanced by a mean of 77.5 (10–197) days compared with conventional follow up and implied adaption of antiarrhythmic medication in eight patients, electrical cardioversion in two, overdrive pacing in one and radiofrequency ablation in two patients. A coronary sinus lead fracture was identified in one patient followed by successful replacement.

Conclusions: RM enables early detection of tachyarrhythmias followed by optimization of medical treatment and potentially lifesaving antitachycardic interventions in adults after atrial repair of TGA.

XVI-8

Spätes Aortenaneurysma nach Stentfraktur bei postoperativer Aortenisthmusstenose und chronischer Niereninsuffizienz

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Hintergrund: Späte Aneurysmen durch Stentfrakturen im Bereich des Aortenisthmus sind selten. Die Bildgebung ist bei niereninsuffizienten Pat. durch den Verzicht auf Kontrastmittel erschwert.

Fall: Im Alter von 3 Wochen wurde bei einem heute 24 J. alten Pat. eine End-zu-End Anastomose bei Aortenisthmusstenose durchgeführt. Wegen Reststenose wurde 1 Tag später reoperiert, ein postop. Nierenversagen über 1 Woche hämodialysiert. In den folgenden Jahren bestand eine Normotonie mit Gradienten zwischen oberer und unterer Extremität von ca. 10 mmHg. Erstmals fand sich 2005 ein Hypertonus, der trotz 2-fach medikamentöser Therapie nicht gut einzustellen war, es bestand eine kompensierte Niereninsuffizienz (Kreatinin 2,1 mg/dl). Ein MR-Angio des Aortenbogens zeigte ein langstreckiges hypoplastisches Segment, weshalb 2006 eine Stent-Implantation erfolgte. Danach war der Hypertonus medikamentös gut einstellbar, es bestand echokardiographisch und in der RR-Messung kein Restgradient mehr. Wegen weiter ansteigenden Kreatinins wurde nach 2008 kein MR- oder CT-Angio durchgeführt. Zwischen 2009–2011 erschien der Pat. zu keinen weiteren Kontrollen. Anfang 2012 erfolgte von der Nephrologie die Zuweisung an unsere EMAH-Ambulanz zur Evaluation vor Nieren-TX (Kreatinin 6,2 mg/dl). Ein natives MR-Angio bestätigte ein 2 × 3 cm großes Aneurysma im Stentbereich, ein Rö-Thorax zeigte mehrere Stentfrakturen. Es erfolgte die operative Entfernung des Stents und die Implantation eines Interponates. Postop. musste über 8 Tage hämodialysiert werden, die Nieren-TX wurde postponiert.

Diskussion: Langfristige und regelmäßige Kontrollen nach Stent-Implantation mittels Thorax-Rö und MR/CT sind notwendig. Für niereninsuffiziente Pat. steht die native MR-Angio zur Verfügung.

Postersitzung XVII: Herzinsuffizienz 2

XVII-1

Elevated neopterin is associated with disease severity and prognosis in chronic heart failure

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Purpose: Accumulating evidence indicate an important role of inflammation for the progression of heart failure. Neopterin is an established marker of cellular immune activation. We aimed to investigate the relationship between serum levels of neopterin, disease severity and prognosis in patients with stable non-ischemic heart failure.

Method: Clinical and laboratory parameters of 141 patients (age 48 ± 14 years; 70 % male; NYHA class I 29 %, NYHA class II 41.3 %, NYHA class III/IV 29.7 %; LV-EF 30 [21–44]; NT-proBNP 1,044 [342–2,655]), who underwent elective invasive testing were evaluated. Central venous pressure (CVP), pulmonary capillary wedge pressure (PCWP), mean pulmonary artery pressure (PAPm) and cardiac output (CO) were measured via right heart catheterization. Long-Term follow-up (20.8 ± 12 months) was availible in 133 patients. The endpoints were defined as death of any cause or heart transplantation.

Results: Median neopterin level was 6.7 nmol/L (IQR 4.9–9.2). Prevalence of elevated serum neopterin (> 10 nmol/L) was 19 % in men and in women. A significant dose-response relationship was found between neopterin levels and increasing NYHA class (I: 5.9 [4.4–7.7], II: 6.7 [4.7–9.2], III/IV: 7.0 [5.8–10.4]; $p = 0.024$). Also, Neopterin was significantly correlated with NT-proBNP ($r = 0.31$, $p < 0.001$), CVP ($r = 0.26$; $p < 0.001$), PAPm ($r = 0.27$; $p < 0.001$), CO ($r = 0.16$; $p = 0.004$). Elevated neopterin levels were associated with a 6-fold increased risk of death or heart transplantation (95 %CI 1.4–25.3; $p = 0.014$). This association remained robust after adjustment for age and sex.

Conclusion: We found an independent relationship between neopterin levels, disease severity and prognosis in stable patients with non-ischemic heart failure. These findings further highlight the importance of immune mechanisms in chronic heart failure.

XVII-2

Parathyroid hormone is associated with markers of bone metabolism and disease severity in chronic heart failure

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Background: Increased parathyroid hormone (PTH) levels are known to be associated with incident heart failure, disease severity and poor outcome in patients with prevalent heart failure. Our

aim was to investigate the crosslink between PTH elevations, bone metabolism and severity of heart failure.

Methods: Clinical and laboratory parameters of 208 patients (age 41±15 years; 70 % male; NYHA class I 31 %, class II 43 %, class III/IV 26 %; LV-EF 34±15 %, NT-proBNP 1,071.0 [IQR 275.3–2,579.8]) were measured. Bone turnover was assessed by 25-hydroxyvitamin D [25(OH)D], osteoprotegerin (OPG), crosslaps (s-CTX), serum alkaline phosphatase (ALP), calcium (Ca^{++}) and inorganic phosphate (Pi).

Results: Median PTH levels were 33.19 ng/L (IQR 25.56–48.65). A significant dose-response relationship was found between PTH levels and increasing NYHA class (I: 27.92 [20.85–35.29], II: 34.40 [29.03–48.25], III/IV: 41.19 [26.20–66.15]; $p<0.001$). Also, PTH was correlated with NT-proBNP ($r=0.305$, $p<0.001$) and LV-EF ($r=-0.203$, $p<0.001$). In bivariate analysis, PTH was directly correlated with OPG ($r=0.103$, $p=0.029$), s-CTX ($r=0.147$, $p=0.002$) and ALP ($r=0.099$, $p=0.036$) and indirectly associated with 25(OH) D ($r=-0.263$, $p<0.001$) and Ca^{++} ($r=-0.19$, $p=0.012$). No correlation was found with Pi. Correlations with s-CTX and 25(OH)D were independent of age, sex and eGFR. By contrast, 25(OH)D was not associated with markers of bone metabolism.

Conclusion: PTH is independently associated with disease severity in chronic heart failure. Furthermore, we found a strong association of PTH with bone turnover in these patients. Our data highlight the importance of PTH for metabolic bone disorders in the heart failure syndrome.

XVII-3

Parathyroid hormone is associated with hemodynamics and disease severity in chronic heart failure

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Background: Increased parathyroid hormone (PTH) levels are known to be associated with incident heart failure and poor outcome in patients with prevalent heart failure. We investigated the association of PTH with hemodynamics and disease severity in chronic heart failure.

Methods: Clinical and laboratory parameters of 208 patients (age 41±15 years; 70 % male; NYHA class I 31 %, class II 43 %, class III/IV 26 %; LV-EF 34±15 %, NT-proBNP 1,071.0 [IQR 275.3–2,579.8]) who underwent elective invasive testing were assessed. Central venous pressure (CVP), pulmonary capillary wedge pressure (PCWP), mean pulmonary artery pressure (PAPm) and cardiac output (CO) were measured via right heart catheterization.

Results: Median PTH level was 33.19 ng/L (IQR 25.56–48.65). Prevalence of elevated serum PTH (>65 ng/L) was 8.1 % in men and 14.8 % in women. A significant dose-response relationship was found between PTH levels and increasing NYHA class (I: 27.92 [20.85–35.29], II: 34.40 [29.03–48.25], III/IV: 41.19 [26.20–66.15]; $p<0.001$). Moreover, PTH was correlated with LVEF ($r=-0.203$, $p<0.001$) and NT-proBNP ($r=0.305$, $p<0.001$). The association with NT-proBNP remained robust after adjustment for age, sex and eGFR. Increasing PTH levels were directly correlated with CVP ($r=0{,}147$, $p=0{,}004$), PCWP ($r=0.285$, $p<0.001$), PAPm ($r=0.241$, $p<0.001$) and indirectly correlated with CO ($p=-0.227$, $p<0.001$).

Conclusion: We found an independent relation of PTH with hemodynamics and disease severity in patients with chronic heart failure, most of whom had PTH levels within the normal range. These findings further highlight the importance of PTH in heart failure.

XVII-4

Pericardiocentesis for severe pericardial effusion due to suspected inflammatory etiology

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Introduction: Severe pericardial effusion (PE) may result from different etiologies. We here report our single-centre experiences on findings and management in patients with suspected inflammatory PE.

Methods and results: Between 2006 and 2012 pericardiocentesis was performed in 79 patients. Inflammatory disease was suspected in 44 (56 %) patients. Established etiologies were grouped into infectious ($n=19$), immunologic ($n=11$), and idiopathic ($n=14$).

Diagnosis of infectious disease (age 60±15.9; female 42 %) was based on positive virus-PCR ($n=7$) and positive bacterial culture ($n=1$) from PE, respectively and timely association with pneumonia/respiratory infections ($n=7$) and perimyocarditis on CMR ($n=4$). Immunologic etiology (age 51±18.3; female 64 %) was ascribed to patients with aseptic pericardial effusions and underlying connective tissue disease ($n=5$), graft versus host reaction (GvHD) following allogeneic stem cell transplantation ($n=3$) and postcardiotomy syndrome ($n=3$). Idiopathic etiology ($n=14$; age 60.4±17.6; female 42.9 %) was suspected when no definite diagnosis was found.

Intrapericardial cell counts were significantly different between groups (2,802, 256, and 594/µl, respectively; $p<0.05$), whereas no relevant differences were found for intrapericardial pressures, volumes and intrapericardial protein and LDH levels.

Saline rising and intrapericardial application of gentamycin (80 mg) were performed in all patients. Intrapericardial therapy with triamcinolon (300 mg/qm BSA) was applied in 47, 73, and 64 % of patients, respectively. Oral colchicin (up to 1 mg/d) for at least 3 months was prescribed in 58, 36, and 93 % of patients.

Conclusions: Etiologies vary among patients with severe pericardial effusions who are suspected for inflammatory disease. Pericardiocentesis can aid to establish specific diagnosis and goal-directed therapy.

XVII-5

Fibroblast growth factor-23 is associated with disease severity in patients with stable heart failure

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Background: Elevated levels of fibroblast growth factor-23 (FGF-23), a bone-derived phosphaturic hormone of the fibroblast growth factor family, are associated with all-cause mortality and incident heart failure in individuals with or without chronic kidney disease. We aimed to investigate the association of serum FGF-23 concentrations with disease severity in patients with stable heart failure.

Materials and methods: Serum C-term FGF-23 concentrations of 231 stable heart failure patients who underwent elective invasive testing were measured (age 41±15 years; 70 % male; NYHA class I 30.4 %, NYHA class II 42.6 %, NYHA class III/IV 25.7 %, LV-EF 34±15 %, eGFR 85.5±24.3 mL/min/1.73 m^2).

One-way analysis of variance was used to calculate differences in FGF-23 levels between NYHA classes. Correlations were calculated using partial regression analyses.

Results: Median FGF-23 levels were 15.69 pg/mL (5.6–38.2 pg/mL). A significant dose-response relationship was found between median FGF-23 levels and increasing NYHA class (I: 7.8 pg/mL, II: 15.4 pg/mL, III/IV: 38.6 pg/mL; $p<0.001$).

FGF-23 was directly correlated with NTproBNP ($r=0.289$, $p<0.001$), central venous pressure ($r=0.313$, $p<0.001$), mean pulmonary arterial pressure ($r=0.244$, $p=0.001$), pulmonary wedge pressure ($r=0.249$, $p=0.001$) and indirectly correlated with cardiac output ($r=-0.297$, $p=0.001$). Correlations were independent of eGFR and serum phosphate levels.

Conclusion: The phosphatonin FGF-23 is independently correlated with hemodynamics and disease severity in patients with stable heart failure. Further studies are needed to evaluate the role of FGF-23 as a potential biomarker in heart failure.

XVII-6

Iron overload cardiomyopathy diagnosed by CMR (cardiac magnetic resonance)

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Introduction: Juvenile hemochromatosis is characterized by onset of severe iron overload occurring typically in the first to third decade of life. Prominent clinical features include hypogonadotropic hypogonadism, cardiomyopathy, arthropathy, and liver fibrosis or cirrhosis.

A 29-year-old Caucasian male patient referred to the emergency department with acute diffuse abdominal pain and right-sided flank pain.

Laboratory on admission revealed elevated WBC count (9.940) and moderately elevated liver enzymes (AST, ALT)

The ECG on admission showed a normofrequent sinusrhythm with unspecific ST segment alterations. An abdominal CT-scan was performed and a renal infarction in the upper region of the right kidney was detected. An echocardiography showed a severely impaired ejection fraction (LVEF 26 %) with diffuse wall motion abnormalities, a thickened myocardium and signs of restrictive filling. Suprisingly cardiac magnetic resonance imaging (MRI) revealed a deposition of iron in the myocardium and liver and established the diagnosis of a hemochromatosis-related cardiomyopathy with its typical alteration in the T2 sequences.

The iron status revealed a high serum iron of 317 µg/dl (normal range 59–158) and a Serum ferritin level >2,420 ng/mL (normal range 30–400) An iron chelating therapy and periodic phlebotomies (9×250 mL in 7 weeks) were performed and a standard heart failure therapy was established. Moreover an oral anticoagulation therapy with Phenprocoumon was begun. Initially the iron levels remained high, but clinical aspect got remarkable better. During the hospital stay several episodes of non-sustained ventricular tachycardias were observed. The implantation of an ICD was recommended, but the patient refused.

Further weekly controls and phlebotomies ad the hematology department were arranged.

After hospital discharge periodic controls showed a significant improvement of the left ventricular ejection fraction (LVEF 56 %) and a significant decrease of ferritin and serum iron.

Discussion: Although genetic testing for hemochromatosis remained negative (further investigations are in progress) in the presented case the diagnosis of juvenile hemochromatosis is most likely, because of the constellation of findings and the early onset of the first symptoms.

Conclusion: Iron overload cardiomyopathy is an important and potentially reversible cause of heart failure. MRI is a useful non-invasive tool to diagnose and quantify an iron overload cardiomyopathy. Iron chelation therapy and periodic phlebotomies in combination with an optimized heart failure treatment may improve left ventricular function and prognosis.

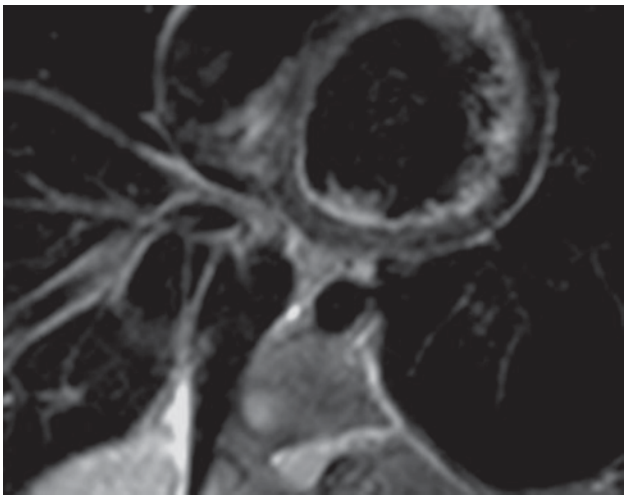

Fig. 1 Typical reduced signalling of the myocard and liver (T2 sequence)

XVII-7

Guideline adherence in CHF: does dosage matter?

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Purpose: Treatment guidelines that consider results of large placebo-controlled, randomized trials have been published to improve the management of chronic heart failure (CHF). Guideline adherence is associated with a decrease in cardiovascular hospitalizations and reduced mortality. The aim of our study was to investigate dosage effects of neurohormonal medication on outcome.

Methods: Data from the HIR-Austria, which is a prospective, multicentre, observational registry of patients presenting in heart failure outpatient clinics in Austria were analyzed. Patients (age 65 [55–74], male 72.6 %, NYHA class I 17.2 %, NYHA II 57.3 %, NYHA III/IV 25.5 %, LV-EF <40 % 74.1 %) were recruited between June 2006 and June 2011. One-year clinical follow-up including a complete data set was available in 1,392 patients. Long-term follow-up until all-cause death or data censoring was 2.7 (1.7–4.1) years. A guideline adherence indicator (GAI-3 [0–100 %]) was calculated at baseline and at follow-up (FU) visit considering indications and contraindications for ACE/ARB, beta-blocker, and MRA according to the ESC guidelines 2008. Patients were considered delta-GAI-3 positive if GAI-3 improved to or remained at a high level (≥80 %) during follow-up. Delta-GAI-3/50 positive was ascribed to patients fulfilling the above criteria but given a final dosage of >50 % of suggested target dosages.

Results: Delta-GAI-3 was positive in 74 % and delta-GAI-3/50 in 62 % of patients, which was paralled by a significant improvement in NT-proBNP (1,448 [504–3,390] to 875 [305–2,058]; $p<0.001$). In univariate Cox regression analysis improvements in GAI-3 and GAI-3/50 were associated with a 35 % (95 % CI 0.46–0.91; $p<0.05$) and 47 % (95 % CI 0.38–0.72; $p<0.001$) reduction in mortality risk, respectively. In a sex-stratified multivariate model adjusted for age,

NYHA class, NT-proBNP, ischemic etiology, diabetes, hypertension, glomerular filtration rate, ICD-implantation, and hospitalization for heart failure during one-year follow-up improvements in GAI-3/50 but not in GAI-3 was independently predictive of lower mortality risk: HR 0.64 (95 % CI 0.43–0.97; $p<0.034$) vs HR 0.84 (95 % CI 0.55–1.27; $p=0.4$).

Conclusions: Improvement of guideline adherence in individual patients with mild to moderate heart failure is associated with a decrease in mortality risk when dose escalation of medication is considered. The beneficial effects on prognosis are independent of baseline characteristics and interim hospitalizations for heart failure.

XVII-8

Increasing levels of GGT predict survival in chronic heart failure

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Purpose: Elevated serum levels of gamma-glutamyltransferase (GGT) have been associated with a high mortality risk in chronic heart failure (CHF). However, there is no data on the prognostic relevance of changes over time of this parameter. We therefore aimed to investigate the prognostic significance of changes in GGT levels over a follow-up period of 1 year.

Methods: Data from the HIR-Austria, which is a prospective, multicentre, observational registry of patients presenting in heart failure outpatient clinics in Austria were analyzed. Patients (male 73.1 %, age 65 [55–74], NYHA class I 17.7 %, class II 60.3 %, class III/IV 22.0 %, LV-EF < 40 % 69.4 %) were recruited between June 2006 and June 2011. One-year clinical follow-up was available in 1,264 patients. Long-term follow-up until all-cause death or data censoring was 2.5 (1.6–3.8) years. Uni- and multivariate, sex-stratified Cox proportional hazards models adjusted for age, ischemic etiology, NYHA class, LV-EF, systolic blood pressure, heart rate, glomerular filtration rate, anemia, body mass index and diabetes were performed to calculate hazard ratios (HR) and 95 % confidence intervals for GGT.

Results: In 36.6 % of the patients serum levels of GGT increased by ≥ 10 % between baseline (BL) and follow-up visit (FU). In this patient group mean NYHA class (2.05 ± 0.65 at BL) decreased to 1.95 ± 0.66 at FU, as compared to 1.88 ± 0.66 in patients with declining or only slightly increasing levels ($p=0.063$).

The endpoint of all-cause death was recorded in 117 patients (9.3 %). In univariate analysis, at ≥ 10 % GGT level increase was associated with a 51 % higher mortality risk (HR 1.51 [1.05–2.18]; $p=0.026$). Multivariate, sex-stratified cox regression analysis revealed an increase of GGT levels ≥ 10 % to be independently associated with a poor outcome (HR 1.89 [1.27–2.82], $p=0.002$). These findings even remained robust in a model with additional adjustment for respective changes in NT-pro-BNP levels.

Conclusions: In ambulatory patients with mild to moderate heart failure an increase in GGT serum levels by ≥ 10 % in the course of 1 year is independently associated with a poor prognosis. Our findings further highlight the clinical importance of GGT in CHF.

Postersitzung XVIII: Herzinsuffizienz 3

XVIII-1

Intraoperative dp/dt Messung zur Bestimmung des hämodynamisch- optimalen Stimulationsvektors unter Verwendung einer vierpoligen LV-Elektrode

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Einleitung: Trotz aller Erfolge der CRT liegt die non-Responder Rate nach Studienlage bei ca. 30 %. Der Erfolg der CRT ist auch von der linksventrikulären (LV)-Sondenposition, bzw. dem Stimulationsort abhängig. Mit der quadripolaren LV Sonde QuartetTM 1,458T (St. Jude Medical), kann LV-Stimulation über zehn verschiedene Stimulationsvektoren, bzw. unterschiedliche Stimulationsorte erfolgen. Wie sich die unterschiedlichen Stimulationsorte auf die Hämodynamik auswirken und dies zu einer Verbesserung der non-Responder Rate führt ist Ziel dieser Studie.

Methode: Bei 18 Patienten (64,2 J, 65 % m, NYHA 2,9 ± 0,32, LVEF 21,11 ± 7,44 %, DCM 13, ICM 1, KHK 4, QRS 161 ± 18,4 ms, längste QRS-Dauer 198 ms, kürzeste QRS-Dauer 126 ms. LSB 15, RSB 3, SR 100 %, AVB I 4, AVBII 1, AVB III 3) wurde erfolgreich und komplikationslos ein CRTD (Promote Quadra, SJM) implantiert. Alle LV-Sonden wurden lateral, bzw. posterolateral platziert. Intraoperativ wurde ein Certus® Druckdraht (Firma RADI) im LV platziert. Der LV-Druck und dp/dtmax wurde unter ER, bei LV- und biventrikulärer Stimulation gemessen. Die quadripolare LV Elektrode hat einen maximalen Polabstand von 4,7 cm, zwischen dem ersten distalen und dem letzten prioximal Pol und ermöglicht 10 verschiedene Stimulationsvektoren. Die AV-Zeit (A-sens) wurde nach der Oberflächen-EKG Methode (Koglek) optimiert. Nach einem standardisierten Protokoll wurde die links- u. biventrikuläre Stimulation mit verschiedenen VV-Dealys (0, −20, −40 ms) durchgeführt. Als positiver CRT Respons wurde eine Zunahme von ≥ 10 % dp/dtmax, in einem Vektor unter Stimulation, gegenüber dem Ausgangswert ohne Stimulation, definiert.

Ergebnisse: 3 Pat. (16,7 %) hatten in keinem Vektor eine Zunahme von ≥ 10 % dp/dtmax und wurden als non-Responder gewertet (1 Pat. mit DCM, RSB, QRS 146 ms. 1 Pat. KHK LSB, QRS 167 ms. 1 Pat. DCM, LSB, QRS 128 ms). 15 Pat. zeigten unter biventrikulärer Stimulation im besten Vektor, eine deutliche Verbesserung der Hämodynamik (↑ dp/dtmax 34,5 %). Die einzelnen Stimulationsvektoren führten zu deutlichen Unterschieden in der Hämodynamik. Im schlechtesten Vektor betrug die Verbesserung der Hämodynamik (↑ dp/dtmax 13,5 %). Bei 7 Patienten war im schlechtesten Vektor der dp/dt Anstieg < 10 %. Bei 8 Patienten zeigte sich der bipolare Standardvektor als der schlechteste Stimulationsvektor.

Diskussion: Die neue, vierpolige LV-Elektrode erlaubt über 10 unterschiedliche Stimulationsvektoren die Auswahl des optimalen Stimulationsortes und führt zu einer deutlichen Verbesserung der Hämodynamik. Bei dieser Untersuchung führte dies zur Halbierung der non-Responderrate. Dadurch lässt sich bei Patienten mit lokal unterschiedlicher Erregungsausbreitung der CRT Respons wesentlich steigern.

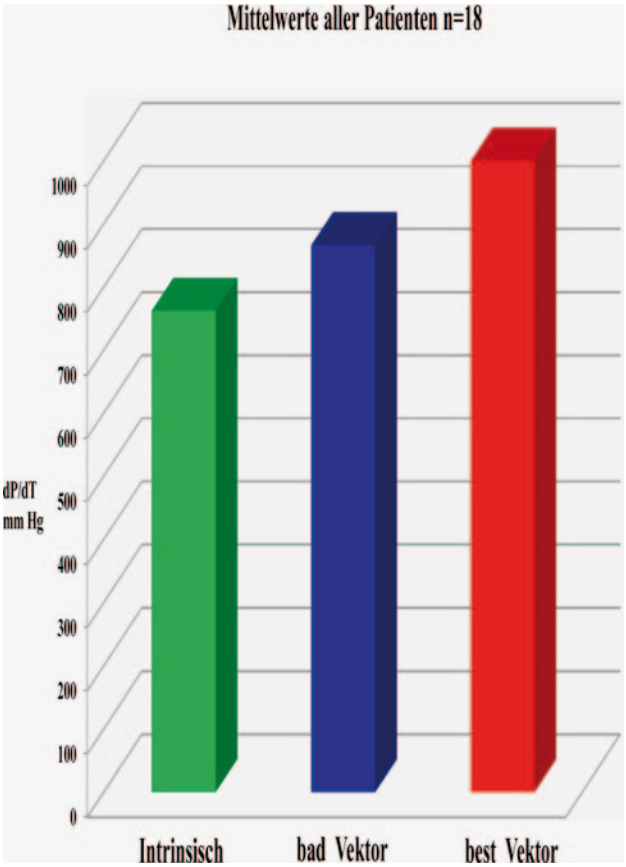

Fig. 1 Unterschiedliche Stimulationsvektoren führen zu einer deutlichen Verbesserung der Hämodynamik

XVIII-2

Epicardial fat volume is inversely correlated with the degree of diastolic dysfunction and outcome in patients with heart failure with preserved ejection fraction

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Introduction: Epicardial adipose tissue has been linked to cardiovascular metabolism and inflammation and has been shown to predict prevalence and progression of coronary artery disease.

The aim of the present study was to assess epicardial fat volume in patients with heart failure with preserved ejection fraction (HFPEF) in terms of quantification and predictive value.

Methods: One hundred patients with suspected HFPEF were enrolled in this prospective, observational study. Confirmatory diagnostic tests, cardiac magnetic resonance (CMR) imaging, and invasive hemodynamic assessments were performed at baseline. Sixty-one patients with confirmed HFPEF (mean age: 70.5 years; female: $n=39$) entered a longitudinal outcome-monitoring phase (median 12.9 months), during which 14 had a cardiac event.

CMR studies included the assessment of cardiac function and dimensions by standard cine sequences. Epicardial fat volume was quantified offline, using dedicated software (cmr42®).

Results: Epicardial fat volume ranged from 23 to 89 mL (mean 49.3±16.2 mL; patients: 43.8±13.4 mL, controls: 58.6±16.6 mL; $p<0.001$). Epicardial fat volume was significantly correlated with E/é ($R=-0.37$; $p<0.001$), NT-proBNP ($R=-0.27$; $p=0.012$), right ventricular size and function ($R=-0.32$; $p=0.002$ and $R=0.40$; $p<0.001$), left ventricular ejection fraction ($R=0.36$, $p<0.001$), left and right atrial size ($R=-0.27$, $p=0.01$; $R=-0.34$; $p=0.001$), mean pulmonary arterial pressure ($R=-0.36$, $p=0.006$), pulmonary capillary wedge pressure ($R=-0.33$; $p=0.013$), and pulmonary vascular resistance ($R=-0.34$; $p=0.01$). Epicardial fat volume was not correlated with gender, age, renal function, or body mass index.

All study participants were followed for 356±198 days. By Kaplan–Meier analysis, event-free survival was significantly worse in subjects with epicardial fat volume below the median of 43 mL (log rank $p=0.038$).

Conclusion: Epicardial fat volume is inversely correlated with diastolic dysfunction, serum NT-proBNP, invasive measures of pulmonary hypertension, but not total body fat. Decreasing epicardial fat volume predicts adverse outcome in HFPEF patients. The mechanism causing decreasing epicardial fat volume in advanced disease remains to be determined.

XVIII-3

Für Patienten nach Implantation eines linksventrikulären Unterstützungssystem ist ein intensives Trainingsprogramm mit Steuerung der Belastungsintensität durch Selbsteinschätzung (Borg Skala) sicher und erfolgreich

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Einleitung: Linksventrikuläre Unterstützungssysteme (Left Ventricular Assist Devices, LVADs) werden zunehmend bei Patienten mit terminaler Herzinsuffizienz implantiert. Bis jetzt existieren nur wenige Daten über Sicherheit und Durchführbarkeit eines intensiven Trainingsprogrammes.

Methode: 41 Pat. 48±38 Tage nach Implantation eines LVAD wurden 32±6 Tage von 1/2011 bis 3/2012 stationär rehabilitiert (Alter 54.8±11.56 J.; weibl. 20%). Die medizinische Trainingstherapie bestand aus Fahrradergometer- (Intervallmethode), Krafttraining, Gymnastik- und Wandergruppen. Die Zunahme des Trainingsumfanges und der Belastung beim Fahrradergometertraining (bestehend aus 12 Modulen mit ansteigender Belastung z. B. Modul 1=1/5W, 60/30 s bis zum Modul 12=5/150W, 60/20 s), der Wechsel in eine leistungsstärkere Wander- bzw. Gymnastikgruppe und der Kraftzuwachs wurde registriert. Aufgrund der technischen und biophysikalischen Gegebenheiten ist eine Messung der Herzfrequenz manuell oder mit Pulsuhr nicht durchführbar, sodass die Intensitätssteuerung nach der subjektiven Belastungsempfindung des Pat. nach der Borg-Skala erfolgte, wobei diese als mittelschwer beurteilt werden sollte. Trainingsbezogene Komplikationen wurden dokumentiert.

Bei einer Subgruppe von 15 Pat. wurde am Beginn und Ende eine Spiroergometrie durchgeführt.

Zur Unterstützung des „reversed remodellings“ wurde die medikamentöse Herzinsuffizienztherapie adaptiert, mit Dosisangaben dokumentiert und zur Verlaufskontrolle das pro BNP bestimmt.

Ergebnisse: Es kam zu signifikanten Steigerungen der Dauer (19±4 vs. 14±2 min) und der Belastung (Modul 6,2±2,8 vs. Modul 2±1,9) beim Fahrradergometertraining und zum Kraftzuwachs in

den trainierten Muskelgruppen (Beinpresse: 34±15 vs. 27±12 kg, Beinstrecker 10±6 vs. 7±4 kg, Beinbeuger 10±6 vs. 7±4 kg, Abduktor: 16±9 vs. 13±8 kg, Adduktor: 16±7 vs. 13±8 kg. Es wurde nur eine trainingsbezogene Komplikation, eine nicht anhaltende ventrikuläre Tachykardie, beim Fahrradergometertraining beobachtet.

Die Spiroergometrie am Beginn und Ende der 15 Patienten zeigte eine signifikante Zunahme des max. VO_2 (14.5±5.2 vs. 11.3±4.1 mL/kg/min) und der maximal erreichten Watt (61.5±24.6 vs. 44.4±17.6 W).

Die Anzahl der Patienten, die mit Betablocker und ACE-Hemmern therapiert wurden, konnte vermehrt werden. Es benötigten mehr Patienten Furosemid, zuletzt auch in höherer Dosis. Bei 28 Patienten konnte ein Abfall des pro BNP von – 1764±2112 gemessen werden, bei 9 Pat. ein Anstieg von 1011±1040, (bei 4 Patienten erfolgten keine zwei Messungen).

Zusammenfassung: Ein intensives Rehabilitationsprogramm mit Steuerung der Belastungsintensität durch Patientenselbsteinschätzung nach der Borg Skala kann erfolgreich und sicher durchgeführt werden. Bei den meisten Pat. ist ein Abfall der pro BNP Werte, bei manchen ein Anstieg zu verzeichnen, möglicherweise als Ausdruck einer Rechtsherzinsuffizienz.

XVIII-4

Mild hypothermia improves mixed venous oxygen saturation during experimental reductions of cardiac power output in pigs

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Background: A decrease of cardiac power output (CPO) is the strongest predictor of in-hospital mortality during cardiogenic shock, with 0.53 W being a critical threshold. We have previously shown that the induction of mild hypothermia (MH) decreases systemic oxygen demand and thereby improves the systemic oxygen supply-demand balance during experimental cardiac dysfunction in pigs. We now tested whether MH alters the relationship between CPO and mixed venous oxygen saturation (SvO_2), a measure of appropriate systemic oxygen supply.

Methods: We retrospectively analyzed data obtained in experimental studies on the hemodynamic effects of MH. Anaesthetized pigs (total $n=45$) were instrumented with Swan-Ganz and left ventricular pressure-volume catheters. Animals were cooled from 38 °C (normothermia, NT) to MH (33 °C) by an intravascular cooling device for 6 h after resuscitation from cardiac arrest (Resus), for 6 h after left ventricular (LV) myocardial infarction (MI), or for 8 h during endotoxemia (LPS, a model of sepsis).

Results: We first confirmed that CPO (cardiac output multiplied by mean aortic pressure) accurately reflects external LV work (derived as minute LV stroke work from pressure-volume measurements) by linear regression analysis ($r^2=0.90$, data not shown). We then plotted SvO_2 as function of CPO indexed to body weight, comprising all animals studied at NT. We observed a close linear relationship here ($r^2=0.80$, see graph), implying that evolving systemic oxygen supply-demand imbalance underlies the prediction of mortality by CPO. Data points obtained during MH after the induction of cardiac dysfunction all fell above the 95 % confidence interval of the CPO-SvO_2 relationship.

Conclusion: Experimental reductions of CPO are linearly correlated to a fall of SvO_2. The induction of MH leads to a pronounced increase of SvO_2 for a given reduction of CPO. These data indicate that during MH substantially lower values of CPO may be compatible with survival than during NT. The induction of MH may thus be a therapeutic option for the treatment of cardiogenic shock.

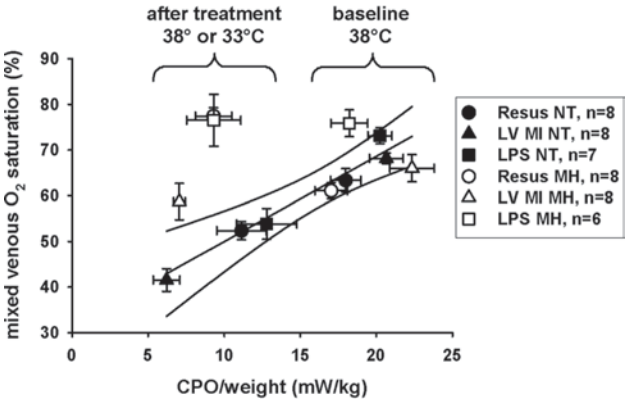

Fig. 1 MH alters the relationship between CPO and mixed venous oxygen saturation (SvO_2)

XVIII-5

Life quality in anemic patients with chronic heart failure and cardiorenal syndrome II type

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Despite the interest of researchers to the problem of cardiorenal relationship, the question remains poorly understood changes in quality of life (LQ) in patients with decompensated chronic heart failure (CHF), depending on the clinical and functional status of the kidneys.

The purpose of the study—to evaluate the LQ of patients with anemia of varying severity, developed against the background of chronic heart failure, depending on the presence or absence of chronic kidney disease (CKD) using a questionnaire FACT-An.

Results: One hundred and forty patients with CHF II-IV FC due to ischemic heart disease were examined. The first group included 71 anemic patients with CHF and was diagnosed with CKD, the second—69 patients with no signs of anemia of CKD. To assess the quality of life in anemic patients with CHF questionnaire used FACT-An. The questionnaire includes 47 questions by category: PWB—physical condition, SWB—social/family relationships, EWB—emotional well-being, FWB-being in everyday life, AnS—additional indicators, reflecting the scale of anemia, FACT-G—the total scale of weakness, FACT-An total—the total scale of weakness and anemia. Overall score from 0 to 180. Highest score reflects higher quality of life. When comparing the quality of life parameters in patients with the same degree of severity of anemia, depending on the presence or absence of signs of renal dysfunction observed differences. Thus in patients with heart failure and CKD anemic syndrome observed a significant decrease parameters PWB, EWB, FWB, FACT-G, AnS and FACT-An total compared to patients with CHF and CKD in the presence of the same degree of severity of anemia ($p<0.05$). Group 1 patients found direct links between Hb and PWB ($r=0.37$), FACT-G ($r=0.22$), FACT-An total ($r=0.23$); CPU and PWB ($r=0.39$), EWB ($r=0.23$), FWB ($r=0.34$), FACT-G ($r=0.35$), FACT-An total ($r=0.28$); level of red blood cells and SWB ($r=0.36$), FWB ($r=0.36$). Reduction indicators hemogram in patients with anemia of CHF and CKD is accompanied by changes in the parameters that reflect the physical condition, emotional well-being and social activity, as well as the total scale of

weakness, fatigue and anemia. The greatest number of connections in one group, identified in the color index. Two groups of patients found direct links between the level of red blood cells and FWB (r=0.20), AnS (r=0.28), FACT-An total (r=0.23); Hb level and AnS (r=0.17), CPU, and SWB (r=0.27). In patients with CHF reduction of red blood cells, Hb associated with decreased total scale of weakness and anemia, anemia scale, the parameters of the physical condition, reducing color index—with the parameters of social activity.

Conclusion: Low hemoglobin levels are associated with a reduction in the physical state of the parameters, the total scale of weakness and anemia in both groups of patients. Color index has a significant effect on the physical, functional, and emotional well-being in patients with CHF, CKD and anemia, as well as the level of social and family relationships in patients with anemia, developed with CHF without evidence of CKD.

XVIII-6

Predictors of adverse outcome in patients with heart failure and preserved ejection fraction

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Background: Patients with heart failure and preserved left ventricular ejection fraction (HFPEF) face an adverse outcome. The aim of the present study was to identify factors that determine prognosis.

Methods: Consecutive patients with HFPEF diagnosed according to current ESC guidelines were recruited in our prospective registry, which was approved by the local ethics committee. Death and/or hospitalization for heart failure were defined as primary outcome variables. Outcome groups were compared with respect to potential prognostic predictors using the Student's t-test and the Chi-square test. Multivariable logistic regression analysis was applied to determine whether parameters of interest were associated with adverse outcome. $P<0.05$ indicated statistical significance.

Results: Between December 2010 and January 2013, 102 HFPEF patients (71 f/31 m, mean age 70±8 years) were registered. After a mean follow-up of 13±9 months, 24 (24%) patients were hospitalized or died. Patients in the adverse outcome group were characterized by a shorter 6 min walk distance in metres (254±117 versus 347±112, p=0.002), a higher borg dyspnea score (BDS, 6±2 versus 3±2, $p<0.001$), lower haemoglobin values in gram per deciliter (11.6±1.3 versus 12.7±1.9, p=0.011), higher NT-proBNP in pg/mL (2,107±1,409 versus 1,363±1,243, p=0.017) and a lower forced expiratory volume in 1 s in % (69±24 versus 81±24, p=0.042) at enrolment. Diabetes mellitus II (DM II, 58 versus 27%, p=0.005) was more prevalent among patients with adverse outcome. With respect to hemodynamic parameters a higher mean pulmonary arterial pressure in millimeter of mercury (39±9 versus 33±9, p=0.009), a higher mean pulmonary capillary wedge pressure (mPCWP in millimeter of mercury, 20±4 versus 23±5, p=0.006), a higher mean right atrial pressure in millimeter of mercury (16±7 versus 12±5, p=0.008) and a higher transpulmonary gradient (TPG >12 mmHg, 83 versus 55%, p=0.013) were detected. In the multivariable regression model, DM II (odds ratio: 5.5 [95% confidence interval 1.5–20.2]; p=0.010), the BDS (odds ratio: 6.2 [95% confidence interval 1.7–22.1]; p=0.005), the mPCWP (odds ratio: 1.2 [95% confidence interval 1.0–1.3]; p=0.007) as well as TPG >12 mmHg (odds ratio: 3.9 [95% confidence interval 1.0–15.1]; p=0.046) remained independent predictors of adverse outcome.

Conclusions: Presence of DM II, a higher BDS, a higher mPCWP and a TPG >12 mmHg predict adverse outcome in HFPEF patients.

XVIII-7

Prevalence of tricuspid regurgitation in patients with heart failure and preserved ejection fraction

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Background: Heart failure (HF) with preserved ejection fraction (HFPEF) is commonly observed in elderly female patients and is responsible for approximately 50% of all HF cases. An elevated left ventricular end-diastolic pressure leads to a rise in pulmonary arterial pressure, resulting in right ventricular dilatation, and the development of tricuspid regurgitation (TR). Little is known about the prevalence and characteristics of TR in HFPEF patients.

Methods: Consecutive patients with HFPEF diagnosed according to ESC guidelines were enrolled in our prospective Viennese registry, which was approved by the local ethics committee of the Medical University of Vienna. All patients underwent invasive hemodynamic work-up. According to TR severity, patients were dichotomized into two groups: TR < moderate and TR ≥ moderate. Groups were compared with Student´s t-test and a Chi-square analysis for categorical data. $P<0.05$ indicated statistical significance.

Results: Between December 2010 and January 2013, a total of 102 patients (71 f/31 m, mean age 71±9) were enrolled, of whom 62 (61%) were diagnosed with ≥ moderate TR. Patients with TR ≥ moderate were characterized by older age in years (72±8 versus 68±10, p=0.024) and higher NT-proBNP values in picogram per milliliter (2,113±2,388 versus 1,233±1,235, p=0.034). Atrial fibrillation (79 versus 40%, $p<0.001$) was more prevalent among patients with TR ≥ moderate. With respect to echocardiographic parameters a larger left atrial diameter in millimeter (67±8 versus 63±8, p=0.037), a larger right atrial diameter in millimeter (68±11 versus 60±7, $p<0.001$), and a larger right ventricular end-diastolic diameter in millimeter (40±8 versus 36±6, p=0.004) were detected. Furthermore patients with TR ≥ moderate displayed a higher pulmonary capillary wedge pressure and transpulmonary gradient compared with the remaining group (Table 1).

Conclusion: Relevant TR is present in more than half of patients with HFPEF and is associated with poor pulmonary hemodynamic parameters.

Table 1. Hemodynamic findings according to tricuspid regurgitation severity

Variables	Tricuspid regurgitation < moderate (n=40)	Tricuspid regurgitation ≥ moderate (n=62)	P value
Hemodynamic parameters			
Mean pulmonary arterial pressure (mmHg)	31±7	37±11	0.003
Mean right arterial pressure (mmHg)	11±6	14±5	0.006
Pulmonary vascular resitance (dynes/s/cm^5)	201±94	272±180	0.031
Pulmonary capillary wedge pressure (mmHg)	19±4	21±5	0.046
Transpulmonary gradient (mmHg)	12±4	16±8	0.003

XVIII-8

Short telomere length predicts adverse outcome in patients with heart failure

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Background: Heart failure affects more than 15 million patients in Europe and is the main cardiovascular discharge diagnosis in the United States. A major risk factor for heart failure is age. Age can be defined chronologically or, via measuring telomere length, biologically. The aim of our current study was to evaluate if biological age is a better predictor for disease progression and adverse outcome in a heart failure cohort compared to chronological age.

Methods: We enrolled 40 patients (67 % male) with advanced heart failure. Mean age was 70±12 years, BNP levels were 415.97±249 pg/mL. Seventeen patients (43 %) died due to cardiovascular reasons during the follow up. To measure biological age we isolated DNA from buffy coats and measured relative telomere length by rt-PCR. To determine, if telomere length correlates with inflammation we measured TNF-alpha, MCP-1, G-CSF and M-CSF by ELISA.

Results: Telomere length and age did not correlate in patients with heart failure ($r=-0.141$, $p=0.4$). In addition telomere length did not correlate with plasma levels of TNF-alpha ($r=-0.156$, $p=0.3$), MCP-1 ($r=-0.139$, $p=0.4$), G-CSF ($r=-0.04$, $p=0.8$) or M-CSF ($r=-0.07$, $p=0.7$). However, telomere length was significantly reduced in patients with cardiovascular mortality (relative telomere length of 0.5 in patients suffering cardiovascular mortality compared to 1.8 in survivors, $p=0.05$). Interestingly, chronological age was not significantly associated with cardiovascular mortality in this analysis.

Conclusions: Relative telomere length predicts adverse outcome in patients with heart failure. A correlation of biological age measured by telomere length and chronological age is lost in heart failure patients. In addition, telomere length does not correlate with markers of current inflammation in patients. We suggest that telomere length describes the remaining life-time more precisely than chronological age. Furthermore, telomere length seems to describe the overall stress burden of a patient and is not correlated with cytokine levels.

Postersitzung XIX: Interventionelle Kardiologie 2

XIX-1

The course of NT-proBNP in real-life patients who underwent percutaneous transcatheter aortic valve implantation

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Background: Natriuretic peptides have been shown to predict outcome in patients with severe aortic stenosis before and after aortic valve replacement. The aim of this study was to evaluate the course of N-terminal pro B-type natriuretic peptide (NT-proBNP) in patients who underwent percutaneous transcatheter aortic valve implantation (TAVI).

Methods: Between May 2007 and January 2012, 109 symptomatic pts with severe aortic stenosis successfully underwent TAVI (86 pts received a Edwards Sapiens valve, 23 pts a CoreValve). NT-proBNP (Roche Elecsys) was assessed before and 30 days, 3-, 6-, and 12-months, 18-months, 2 and 3 years after TAVI.

Results: Patients had an age of 82.8±6 years, the baseline aortic valve area 0.6±0.2 cm^2, and the mean gradient 58±19 mmHg. Baseline NT-proBNP was significantly correlated to the logistical EuroScore (rho=0.3, $p=0.008$), but not to age. After TAVI NT-proBNP decreased in trend from 2,325 pg/mL ($n=91$; IQR 1,204–5,011) to 1,683 pg/mL ($n=45$; IQR 911–3,014; $p=0.052$) after 30 days, to 1,496 pg/mL ($n=46$; IQR 880–3,103; $p=0.356$) after 3 months, to 1,250 pg/mL ($n=43$, IQR 585–3,056; $p=0.009$) after 6 months, to 1,424 pg/mL ($n=30$, IQR 770–3,070; $p=0.164$) after 12 months, to 1,372 pg/mL ($n=19$, IQR 524–3,690; $p=0.123$) after 18 months, to 1,354 pg/mL ($n=15$; 383–5,105; $p=0.155$) after 2 years, and to 1,294 pg/mL ($n=13$; 1,097–2,072; $p=0.099$).

Conclusion: After TAVI, NT-proBNP levels tended to decrease. Baseline NT-proBNP seems to be a predictor for outcome after TAVI. These data should be confirmed in larger patient populations.

XIX-2

Late stent malapposition and endothelial coverage of drug-eluting-stents with and without bioabsorbable polymer: a prospective optical coherence tomography study

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Background: Uncovered stent struts of drug-eluting stents (DES) are associated with late stent thrombosis. Early and late malapposition of stent struts may be the major mechanisms for uncovered struts. Durable polymer may contribute to late acquired stent malapposition. Optical coherence tomography (OCT) enables the evaluation of stent strut apposition due to high-resoluted intravascular images.

Aims: This study examines malapposition of DES with and without bioabsorbable polymer in patients who underwent elective percutaneous coronary intervention (PCI).

Methods: Fifty patients treated with 60 DESs (25 Everolimus-eluting stents [EES], 18 Zotarolimus-eluting stents [ZES], 17 Biolimus-eluting stents [BES] underwent OCT directly after implantation and after 12 months.

Results: Postintervention acute stent malapposition (ASM) occurred in 27 stents (45 %), distributed to 25 EES, 18 ZES, and 17 BES. Of these, malappositions in 19 stents resolved completely (70 %), whereas 8 malappositions persisted after 1 year (malapposed segments in 6 stents resolved partly whereas malappositions in 2 stents persisted completely). At this time-point, a total 18 stents (30 %) with late stent malappositions were detected due to late acquired stent malapposition (LASM) in additional 10 stents (17 %). The occurrence of LASM was significantly higher in stents without bioabsorbable polymer (10 in EES and ZES—100 %) than in stents with bioabsorbable polymer (0 BES—0 %; $p=0.0492$).

Conclusion: The use of bioabsorbable polymer may reduce late acquired stent malapposition.

Table 1. Malappositon of DES with and without bioabsorbable polymer

	Pat. with bioabsorbable Polymer DES ($n=13$)	Pat. with durable Polymer DES ($n=37$)	Total ($n=50$)
Age at 1 year FUP	56.4 (IQR: 51.5–60.0)	61.6 (IQR: 54.2–70.0)	60.2 (IQR: 53.0–66.0)
Gender (m/f)	14/3	38/5	42/8
FUP period	364.2 (±17,3)	363.3 (±18,4)	363.5 (±18.0)
Stents implanted	*n=17*	*n=43*	*n=60*
Stent length	22.94 (±7.25)	23.3 (±8.07)	23.2 (±7.79)
Stent diameter	2.99 (±0.38)	2.97 (±0.4)	2.7 (±0.39)
Struts total 1 year[a]	3.291 193.6 (±80.1)	12.385 288.0 (±168.9)	15.676 261.3 (±154,6)
-cont./app + cvd	3.216 189.0 (±77.3)	11.754 273.4 (±147.4)	14.970 249.0 (±136.2)
-app + uncovd	45	73	118
-malapp. + covd.	6	348	354
-malapp. + uncvd	9	9	18
-thereof LASM	0	289	289
LASM	0	10	10
No LASM	17	33	50
Total	17	43	60

[a]"Struts total 1year" were counted in every fourth frame

XIX-3

The TAVI-HEART team approach in an interventional cardiology centre without on-site cardiac surgery

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Introduction: Transcathether aortic valve implantation (TAVI) has become a standard procedure for high risk patients with severe aortic stenosis (AS). Accordingly, in the current ESC-guidelines, it is recommended (class IB) for patients who cannot undergo surgery. TAVI is commonly performed in hospitals with cardiac surgery on-site and a heart team that assesses the patient's risk. At our hospital on-site cardiac surgery is not available, but the heart team approach includes extensive collaboration with technicians, interventional cardiologists, anaesthesiologists, heart- and vascular surgeons, respectively. The TAVI-programme started 2 years ago at our centre. Aims of the Wilhelminen hospital TAVI-registry include permanent quality control including safety and efficacy monitoring. This report describes the 12 months outcome of patients, admitted to our department for severe inoperable AS.

Methods: Since August 2010 a total of 70 consecutive patients with severe inoperable AS were admitted to our department. Forty-seven patients were intended to receive TAVI (intention-to-treat group). Of these, seven died before the procedure could be performed. Forty received a CoreValveTM bioprosthesis within 5 (4–8) weeks after screening (on-treatment group). The remaining 23 patients were either assigned to conservative treatment ($n=12$) or refused to give written informed consent ($n=11$). Consequently they served as control-group on optimal medical therapy.

Results: The mean age of screened patients was 84.7±5.9 years, 70% were female. Baseline echocardiography of on-treatment TAVI patients unveiled a mean transvalvular gradient of 45.4±13.2 mmHg compared to 8.4±2.6 mmHg ($p<0.001$) 1 year later. The mean valvular opening area increased from 0.8±0.2 cm^2 before TAVI to 1.6±0.3 cm^2 1 year after intervention ($p<0.001$). Mean EF remained constant over time (50.7±7.7 vs. 50.9±8.3%, $p=0.95$). Importantly, NYHA levels decreased significantly from 3 (3–3) to 1 (1–2, $p<0.001$). Furthermore, mini mental state examination results were stable over time (27.6±2.1 vs. 27.7±4.2, $p=0.918$). Survival of the intention-to-treat group was 83% after 1 month, and 54.5% after 1 year compared to conservatively managed patients with survival rates of 87% after 1 month and 11.1% after 1 year ($p=1$ and $p=0.002$, respectively). Survival of the on-treatment group was 90% after 1 month and 69.2% after 1 year compared to the conservatively managed patients with 87% after 1 month and 11.1% after 1 year ($p=0.699$ and $p<0.001$, respectively). Kaplan–Maier analyses confirmed these results.

Conclusion: Our data underline the poor prognosis of severe symptomatic AS in inoperable patients, especially when TAVI cannot be offered timely. Our findings show similar results compared to previously published international data. Patients receiving TAVI have a significantly improved outcome in contrast to conservatively managed patients with severe inoperable AS. The high early mortality rate of this patient population indicates that the TAVI procedure should be offered to patients as early as possible after screening. Our data not only underline the feasibility to safely perform TAVI procedures at medical centres without on-site cardiac surgery, but also emphasize the importance of a well organized cath lab procedure under presence and in close cooperation of the complete Heart Team consisting of cardiologists, cardiac and vascular surgeons as well as anaesthesiologists.

XIX-4

Effektivität und Sicherheit einer personalisierten Reduktion der dualen Plättchenhemmung bei Blutungskomplikationen nach perkutaner Koronarintervention und „Overresponse" auf Clopidogrel und Aspirin

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Einleitung: Blutungskomplikationen nach perkutaner Koronarintervention (PCI) stellen ein klinisches Problem hinsichtlich Weiterführung der dualen Anti-Plättchentherapie (DAPT) dar. Die Effektivität und Sicherheit einer personalisierten Reduktion der DAPT bei Auftreten von Blutungskomplikationen wurde noch nicht untersucht.

Methoden und Patienten: Es handelt sich um eine Subgruppen Analyse der prospektiven monozentrischen Kohortenstudie (Indi-

vidualizing Dual Antiplatelet Therapy After Percutaneous Coronary Intervention – The IDEAL-PCI Registry) an 747 Clopidogrel Respondern. Die Plättchenreaktivität wurde mit Impedanzaggregometrie (Multiplate©) nach Stimulation mit Adenosin Diphosphat (ADP) Arachidon-Säure (ASPI) und Thrombin-Rezeptor Agonist (TRAP) bestimmt. Bei Patienten mit spontanen Blutungskomplikationen die als „duale Overresponder" identifiziert worden sind (ADP <25 U, ASPI ≤15 U), wurde die Clopidogrel und Aspirin Erhaltungsdosis schrittweise bis zum Erreichen des therapeutischen Fensters (ADP: 26–49 U, ASPI: 16–30 U) reduziert. Die klinische Beobachtung erfolgte über 12 Monate.

Ergebnisse: „Duale Overresponder" (26 % der Clopidogrel-Responder) wiesen eine hochsignifikant geringere Plättchenreaktivität im Vergleich zu „Normal Ansprechern" auf (ADP: 17±5 vs. 33±9 U, ASPI: 8±4 vs. 20±14 U, TRAP: 82±25 vs. 99±22 U, p für alle <0,001), was mit einem deutlich erhöhtem TIMI Blutungsrisiko (13 vs. 8,3 %, p=0,05) einherging, wobei vor allem spontane Blutungskomplikationen signifikant häufiger auftraten (6,7 vs. 2,0 %, p=0,006). Weibliches Geschlecht war ein Prädiktor der Blutungskomplikationen (21 vs. 9 %, p=0,01). Bei acht „dualen Overrespondern" mit spontanen Blutungen wurde die Clopidogrel und Aspirin Erhaltungsdosis schrittweise von 75 mg auf 35±7 mg (p<0,001) bzw. von 100 mg auf 44±28 mg (p<0,001) reduziert. Damit konnte die Plättchenreaktivität signifikant bis zum Erreichen des therapeutischen Fensters gesteigert werden (ADP: von 14±8 auf 31±10 U, p<0,001; ASPI: von 7±6 auf 19±5 U, p<0,001; TRAP: von 83±34 auf 113±33 U, p=0,02). Dieses Vorgehen führte zum Sistieren von Spontanblutungen, (gastrointestinalen TIMI Major und Minor Blutungen), sowie Rückbildung von ausgeprägten Spontanhämatomen. Bis zur Beendigung der DAPT nach 12 Monaten traten keine weiteren Blutungen oder ischämische Ereignisse auf.

Schlussfolgerungen: Spontane Blutungskomplikationen nach PCI treten unter DAPT mit Clopidogrel und ASS signifikant häufiger bei Patienten mit „dualem Overresponse" auf. Eine personalisierte, Multiplate© gesteuerte Reduktion der Clopidogrel und Aspirin Erhaltungsdosis zur Erreichung des therapeutischen Fensters bis zur geplanten Beendigung der DAPT erscheint sowohl effektiv hinsichtlich Minimierung der Blutungsneigung, wie auch sicher hinsichtlich ischämischer Komplikationen.

XIX-5

Impact of bivalirudin monotherapy vs. other antithrombotic strategies on mortality, bleeding and hospitalization in patients admitted with acute coronary syndromes (ACS) for percutaneous coronary intervention (PCI)

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Background: The role of bivalirudin monotherapy vs. unfractionated heparin + GP IIb/IIIa-receptor inhibition (UFH + GPI) in patients (pts.) undergoing PCI has been studied extensively in randomized controlled trials. A comparison vs. UFH monotherapy does not exist and in general „real-world" clinical data are scarce.

Methods: In a posthoc analysis of a permanent prospective registry, antithrombotic therapy and baseline variables were evaluated in 1,201 consecutive pts. admitted between January 2003 and February 2011 with an ACS referred for PCI with stent implantation.

Primary endpoints were a composite of in-hospital minor or major bleeding hazards and long-term all-cause mortality. As secondary endpoint we investigated the length of hospitalization. For the evaluation of bleeding complications levels of hemoglobin and hematocrit were measured during the index hospitalization. All pre-defined endpoints were compared between pts. receiving peri-interventional anticoagulation with bivalirudin alone, UFH alone, or UFH + GPI, respectively. As GPI we used exclusively abciximab in the recommended dosage (bolus + infusion for 12 h). All patients received aspirin and a P2Y12-receptor antagonist (mainly Clopidogrel) as basal antiplatelet strategy.

Results: From the whole patient cohort, 127 (10.6 %) pts. received bivalirudin monotherapy, 665 (55.4 %) pts. UFH alone, and 408 (34 %) pts. UFH + GPI, respectively. Within the wide range of registered baseline characteristics, age, gender, current smoking, peripheral vascular disease, renal failure, presence of atrial fibrillation, history for malignant tumors and baseline hemoglobin were significantly different between the study groups. The mean follow up in our cohort was 59±27 month. All-cause mortality was 9.4, 18, and 13.5 % in the bivalirudin alone, UFH alone, and UFH + GPI group. In the cox proportional-hazards model peri-interventional anticoagulation with bivalirudin monotherapy, as compared to UFH + GPI, resulted in similar rates of all-cause death (HR 0.61, 95 % CI 0.33–1.14, p=0.12). Notably, peri-interventional anticoagulation with bivalirudin monotherapy, as compared to heparin monotherapy, resulted in a 50 % relative risk reduction in long-term all-cause mortality (HR 0.50, 95 % CI 0.27–0.9, p=0.02). Minor or major bleeding occurred in 7.8 % of pts. in the bivalirudin alone group, 8.9 % of pts. in the heparin alone group, and 14.5 % of pts. in the UFH + GPI group, respectively. After adjustment for baseline characteristics in the logistic regression model bivalirudin monotherapy, as compared to UFH + GPI, was associated with significantly lower rates in the composite of minor or major bleedings (OR 0.38, 95 % CI 0.17–0.86, p=0.02). However, composite bleeding rates were similar between bivalirudin monotherapy and UFH monotherapy (OR 0.69, 95 % CI 0.31–1.55, p=0.53). Moreover, anticoagulation with bivalirudin alone, compared with UFH + GPI accounted for a 38 % reduction of hospitalization (days between PCI and hospital discharge; B = – 1.38, 95 % CI – 1.15; – 1.64, p<0.01)

Conclusion: In this "real-world" setting, we were able to confirm the beneficial action of bivalirudin vs. other peri-interventional antithrombotic strategies. These data support the more frequent use of bivalirudin in interventional cardiology, which is also highly recommended by international guidelines.

XIX-6

Individualizing dual antiplatelet therapy after percutaneous coronary intervention: the IDEAL-PCI registry

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Aims: To evaluate the impact of tailoring dual antiplatelet therapy with multiple electrode aggregometry on clinical outcome in an all-comers PCI population, including STEMI patients, as high on-treatment platelet reactivity to ADP is associated with adverse ischemic events after PCI.

Methods and results: Prospective, single-center cohort observation of 1,008 consecutive PCI patients with stent implantation or drug eluting balloon dilatation. STEMI patients without contraindication received 60 mg prasugrel, all others 600 mg clopidogrel loading. On-treatment platelet reactivity was measured by the Multiplate Analyzer, a new generation impedance aggregometer, latest at the time of PCI (but not earlier than 12 h after loading). In case of

PCI within 6 h after loading and/or significant thrombus burden, a glycoprotein IIbIIIa inhibitor was added and serial measurements until discharge were performed. In case of non-response (>49 U ADP-induced aggregation), antiplatelet therapy was individualized according to the protocol with either prasugrel loading (since June 2009), ticagrelor loading (since March 2011), or clopidogrel reloadings (until June 2009). The primary efficacy end point was definite stent thrombosis, the secondary endpoints probable stent thrombosis and cardiovascular death at 30 days. The safety endpoint was bleeding according to TIMI criteria.

Demographics: Fifty-three percent of the 1,008 consecutive patients presented with ACS (9% STEMI, 44% NSTEMI; 5% in cardiogenic shock). Thirty percent females, 32% diabetics, mean age 65±12, (range 29–90). Seventy-three percent complex lesions (b2/c), 11% LM and 58% LAD interventions. Ninety percent stentimplantation (94% 2nd gen. DES, 5% BMS); 2.2 stents/patient (range 1–12; total stent length 8–241 mm). Twenty-one percent glycoprotein inhibitor usage in ACS.

Platelet reactivity: 94.8% received clopidogrel, 5% prasugrel and 0.2% ticagrelor loading (known clopidogrel allergy). Clopidogrel non-response occurred in 30% (73±19 vs. 28±11 U, $p<0.0001$) and was treated in 70% with prasugrel, 27% with clopidogrel and 3% ticagrelor reloading to reach sufficient levels (22±12 U; $p<0.0001$ vs. initial response). Prasugrel non-response occurred in 2.4% (88±22 vs. 20±12 U, $p<0.0001$) and was successfully treated with ticagrelor reloading (30±13 U; $p<0.006$ vs. initial response).

Clinical endpoints: No acute stent thrombosis (0%) occurred in the total patient cohort. In the ACS cohort one fatal subacute definite stent thrombosis (0.099%; a patient with gram-negative sepsis and diarrhea), two probable stent thrombosis (0.2%; sudden death after discharge without autopsy) and 15 additional cardiovascular deaths (1.5%; 67% due to cardiogenic shock) occurred. In stable patients no stent thrombosis or cardiovascular death occurred (0%). No increase in bleeding complications (TIMI major and minor) could be detected in the individualized (2.7%) versus the standard group (2.5%; $p=0.6$)

Conclusions: A strict protocol of individualizing antiplatelet therapy with the Multiplate Analyzer is able to minimize early thrombotic events in an all-comers PCI population including STEMI patients to a so far unsurpassed degree, without increasing bleeding complications. Based on these findings we strongly recommend the incorporation of Multiplate guidance of dual antiplatelet therapy after PCI in routine clinical practice.

XIX-7

Percutaneous coronary intervention in lesions with intermediate hemodynamic significance in pressure wire

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Background: Recent studies have indicated that optimal medical therapy (OMT) is similarly effective as percutaneous coronary intervention (PCI) of significant stenoses regarding clinical outcome. However the long-term prognosis of intermediate lesions and the corresponding FFR value as indicated by the DEFER (≥0.75) and FAME trial (≥0.80) is still unclear. The aim of our study was to evaluate clinical event rates in patients with borderline lesions as determined by FFR.

Methods: We conducted a demographic analysis of patients with borderline coronary lesions as determined by pressurewire with a FFR ≥0.75 and ≤0.85. Between 2010 and 2012 eighty-six patients with objective evidence of myocardial ischemia who underwent angiography and subsequent FFR measurement were included. The primary outcome was a composite endpoint of death of all cause and myocardial infarction (MI) during a follow-up period of up to 2 years.

Results: There were no differences in clinical characteristics between the two groups. Complete follow-up was obtained in 97%. The observational period was up to 24 month. Among those patients 21.4% underwent PCI at baseline. There was a trend towards a lower incidence of MI in the conservative group with (9.1 vs. 16.7%, ns) with no deaths in both groups. There was no difference concerning secondary endpoints such as hospitalisation and serious adverse events except of MI.

Conclusion: OMT in patients with coronary stenoses of borderline significance is associated with a lower rate of myocardial infarction during our follow-up period. Longer prospective trials are needed to verify the role of PCI in this subgroup.

XIX-8

Late malapposition and endothelial coverage of drug-eluting-stents: a prospective optical coherence tomography analysis

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Introduction: Uncovered stent struts of drug-eluting stents (DES) are associated with late stent thrombosis. Early and late malapposition of stent struts may be the major mechanisms for uncovered struts. Data regarding coverage of malapposed struts are missing.

Material and methods: This study examines malapposition of DES and the coverage of late malapposed struts in patients who underwent elective percutaneous coronary intervention (PCI).

Fifty patients treated with 60 DES (25 Everolimus-eluting stents [EES], 18 Zotarolimus-eluting stents [ZES], 17 Biolimus-eluting stents [BES]) underwent optical coherence tomography (OCT) directly after implantation and after 12 months.

Results: Postintervention acute stent malapposition (ASM) occurred in 27 stents (45%). Of these, 19 stents resolved completely whereas 6 stents resolved partly (as well resolved a persisting segments). At this time-point, a total of 18 stents (30%) with late stent malappositions (LSM) were detected due to late acquired stent malapposition (LASM) in additional 10 stents. Fifteen of these 18 stents showed complete or almost complete (>80%) coverage of the malapposed struts, whereas 3 stents had no coverage of any malapposed strut.

Discussion: More than a quarter of electively implanted DES is associated with LSM. Uncoverage of malapposed struts applies only to a minority of stents with LSM. The reason for coverage/uncoverage and the clinical impact has to be determined.

XIX-9

Coronary computered tomography for systematic screening of coronary stent fractures in patients at high risk

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Background: Fracture of drug-eluting stents (DES) may mediate in-stent restenosis as well as stent-thrombosis, which clinically presents as myocardial infarction or sudden death. Coronary computered tomography (CCT) may be an appropriate method for the detection of a stent fracture (SF).

Aim: This study prospectively evaluated the incidence of stent fractures in high-risk patients using CCT and assessed the clinical relevance of this finding using catheter coronary angiography (CCA).

Methods: Patients with two or more risk factors for a stent fracture defined as (1) stent length ≥28 mm, (2) overlapping stents, (3) stent localization in the right coronary artery or saphenous vein graft and (4) vessel angulation ≥75° before implantation or stent angulation ≥45° after implantation were invited to undergo a CCT 6 months after the procedure. To differentiate between stent fracture and overlap failure all stents were identified on the CCT image by measuring the distance between edges and comparing these measurements with the known stent lengths. A coronary angiography including optical coherence tomography was recommended in patients with a partial or total stent gap. Patients without stent gaps but with pathological findings in the CCT who underwent coronary angiography served as controls.

Results: In 19 out of 65 patients (29 %) coronary CCT revealed a stent gap including 11 patients with a stent fracture (17 %) and 8 patients with an overlap failure (12 %). In the following CCA all stent gaps were confirmed by optical coherence tomography. A clinically relevant stent-related pathology could be detected in 4 out of 11 patients (36 %) with SF (in-stent-restenosis in two patients, chronic total occlusion and coronary aneurysm in one patient, respectively), but in none out of 9 controls (chi-square—$p<0.01$).

Conclusion: Stent gaps are frequent in high-risk patients. The majority of these gaps result from a stent fracture, which is often associated with a clinically relevant pathology. Therefore, screening for stent fractures using CCT in high-risk patients might be beneficial.

XIX-10

Malapposition, underexpansion and edge dissection in bioabsorbable vascular scaffolds (ABSORB™) and XIENCE™ stents: a comparison based on optical coherence tomography

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Background: In addition to the lesion characteristics, post-stenting results depend on the characteristics of the stent and on the inflating pressure of the stent balloon or post-dilatation balloon. The biodegradable ABSORB scaffold is characterized by a greater strut thickness (152.4 versus 81.3 µm), nevertheless, it has a greater flexibility (lower maximum compressive load required to deflect the device) compared to the XIENCE stent. Due to the fragility of the biodegradable scaffold the inflating pressure of the stent balloon or post-dilatation balloon is limited and suitable lesions have to be well pre-dilated before implantation.

Aim: To compare post-implantation results of the ABSORB scaffold and the XIENCE stent by using Optical Coherence Tomography (OCT).

Methods: Ten patients who underwent OCT after elective implantation of a bioabsorbable ABSORB scaffold were matched with 11 patients who underwent OCT after elective implantation of a XIENCE stent according to diameter and length of the device. Occurrence of malapposed stent-struts, stent-underexpansion and edge-dissection was compared between groups.

Results: Lesion characteristics were comparable between groups. Stent diameter and length were similar in ABSORB scaffolds (3.35±0.24 and 20.80±6.61 mm) and XIENCE stents (3.29±0.53 and 20.00±7.05 mm). The inflation pressure of the stent-balloon (ABSORB 13.1±2.4 versus XIENCE 14.0±3.1 atm) and the frequency of post-dilatation with a high-pressure balloon (ABSORB $n=6$ versus XIENCE $n=5$) were similar between groups. However, the diameter of the pre-dilatation balloon was greater in the ABSORB group (3.0±0.4 mm) compared to the XIENCE group (2.5±0.5 mm, $p=0.03$), the inflation time of the stent balloon was longer in the ABSORB group (52.7±14.0 s) than in the XIENCE group (31.0±8.1 s; $p<0.001$), and the inflation pressure of the post-dilatation high-pressure balloon was similar in both devices (15.67±4.97 versus 16.60±2.97 atm). The count of malapposed stent-struts between both groups (ABSORB 33.8±38.9 versus XIENCE 62.1±69.6) was not significantly different, although a trend can be suggested. Similarly, the incidence of stent-underexpansion (ABSORB $n=3$ versus XIENCE $n=6$) was not significant. The incidence of edge dissections was high in both groups (ABSORB $n=6$ versus XIENCE $n=6$).

Conclusion: The different characteristics of the devices require different deployment strategies. However, OCT post implantation demonstrated no adverse results concerning the biodegradable ABSORB scaffold compared to the XIENCE stent.

Postersitzung XX: Koronare Herzkrankheit

XX-1

Significant impact of gender on the association of HbA1c with angiographically diagnosed coronary atherosclerosis

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Introduction: The association of HbA1c with angiographically determined coronary atherosclerosis is unclear. In particular, it has not been investigated so far whether gender modulates the association of HbA1c with angiographically diagnosed coronary atherosclerosis. We therefore aimed at clarifying this issue.

Materials and methods: We enrolled a large consecutive series of 1,449 patients, 484 women and 965 men, who did not have previously known diabetes and who underwent coronary angiography for the evaluation of stable coronary artery disease. Significant coronary atherosclerosis was diagnosed in the presence of significant coronary stenoses with lumen narrowing ≥50 %.

Results: HbA1c values of <5.7% (normal according to ADA criteria), 5.7–6.4% (at risk of diabetes according to ADA criteria), and ≥6.5% (diabetes according to ADA criteria) were found in 36.4, 56.2, and 7.4% of women and in 44.2, 46.6, and 9.1% of men, respectively. The prevalence of angiographically diagnosed coronary atherosclerosis in these HbA1c categories was 31.2, 38.2, and 47.2% among women (ptrend = 0.041) and 63.2, 65.3 and 64.8% among men (ptrend = 0.589). In logistic regression models, HbA1c as a continuous variable was a strong predictor of coronary atherosclerosis among women (adjusted OR for a 1% increase in HbA1c 1.61 [95% CI 1.07–2.43]; $p=0.024$) but not among men (OR 0.92 [0.74–1.13]; $p=0.416$). The interaction HbA1c by gender was significant ($p=0.022$), indicating that HbA1c was a significantly stronger predictor of coronary atherosclerosis among women than among men.

Discussion: We conclude that gender has a significant impact on the association of HbA1c with angiographically diagnosed coronary atherosclerosis among subjects without previously known diabetes.

XX-2

Gender does not significantly modulate the association between markers of inflammation and the metabolic syndrome among patients with stable coronary artery disease

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Introduction: The metabolic syndrome (MetS) confers a stronger increase in cardiovascular event risk among women than among men. The MetS is associated with elevated markers of inflammation, and inflammatory markers have been linked to cardiovascular event risk in MetS patients. We therefore tested the hypothesis that CRP and leukocyte count are more strongly associated with the MetS among women than among men.

Materials and methods: We measured CRP and leukocyte counts in a large high-risk cohort of 1,041 patients with angiographically proven stable coronary artery disease, enrolling 371 women and 670 men. The MetS was diagnosed according to National Cholesterol Education Panel III criteria. Interaction analyses were performed using analysis of covariance models, applying a general linear model approach.

Results: The prevalence of the MetS was significantly higher among women than among men (40.2 vs. 31.2%; $p=0.004$). Both CRP and leukocyte counts were significantly higher in patients with the MetS than in those without MetS among women (0.50±0.58 vs. 0.41±0.83 mg/dl; $p=0.001$ and 6.9±1.7 vs. 6.3±1.8 G/l; $p<0.001$, respectively) and also among men (0.47±0.67 vs. 0.40±0.72 mg/dl; $p<0.001$ and 7.1±1.8 vs. 6.6±1.8 G/l; $p<0.001$, respectively). Formal interaction analyses did not show a significant MetS by gender interaction neither with regard to CRP ($p=0.788$) nor to leukocyte count ($p=0.333$), indicating that the associations between CRP and leukocyte count did not differ significantly between women and men.

Discussion: From the data of this large study we conclude that gender does not significantly modulate the association between CRP or leukocyte count and the MetS among patients with stable coronary artery disease.

XX-3

Serum omentin significantly predicts cardiovascular events both in patients with the metabolic syndrome and in subjects who do not have the metabolic syndrome

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Introduction: Some recent small cross-sectional studies have described associations of the novel adipocytokine omentin with atherosclerosis. However, no prospective data on the power of omentin to predict cardiovascular events are available.

Materials and methods: We therefore measured serum omentin in a series of 297 patients undergoing coronary angiography for the evaluation of established or suspected stable CAD; the metabolic syndrome (MetS) was defined according to national cholesterol education programme adult treatment panel III criteria; cardiovascular events were recorded over a mean follow-up period of 3.2 years.

Results: During the follow-up period, 18.4% of our patients suffered cardiovascular events, corresponding to an annual event rate of 5.8%. In the total study population, serum omentin significantly predicted cardiovascular events both univariately (standardized adjusted HR = 1.47 [1.21–1.78]; $p<0.001$) and after adjustment for age, gender, BMI, diabetes, hypertension, LDL cholesterol, HDL cholesterol and smoking (HR = 1.49 [1.21–1.82]; $p<0.001$). From our patients, 98 had the MetS and 199 did not have the MetS. In both of these patient subgroups serum omentin strongly predicted cardiovascular events both univariately (HRs = 1.51 [1.15–2.00]; $p=0.003$ and 1.41 [1.08–1.84]; $p=0.011$, respectively) and after adjustment for age, gender, BMI, diabetes, hypertension, LDL cholesterol, HDL cholesterol and smoking (1.56 [1.09-2.25]; $p=0.016$ and 1.48 [1.12–1.97]; $p=0.006$, respectively).

Discussion: From this first prospective evaluation of the cardiovascular risk associated with serum omentin we conclude that elevated serum omentin is a strong predictor of cardiovascular events both among patients with the MetS and among subjects who do not have the MetS.

XX-4

The metabolic syndrome significantly affects the association between resting heart rate and cardiovascular mortality in women

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Introduction: Epidemiological studies suggest that the resting heart rate (RHR) is an independent predictor of cardiovascular events. However, the power of the RHR to predict cardiovascular events in women with the metabolic syndrome (MetS) is not known.

Materials and methods: We therefore prospectively investigated the relationship between RHR and cardiovascular events in 243 consecutive female patients undergoing coronary angiography for the evaluation of coronary artery disease (CAD) over a follow-up period of 7.1±0.1 years. The MetS was defined according to National Cholesterol Education Programme Adult Treatment Panel III criteria.

Results: During follow-up, 13.2% of our women died from cardiovascular disease. In the total study population, the RHR significantly predicted cardiovascular mortality (standardized adjusted

HR 1.55 [1.08–2.22]; $p=0.015$). Also, among female patients without the MetS ($n=158$), a higher baseline RHR indicated a significantly increased risk of cardiovascular mortality (HR=2.07 [1.411–3.04], $p<0.001$). However, the RHR did not significantly affect cardiovascular mortality (HR=0.52 [0.19–1.41]; $p=0.200$) in patients with the MetS. An interaction term RHR x MetS was significant ($p=0.003$), indicating that the risk conferred by a high RHR was significantly higher in women without the MetS than in those with the MetS.

Discussion: We conclude that among angiographied female coronary patients, the MetS status significantly affects the association of the RHR with cardiovascular mortality: The RHR is a strong predictor of cardiovascular mortality among women without the MetS, but not among those who have the MetS.

XX-5

Association between hs-CRP (high sensitive C reactive Protein), coronary artery disease severity (CAD), diabetes mellitus (DM) and NT-proBNP

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Background: C-reactive protein (CRP) is an acute phase protein and activated by inflammatory cytokines. Elevated level of high sensitive CRP (hs-CRP) has been proved to predict adverse outcome of ST-segment elevation myocardial infarction (STEMI). A hsCRP level above 2 mg/L has been associated with increased risk of cardiovascular events.

Aim: The aim of our study was to investigate the correlation between circulating hs-CRP value and severity of coronary artery disease (CAD), and the marker of heart failure NT-proBNP in patients with previous STEMI.

Method: Forty-four consecutive patients (84.1% male, 58.7±12.4 years) with previous myocardial infarction (median 24 months, 25–75% interquartile range /IQR/8–62 months) were screened for elevated levels ofhs-CRP between a 6-month period of September 2012 and February 2013.

Results: The median hs-CRP value was 1.09 mg/L (IQR: 0.50–3.9 mg/L), the median NT-proBNP 186 pg/ml (IQR: 93–599 pg/mL). The mean LDL-cholesterol and cholesterol levels were 99.2±43.3 mg/dl and 178.9±584 mg/dl, respectively. Four patients (9.1%) underwent previous coronary artery bypass graft surgery (CABG), three patients (6.8%) had peripheral vascular disease (PVD) and six patients (13.6%) had diabetes mellitus (DM). No correlation was found between hs-CRP value and NT-proBNP, age, elevated levels of LDL-cholesterol or cholesterol, severity of CAD, presence of PVD or previous CABG. Trends towards higher hs-CRP (3.93±3.2 vs 2.39±2.58 mg/L) and NT-proBNP (603±472 vs 382±550 pg/mL) levels were found in diabetic patients. Male patients were younger (57±11 vs 66±17 years, $p=0.091$) and showed a non-significantly elevated hsCRP level (2.73±2.88 vs 1.91±1.40 mg/L) as compared with female patients.

Conclusion: Elevated levels of hs CRP in a limited cohort of patients with history of myocardial infarction was not associated with the severity of CAD, severity of heart failure, reflected by NT-proBNP, or incidence of diabetes mellitus.

XX-6

Performance of a simple five-variable score model for the prediction of invasively evaluated significant coronary artery disease among elective patients

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Background: The evaluation of the probability of the presence of significant coronary artery disease (CAD) belongs to the most common questions in daily cardiological practice. Despite the increasing use of (cost intensive) non-invasive tests, the mainstay of clinical judgement might be reduced to few easily assessable parameters. The aim of this study was to assess the performance of a multivariable derivation model to predict the presence of CAD among elective patients.

Methods: Three thousand five hundred and seven consecutive patients undergoing elective coronary angiography for the evaluation of CAD were analysed. An electrocardiogram was performed for each patient and cardiovascular risk factors were assessed by a standardised questionnaire and routine blood chemistry. CAD was graded by visual estimation of lumen diameter stenosis (significant stenoses were defined as lumen diameter reduction ≥70%) into non-significant CAD, 1-, 2- or 3-vessel disease (VD), or as non-CAD.

Multiple logistic regression analysis was performed on a restricted number of predictors to estimate the probability of the diagnosis of 1-VD, 2-VD or 3-VD. To evaluate model performance the discriminating ability was measured by the concordance (c) -statistic, here equal to the area under the receiver operating characteristic curve, and the calibration by comparing the observed outcomes and the predictions.

Results: Sixty-seven percent (2,355) of the 3,507 patients were men, 58% (2,051) of the patients had a 1-, 2- or 3 VD and 41.5% (1,456) had non- or non-significant CAD. Patients with significant CAD more often had arterial hypertension (57.5 vs 42.5%, $p=0.003$) and were more frequently on statin therapy (36.7 vs 31.6%, $p=0.001$), while no differences were found for diabetes mellitus, nicotine consumption, or positive family history. Moreover, patients with significant CAD were older (64.5±10.5 vs 62.3±11.6 years, $p<0.001$) and had lower high-density lipoprotein levels (51.7±15.5 vs 55.6±18.0 mg/dl, $p<0.001$). After modelling for gender, age, HDL cholesterol, ECG changes (sinus rhythm yes or no) and medical history (presence or absence of any kind of angina pectoris, former percutaneous intervention or bypass-surgery) the c-statistic amounted to 0.77 (95% CI 0.75–0.79), the range of predicted possibilities was rather wide, and the model calibrated well.

Conclusion: The five-variable model performed very well in predicting the diagnosis of significant CAD. Validation on a separate group of patients, at the same institution and/or on a similar patient group elsewhere, would enable composing a definite score model, which enhances the diagnostic tools easily available to cardiologists.

XX-7

The baseline left ventricular ejection fraction significantly modulates the power of CRP to predict cardiovascular and total mortality in patients with coronary artery disease

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Introduction: C-reactive protein (CRP) is an important prognostic marker in patients at intermediate cardiovascular event risk and is elevated both in patients with coronary artery disease (CAD) and in those with impaired left ventricular ejection fraction (LVEF). However, no data on the power of CRP to predict cardiovascular events in CAD patients with impaired LVEF are available.

Materials and methods: Cardiovascular events were recorded over a follow-up period of 8 years in 508 patients with angiographically proven stable CAD. Impaired LVEF was diagnosed when the LVEF was <50 %.

Results: Baseline CRP was significantly higher in CAD patients with impaired LVEF (n=84) than those without impaired LVEF (n=424; 1.1±1.7 mg/dl vs. 0.6±0.6 mg/dl; p=0.004). Prospectively, CRP after multivariable adjustment significantly predicted cardiovascular (standardized HR 1.09 [1.00-1.20]; p=0.042) and total mortality (standardized HR 1.11 [1.03–1.21]; p=0.004) in patients with normal LVEF, but not in those with impaired LVEF (standardized adjusted HRs 0.85 [0.59–1.22]; p=0.381 and 1.03 [0.81–1.31]; p=0.762, respectively). Interaction terms LVEF × CRP were significant for both total and cardiovascular mortality (p=0.014 and p=0.017, respectively), indicating that the respective risks indicated by a high CRP were significantly higher in patients without normal than in those with impaired LVEF.

Discussion: We conclude that the baseline LVEF significantly modulates the power of CRP to predict cardiovascular and total mortality in patients with CAD.

XX-8

Geringere koronare Kalzifikationen bei Extrem-Dippern

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Einleitung: Hypertensives Blutdruckverhalten insbesondere mit veränderter zirkadianen Blutdruckrhythmik gehen mit einem erhöhtem kardio- und zerebrovaskulärem Risiko einher. In dieser Analyse wurde untersucht ob eine Korrelation zwischen den unterschiedlichen zirkadianen Blutdruck-Mustern und dem Auftreten koronarer Kalzifikationen besteht.

Methoden: 305 Patienten aus dem Kollektiv der „Austrian Stroke Prevention Family Study“ wurden kardiologisch exploriert. Die Zuordnung des Dipping-Status erfolgte nach den aktuellen Richtlinien der Österreichischen Gesellschaft für Hypertonie in Dipping (nächtlicher Blutdruckabfall >10 %), Nondipping (nächtlicher Blutdruckabfall <10 %), Extrem-Dipping (nächtlicher Blutdruckabfall >20 %) und Reverse Dipping (nächtlicher Blutdruckanstieg). Das Auftreten oder Fehlen koronarer Kalzifikationen in der Mehrschicht-Computertomographie wurde mittels Agatston Score beurteilt (Agatston-Score >0 vs Agatston-Score =0).

Ergebnisse: Die Patienten (58 % weiblich) hatten ein mittleres Alter von 65±10 Jahren, der mittlere Blutdruck betrug 133±12/78±7 mmHg. Es zeigte sich ein mittlerer Cholesterinwert von 209±41 mg/dl (HDL 68±21 mg/dl; LDL 118±33 mg/dl), 16% Raucher. 92 Patienten waren Nondipper, 26 Reverse-Dipper, 133 Dipper und 54 Extrem-Dipper.

In der Gruppe der Extrem-Dipper zeigten signifikant mehr Patienten einen Agatston Score =0 als in allen anderen Untergruppen (53,7 vs 34,3 %; p=0,007). Alter, Geschlecht, 24 h- und ambulante Blutdruckmessung, Lipid-Status und Raucherstatus waren nicht signifikant unterschiedlich zwischen der Gruppe der Dipper und den Gruppen anderer zirkadianer Blutdruckverläufe.

Konklusion: Patienten mit einem Extrem-Dipping Blutdruckprofil zeigten unabhängig vom 24 h Blutdruckwert, signifikant häufiger blande Koronararterien als Patienten mit anderen zirkadianen Profilen.

Postersitzung XXI: Pulmonale Hypertension 2

XXI-1

Pulmonary vascular reactivity in pulmonary hypertension due to left heart disease

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Purpose: Pulmonary hypertension (PH) due to left heart disease (LHD) is the most common subset of PH. It is defined by an increase of mean pulmonary artery pressure (mPAP) ≥25 mmHg in the presence of a mean pulmonary capillary wedge pressure (mPCWP) >15 mmHg. In the fifth World Symposium on Pulmonary Hypertension in Nice, PH due to LHD (post-capillary PH) was subdivided into two phenotypes, “isolated” post-capillary PH (diastolic pulmonary vascular pressure gradient [DPG] <7 mmHg) and “combined” pre-capillary and post-capillary PH (DPG ≥7 mmHg). Recent data have shown that patients with post-capillary PH and a DPG ≥7 mmHg have an increased mortality and significant pulmonary vascular disease. We hypothesize that these patients may benefit from vasodilator treatment. The aim of this study was to compare the degree of acute vasoreactivity to inhaled nitric oxide (NO) in “combined” pre-capillary and post-capillary PH to that of “isolated” post-capillary PH.

Methods: A prospective data set of 94 patients with PH due to LHD undergoing first diagnostic right heart catheterizations at rest and after inhalation of 40 ppm NO was analyzed. Fifty-seven patients were classified as “isolated” post-capillary PH (DPG <7 mmHg) and 36 as “combined” pre-capillary and post-capillary PH (DPG ≥7 mmHg).

Results: The strongest decrease of mPAP was observed in patients with “combined” pre-capillary and post-capillary PH (−5.4±3.7 mmHg, p<0.001). In contrast, mPAP did not change upon NO inhalation in patients with “isolated” post-capillary PH (−0.2±5.3 mmHg, p=0.738).

Conclusion DPG identifies patients with PH due to LHD who have significant pulmonary vascular disease that is reactive to inhaled NO.

XXI-2

Baseline hemodynamic predictors of treatment response in pulmonary arterial hypertension

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Purpose: Pulmonary arterial hypertension (PAH) is a progressive disease characterized by an increase in pulmonary vascular resistance (PVR), by right ventricular dysfunction, and ultimately, right heart failure and death. Although PVR can be reduced by vaso-

dilator treatment, PVR remains elevated above normal in the vast majority of patients, and prognosis remains poor. Recent data suggest that a threshold PVR has to be reached to effectively prolong survival. The purpose of this study was to identify baseline hemodynamic predictors of treatment response in patients with PAH.

Methods: A retrospective data set of 3,107 all-comers undergoing first diagnostic right and left heart catheterizations at rest was analyzed. One thousand and ninety-four patients were classified as post-capillary pulmonary hypertension (PH) and 137 as pre-capillary PH. Of these, 23 patients had idiopathic PAH (iPAH). Hemodynamic cut-offs for the discrimination between iPAH and post-capillary PH were determined by receiver operating characteristic (ROC) curves. A prospective data set of 541 PAH patients from the United Therapeutics (UT) prospective database receiving treprostinil or placebo was utilized for the validation of hemodynamic cut-offs.

Results: ROC analysis identified mPCWP of 12 mmHg (area under the curve [AUC]: 0.99) and diastolic pulmonary vascular pressure gradient (DPG) of 20 mmHg (AUC: 0.97) as the best hemodynamic values for the differentiation between iPAH and post-capillary PH. Patients with mPCWP <12 mmHg, DPG >20 mmHg or a combination of both had a significant improvement in hemodynamics under treprostinil compared to corresponding placebo groups, with a decrease in PVR of 3.1WU [1.3, 4.9], 2.9WU [1.0, 4.7] and 3.6WU [1.5, 5.8], respectively. By contrast, hemodynamics did not improve in patients with mPCWP ≥12 mmHg or DPG ≤20 mmHg, or both.

Conclusion: An mPCWP of less than 12 and a DPG of over 20 mmHg identify PAH patients who are likely to have a significant benefit under treatment with treprostinil. The data indicate that mPCWP and DPG are useful to identify pulmonary vascular disease that is responsive to prostacyclin.

XXI-3

Splenectomy delays thrombus resolution

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Purpose: Splenectomy is a clinical risk factor for chronic thromboembolic pulmonary hypertension (CTEPH). Recent data suggest that CTEPH is a complication of venous thromboembolism. Therefore, we investigated the effects of splenectomy on venous thrombus resolution.

Methods: We analyzed phospholipid profiles in thrombotic material from splenectomized and non-splenectomized CTEPH patients using mass spectrometry. To study the role of these phospholipids in thrombus resolution, we employed a mouse model of stagnant flow venous thrombosis and performed splenectomy in the study group. We examined murine thrombi using immunohistochemistry, real time PCR and mass spectrometry and murine blood using FACS. To analyze angiogenesis, cell proliferation and sprouting assays were performed.

Results: We observed a different phospholipid profile in splenectomized CTEPH patients compared with non-splenectomized CTEPH patients. In the mouse model, prior splenectomy was associated with larger and more persistent thrombi. FACS revealed higher counts of procoagulant platelet microparticles and increased leukocyte–platelet aggregates compared with animals after a sham splenectomy. Mass spectrometry disclosed a relative enrichment of anionic phospholipids like phosphatidylserine (PS) in murine thrombi proximal to the caval ligation after splenectomy. Thrombus histologies demonstrated fewer vessels. Compared with neutral phospholipids, PS enriched phospholipids inhibited angiogenesis in a cell proliferation assay and in a sprouting assay.

Conclusions: The data confirm that an increase in circulating negatively charged phospholipids as a consequence of splenectomy enhances thrombus growth by amplifying platelet activation, and delays thrombus resolution by inhibition of thrombus angiogenesis.

XXI-4

D-dimer in chronic thromboembolic pulmonary hypertension

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Background: Chronic thromboembolic pulmonary hypertension (CTEPH) is one of the leading subsets of pulmonary hypertension (PH), and is characterized by organized thrombus obstructing major pulmonary arteries. We hypothesized that the inability of thrombus resolution in CTEPH is due to an "inflammatory thrombosis phenotype" triggering ongoing thrombosis.

Objective: We measured D-dimer, fibrinogen, antithrombin (AT), and CRP plasma levels in CTEPH patients, and calculated their role as biomarkers of disease severity.

Methods One hundred and ninety CTEPH patients diagnosed between 1995 and 2010 were included in this retrospective data analysis. Biomarkers at the time of diagnosis were measured by ELISA. Matched patients with dyspnea, and excluded PH served as control group. Statistical analyses were performed using SAS 9.3 and R 2.14.2.

Results: Median D-dimer was 0.53 μg/L (0.23–0.84). A proportional hazard model including age and fibrinogen levels revealed D-Dimer as a predictor of survival (p 0.0012). D-dimer plasma levels ≤0.52 μg/L were associated with a better survival in CTEPH patients compared with higher D-dimer levels. A D-dimer level of 0.61 μg/L was the optimal threshold for predicting an event (lung transplantation or death) within 5 years, with a sensitivity and specificity of 0.74 and 0.76, respectively.

Conclusions D-dimer could serve as a predictor of outcome in CTEPH.

XXI-5

Hemodynamic correlates of right ventricular afterload and pulmonary artery pulsatility under treatment with prostacyclin: retrospective analysis of changes from baseline in pulmonary arterial hypertension patients

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Purpose: Survival in pulmonary arterial hypertension (PAH) is significantly dependent on right ventricular (RV) function. We characterized the change from baseline in hemodynamic correlates of RV afterload that reflects the arterial load to steady flow (pulmonary vascular resistance [PVR]) and parameters of oscillatory load,

including pulmonary arterial compliance (PAC) and pulmonary valve resistance (ZVA).

Methods: Parameters of RV afterload were analyzed in a prospective data base of 933 PAH patients receiving treprostinil or placebo (United Therapeutics prospective data base). Univariate proportional hazards regression model using cubic spine function was constructed to assess the effects of parameters on death and lung. Receiver operating characteristic (ROC) analysis was used to assess the optimal hemodynamic cut-offs.

Results: Within 12 weeks parameters of oscillatory load did not change, while PVR was significantly reduced in patients on treprostinil compared to placebo (Mean, [95 %C.I.]: −2.6WU [−4.2, −1.0]). Because of the fixed time constant in the relation between resistance and compliance, PVR threshold for a significant change in pulsatile parameters was assessed. ROC analysis revealed that PVR has to be reduced by at least 3WU to achieve an improvement in ZVA, (area under the curve [AUC]: 0.84), whereas an increase in PAC is already reached after a reduction of 1WU (AUC: 0.90). However, only baseline PVR ($p<0.001$) and ZVA ($p<0.001$) were predictors of survival/freedom of lung transplantation. Patients with improved PAC and ZVA had a larger reduction in afterload (ΔmPAP (mmHg): −3±7.8, −3.6±7.7; ΔPVR (WU): −3.1±4.5, −3.0±4.6) than patients with worsened PAC and ZVA (ΔmPAP (mmHg): 2.2±8.1, 2.2±8.2; ΔPVR (WU): 2.5±4.5; 2.1±4.7).

Conclusion: PVR is the key steady flow parameter that is changed under treatment with treprostinil, while parameters of pulsatility did not change significantly over 12 weeks. Baseline PVR ($p<0.001$) and ZVA ($p<0.001$) were predictors of survival/freedom of lung transplantation. The data show that a minimum improvement of 3WU for PVR is essential to reach a decrease of pulmonary valve resistance ZVA.

XXI-6

Hemodynamic assessment of patients with pulmonary hypertension due to lung disease and/or hypoxia

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Purpose: Current pulmonary hypertension (PH) guidelines classify PH due to lung disease and/or hypoxia (group 3) as pre-capillary PH (mean pulmonary artery pressure [mPAP] ≥25 mmHg and a mean pulmonary capillary wedge pressure [mPCWP] ≤15 mmHg). In the setting of lung disease, multiple mechanisms of disease play a role apart from classical pulmonary arteriopathy, hypoxia, hypercapnia, mechanical stress of hyperinflated lungs, emphysematous and fibrotic changes, inflammation and toxic effects of cigarette smoke. We hypothesized that a significant proportion of patients with PH due to lung diseases carries a post-capillary component.

Methods: A large database ($n=3,107$) of right and left heart catheterizations was interrogated consecutively.

Results: Of 291 patients with lung diseases and/or hypoxia at first diagnostic right and left heart catheterization, 96 patients had normal hemodynamics ("Non-PH" mPAP <25 mmHg). Of the remaining 195 patients with PH, 53 were classified as pre-capillary PH (mPCWP ≤15 mmHg), and 142 had elevated left ventricular filling pressures (mPCWP >15 mmHg; Fig. 1 and Table 1). Multivariate analysis identified stable ischemic heart disease as an independent predictor of survival ($p=0.014$).

Conclusion: The data demonstrate that a significant proportion of patients with PH due to lung disease suffers from post-capillary pulmonary hypertension. This observation may impact treatment decisions.

Table 1. Age and hemodynamic characteristics of patients with pulmonary hypertension due to lung disease and /or hypoxia

	PH due to lung diseases and/or hypoxia		*p* value
	mPCWP ≤15 mmHg	mPCWP >15 mmHg	
	(*n*=142)	(*n*=53)	
Age	59.9±13.6	63.5±12	0.074
SaO_2 (%)	89.9±10	94.5±2.3	<
SvO_2 (%)	64.1±11.3	61±10.3	0.108
mRAP (mmHg)	7±3.3	12±5.4	<
sPAP (mmHg)	59.2±25.2	58.2±15.7	
dPAP (mmHg)	25.2±10	27.1±8	
mPAP (mmHg)	38.2±15.3	39.2±9.9	
mPCWP (mmHg)	10.6±3.1	25.7±7.4	<
CI (mmHg)	3±1.1	2.5±0.6	
TPG (mmHg)	27.6±16.4	13.6±8.3	<
DPG (mmHg)	14.9±11.2	1.4±6.5	<
PVR (dyne*s/cm^5)	472.5±394.9	247.4±161.6	<

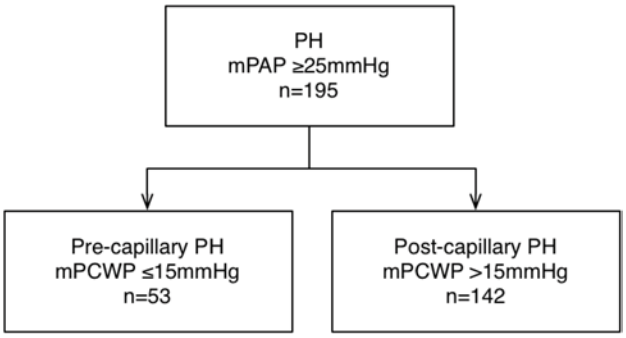

Fig. 1 Patient disposition

XXI-7

Pulmonary hypertension in aortic stenosis

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Purpose: We assessed the prevalence of pulmonary hypertension (PH) in aortic stenosis.

Methods: A data set of 3,107 all-comers undergoing first diagnostic right heart catheterization (RHC) was analyzed.

Results: In 358 patients a diagnosis of severe degenerative aortic valve stenosis had been established (aortic valve mean gradient 48.7±18.2 mmHg, valve area 0.7±0.2 cm^2), with RHC as a routine preoperative procedure preceding diagnostic coronary angiography (58.7 % males, age 69±12 years). In 182 patients with aortic stenosis (51 %) PH (i.e., mean pulmonary artery pressure (mPAP) ≥25 mmHg) was documented. In 178 patients pulmonary capillary wedge pressure was ≥15 mmHg. 162 patients of those were classified as "isolated" post-capillary PH (diastolic pressure gradient [DPG] <7 mmHg) and 16 as "combined" pre- and post-capillary PH (DPG ≥7 mmHg). There was a moderate correlation between

invasively measured systolic pulmonary artery pressure (sPAP) and sPAP estimated by echo ($r=0.684$). In 41 patients (11 %) PH was not detected by echocardiography.

Conclusion: The data of this large unselected patient population with severe degenerative aortic stenosis demonstrate that PH is prevalent in this condition (50 % of patients affected), and that one third of patients with PH classifies as "combined" pre- and post-capillary PH.

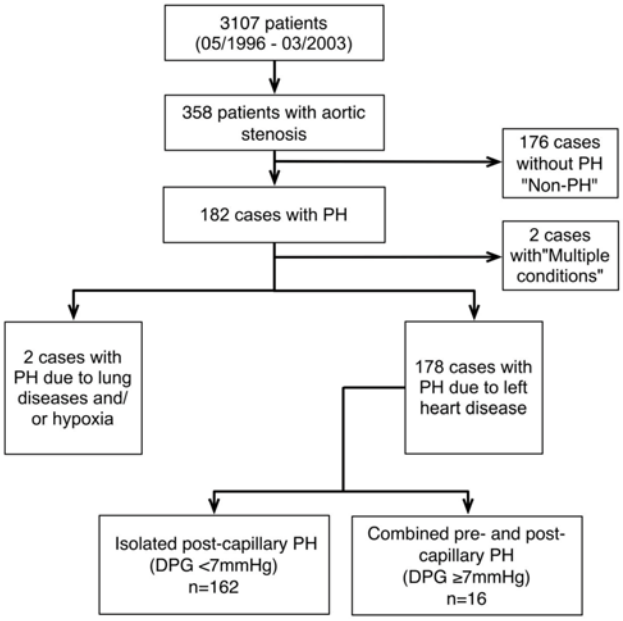

Fig. 1 Prevalence of pulmonary hypertension (PH) in aortic stenosis

XXI-8

Hemodynamic assessment of pulmonary hypertension in corrected versus non-corrected grown-up congenital heart disease

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Purpose: Pulmonary arterial hypertension (PAH) associated with congenital heart disease (CHD) is thought to result from persistent exposure of the pulmonary vasculature to increased blood flow of systemic-to-pulmonary shunts, and comprises a typical pulmonary arteriopathy in association with biventricular heart failure. Endothelial dysfunction has been demonstrated in individuals with congenital heart disease both before and after surgery.

Methods: Three thousand one hundred and seven right and left heart catheterizations were analyzed. Diagnoses were validated on the grounds of patient histories, imaging, clinical data and pathoanatomic evidence (2,369 complete data sets). Two hundred and forty-one data sets were from patients with CHD.

Results: Our database showed pre-tricuspid defects in 162 patients, post-tricuspid defects in 36 patients and complex lesions in 43 patients. Forty-four patients with CHD had undergone any correction. PH was observed in 27 patients with a correction status and in 22 patients with non-corrected CHD. Mean survival of "corrected" patients with PH (7.3 years) was worse than in "non-corrected" patients PH (11.4 years; $p=0.009$, Fig. 1). There was a significant difference in age ($p=0.05$), mixed venous saturation (SvO_2) ($p=0.01$), diastolic pulmonary artery pressure (dPAP) ($p=0.018$) and mean pulmonary capillary wedge pressure (mPCWP) ($p=0.006$) between "corrected" patients with PH and PH patients who did not undergo surgical or interventional correction (Table 1).

Conclusion In an analysis accounting for confounders, grown-up patients with PH due to CHD after any corrective procedure show a worse survival than similar patients without correction.

Table 1. Hemodynamic data of patients with PH due to congenital heart disease classified by correction status

	PH associated with congenital heart disease		*p* value
	Corrected	Non-corrected	
	(*n*=27)	(*n*=22)	
Age (years)	44.4±20.3	55.1±16.1	0.05
SaO_2 (%)	92.3±9.1	93.5±4	0.659
SvO_2 (%)	69±12	78.3±10.2	0.01
Hb (g/dL)	13.5±3.3	12.8±2.5	0.421
CI (L/min/m²)	2.8±1.4	2.9±1.5	0.793
SAP (mmHg)	92.6±13.3	102.9±19.1	0.116
LVEDP (mmHg)	14.8±4.7	14.2±5.6	0.835
mRAP (mmHg)	10.6±5.6	8.7±3.8	0.206
RVEDP (mmHg)	14.2±5.9	12±3.9	0.168
mPAP (mmHg)	50.6±25.9	41.1±13.3	0.124
SVRI (WU)	12.3±5	12±4.2	0.887
PVRI (WU)	4.6±4.3	4.5±3.6	0.943

CI cardiac index, *Hb* hemoglobin, *LVEDP* left ventricular end-diastolic pressure, *mPAP* mean pulmonary artery pressure, *mRAP* mean right atrial pressure, *PVRI* pulmonary vascular resistance index, SaO_2 arterial oxygen saturation, *SAP* systemic artery pressure, SvO_2 mixed venous oxygen saturation, *SVRI* systemic vascular resistance index

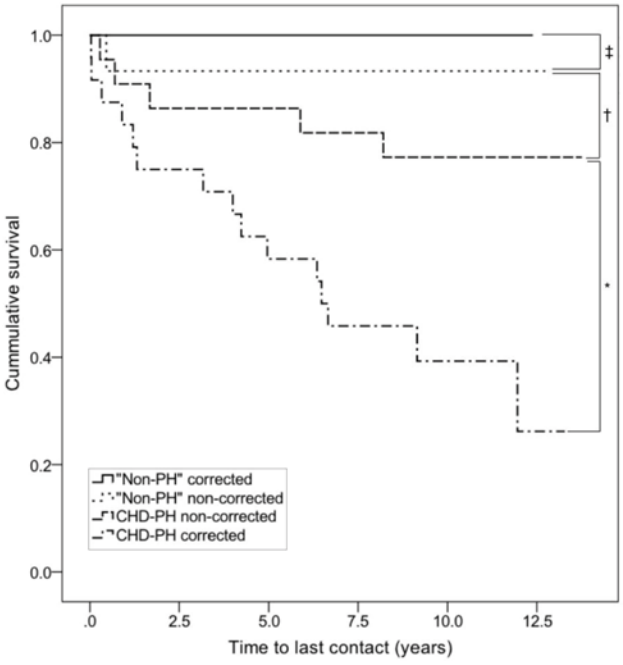

Fig. 1 Mean survival of "corrected" and "non-corrected" patients

XXI-9

Formation of typical vascular lesions in a new experimental model of pulmonary arterial hypertension

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Background: Pulmonary arterial hypertension (PAH) is a severe and progressive disease characterized by obstruction of small pulmonary arteries leading to increased pulmonary vascular resistance. The key pathologic finding in this disease is a negative pulmonary vascular remodeling process with total vessel occlusion and a monoclonal expansion of collateral endothelial cells. It has been proposed that impaired vascular endothelial growth factor (VEGF) signaling plays a significant role in this process. Aim of our study was to investigate whether inhibition of VEGFR-2 (KDR) by direct gene manipulation may replicate classical pulmonary vasculopathy.

Methods: We utilized mice with conditional VEGFR-2/KDR knock-out in endothelial cells (KDR−-/−). KDRflox/flox/Tie-2Cre and KDRflox/flox/Tie-2 mice were injected intraperitoneally with tamoxifen for 3 weeks to induce the knock-out. KDR−/− mice and wild type littermates were held in an environmental chamber with FiO_2 of 10 % or under normoxia for 2, 4, and 6 weeks. We investigated the effect of KDR deletion and chronic normobaric hypoxia on pulmonary hemodynamics and right ventricular hypertrophy.

Results: KDR−/− mice showed significantly increased right ventricular pressures (RVSP's) and Fulton indices after 2, 4, and 6 weeks under normoxic conditions, compared with wild type controls. Both KDR−/− and wild type mice showed increased right ventricular pressures under normobaric hypoxia. KDR−/− mice revealed significantly higher right ventricular pressures (Fig. 1) and Fulton indices than controls after 4 and 6 weeks. Knockout mice showed a significant increase in pulmonary arterial wall thickness after chronic hypoxia compared to control mice. Lung histologies demonstrated neointimal thickening and vessel occlusions in lungs of KDR−/− mice resembling human pulmonary arteriopathy.

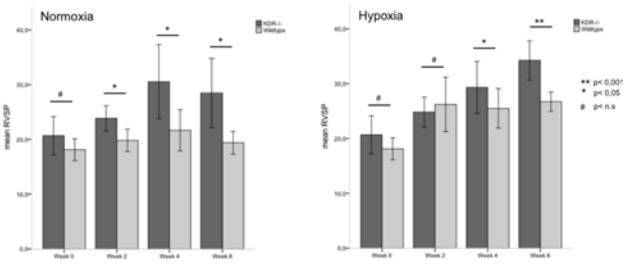

Fig. 1 Effect of KDR deletion and chronic normobaric hypoxia on pulmonary hemodynamics and right ventricular hypertrophy

Postersitzung XXII: Rhythmologie 3

XXII-1

Aldosterone to renin ratio is associated with QTc changes in patients with arterial hypertension: the Styrian hypertension study

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Introduction: Aldosterone to renin ratio (ARR), which reflects inappropriate aldosterone activity, is used as a screening tool for diagnosing primary aldosteronism (PA). Accumulating evidence suggests that even in essential hypertensives a high ARR may indicate an increased cardiovascular risk. The underlying mechanisms are still unclear but might be related to aldosterone effects on the myocardium. We therefore aimed to elucidate whether ARR is associated with the QTc interval.

Materials and methods: We examined a cohort of hypertensive patients derived from a tertiary care centre at the local medical university hospital. We performed 24 h ambulatory blood pressure measurements (ABPM) and calculated QTc according to Framingham and linear regression formulas and by adhering to the AHA/ACCF/HRS 2009 guideline for surface ECG interpretation. Plasma concentrations of aldosterone and renin were measured by Radio-ImmunoAssay (RIA) methods.

Results: We included 172 hypertensive patients (age: 59.6±11.3years; 51.2 % females). In linear regression analyses adjusted for age, sex, body mass index and systolic ABP, ARR was significantly associated with QTc(Framingham) and with QTc(linear regression) (median = 430 ms [IQR = 400–450 ms]; beta coefficient: 0.19; $p = 0.021$ for both). These associations remained significant after additional adjustments for other possible confounders including antihypertensive medications, cardiovascular risk factors, 24 h urinary sodium and serum electrolytes.

Discussion: We found a significant association between ARR and QTc in hypertensive patients. Further studies are needed to elucidate whether QT prolongation contributes to the increased cardiovascular risk in patients with a high ARR and whether cardiovascular protective effects of MR blockers are related to the underlying mechanism of QTc changes.

XXII-2

Long-term pulmonary vein isolation: comparing the efficacy of remote magnetic navigation with conventional lasso-controlled interventions

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Purpose: Remote magnetic navigation (RMN) and ablation in patients with atrial fibrillation (AF) should facilitate these complex interventional procedures, reducing the importance of operator skills. In order to evaluate the efficacy of ablations with the help of RMN (with the Stereotaxis-system) the long-term isolation of pulmonary veins (PV) by RMN was compared with that of conventional

lasso-controlled ablations in redo procedures, evaluating the PV-connections with 20-polar lasso-catheters.

Methods: Some of the patients for pulmonary vein (PV) isolation are scheduled for a procedure with RMN (stereo-group): after single transseptal puncture the ablation catheter is forwarded into the left atrium for 3D mapping and ablation. The ablation is performed circumferentially around the ipsilateral pulmonary veins and verified by an inbuilt „bulls eye" feature of the RMN system: the respective PVs are mapped with the ablation catheter beyond the ablation line circumferentially to verify the line of block. The controls are the patients treated conventionally by lasso-guided ablation (lasso-group): after double transseptal puncture the ablation catheter and a lasso-catheter are forwarded into the left atrium. Ablation is performed circumferentially in the antrum of the PVs with the lasso-catheter in the entrance of the respective PV. Ablation is performed until entrance- and exit-block is confirmed via all 20 electrodes of the lasso-catheter in every PV. PV connections were examined by a lasso-catheter during the redo procedures in the patients.

Results: Out of 82 patients with RMN ablations 44 had redo procedures. Out of these 44 patients 14 (stereo-group; 59±11 years old, 79% paroxysmal AF) were scheduled for a conventional lasso-controlled redo intervention. In case of 214 patients with primarily lasso-controlled PV isolations 43 had redo-procedures and 34 were lasso-controlled (lasso-group; 64±9 years old, 44% paroxysmal AF). The redo procedures were 1.6±0.8 years after RMN index procedure and 1.3±0.8 years after the lasso-controlled index procedure (n.s.). Isolated PVs in the redo procedure:

Table 1. Long-term isolation of pulmonary veins (PV) by RMN compared with conventional lasso-controlled ablations

	Stereo-group	Lasso-group	
	n (%)	*n* (%)	*p*
RSPV	1 (7%)	18 (53%)	<0.001
RIPV	0 (0%)	10 (29%)	<0.001
LSPV	0 (0%)	19 (56%)	<0.001
LIPV	0 (0%)	19 (56%)	<0.001

RS right superior, *RI* right inferior, *LS* left superior, *LI* left inferior

From 54 PVs isolated in the stereo-group one PV (2%) appeared isolated in the redo procedure, evaluated by the lasso-catheter. From 134 PVs isolated in the lasso-group 73 appeared isolated in the redo procedure (55%, $p<0.001$). In the stereo-group 38 PVs primarily had been isolated with the 8 mm tip catheter, 16 PVs with the a cooled tip catheter: in the redo procedure one PV (3%) appeared isolated from those performed with the 8 mm tip catheters in contrast to none (0%) of those performed with the cooled-tip catheter (n.s.).

Conclusions: In respect to long-term PV isolation the lasso-controlled PV isolation appears to be superior to the "bulls-eye" controlled PV isolation performed with remote magnetic navigation.

XXII-3

Pulmonalvenenisolation bei Vorhofflimmern: Ein Vergleich zwischen Cryoballoon- und Radiofrequenz-Ablation

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Einleitung: Die Pulmonalvenen-Isolation (PVI) hat sich in den letzten Jahren zu einer wichtigen interventionellen Methode zur Behandlung von paroxysmalem oder persistierendem Vorhofflimmern (VHF) entwickelt. Für ein optimales Ergebnis sind weite und kontinuierliche Läsionen um die PV-Ostien mit nachgewiesener PVI notwendig. Als Energiequellen stehen hochfrequenter Wechselstrom (Radiofrequenz, RF) und Cryoballon-Technologie (CB) zur Verfügung. In dieser Analyse wurde die Anwendung der beiden in unserer Abteilung verwendeten Verfahren in Hinblick auf Durchführung, Komplikationen und klinischen Erfolg miteinander verglichen.

Methodik: 94 Patienten mit paroxysmalem oder persistierendem VHF und ohne schwerwiegende strukturelle Herzerkrankung wurden in diese Analyse inkludiert. Alle Patienten waren in unserem Zentrum zwischen 2009 und 2011 einer PVI zugeführt und zu regelmäßigen Follow ups einberufen worden. 49 Patienten (55,2±9,5J; 38 M) wurden mit CB, 45 Patienten (58,6±9.4J; 35 M) mit RF behandelt. Prozedurale Daten wurden retrospektiv analysiert, Komplikationen und klinischer Erfolg wurden in Kontrollen nach 3, 6, 9 und 12 Monaten evaluiert.

Ergebnisse: Die CB Patienten wurden im Mittel mit 13,2±4,6 Cryoballon-Ablationen behandelt. Bei 39/49 (80%) der CB Patienten wurde zur Überprüfung der Okklusion intrakardialer Ultraschall und bei 7/49 (14%) Patienten einer invasive Druckmessung an der Spitze des Ballonkatheters verwendet. Bei 19/49 (39%) der CB und bei 41/45 (91%) der RF-Patienten wurde zur Überprüfung der PVI zusätzlich ein Adenosin-Test angewandt.

Es fand sich kein signifikanter Unterschied in der Prozedurzeit zwischen CB und RF (4,01 vs. 4,06 h), die Durchleuchtungszeit war in der CB Gruppe signifikant geringer (49,2±13,7 vs. 59,7±15,6 min; $p=0,01$). Bei 7/49 (14%) der CB Patienten (4 reversible Phrenicus-Paresen, 1 PRIND nach Gasembolie, 1 Perikarderguss, 1 Leistenkomplikation) und bei 4/45 (9%) der RF Patienten (1 Perikarderguss, 3 Leistenkomplikationen) wurde eine Prozedur-bezogene Komplikation beobachtet. 6 Patienten in der CB- (12%) und 5 Patienten in der RF-Gruppe (11%) mussten im Verlauf des Beobachtungszeitraums neuerlich mit einer PVI behandelt werden. Die Anzahl der Episoden wurde durch die CB Behandlung von durchschnittlich 13,2 auf 4,2 und durch die RF-Ablation von 11,3 auf 0,6 jeweils signifikant gesenkt. Die Anzahl der VHF Episoden 6 und 12 Monate nach der Intervention waren nicht signifikant unterschiedlich zwischen den beiden Gruppen, auch unterschieden sich die Anzahl der Antiarrhythmika und der Patienten mit Palpitationen nach 6 und 12 Monaten nicht.

Diskussion: Die PVI mit dem Cryoballoon kann mit einer geringeren Durchleuchtungsdosis durchgeführt werden, die Dauer der Interventionen unterscheidet sich nicht von der mit RF-Ablation, allerdings wurden nach CB mehr Komplikationen (v.a. Phrenicusparesen) beobachtet. Die Effektivität der Prozeduren ist in Hinblick auf Anzahl der VHF-Episoden, Verwendung von Antiarrhythmika und neuerlichen Prozeduren vergleichbar.

XXII-4

Pulmonary vein isolation in patients with paroxysmal and non-paroxysmal atrial fibrillation: importance of diastolic function grading

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Objectives: Clinical and echocardiographic parameters should help to identify patients who have the best long-term benefit from pulmonary vein isolation (PVI).

Background: PVI has become an accepted therapy for patients with atrial fibrillation (AF) and the indications have widened to include non-paroxysmal AF-patients.

Methods: After baseline clinical and echocardiographic evaluation the follow-up strategy in the first year and thereafter, if non-sustained AF has been recorded included: (1) Clinical follow up, 12-lead ECG and 24 h ECG every 3 months, (2) trans-telephonic ECGs twice daily and when symptomatic (over 4 weeks) every 3 months, or (3) continuous monitoring via implanted devices. A recurrence was an atrial arrhythmia lasting >30sec.

Results: All 340 PVI procedures of 229 consecutive patients were analyzed. On average, 1.5 PVI procedures per patient (range, 1–6 PVI) were performed. The mean age was 58±11 years (73% male) with 109 paroxysmal and 120 non-paroxysmal AF cases. Clinical follow-up with 12-lead ECGs, 24 h ECGs, trans-telephonic ECGs and implanted devices was available in 100, 63, 51 and 16% of cases, respectively. The one-year recurrence rate of 59% (range, 24–82%) was dependent on grades of diastolic function (normal—dysfunction grade III) in a multivariate analysis model. Patients with normal diastolic function had the lowest recurrence rates of 24 and 49% after 1 and 3 years of follow-up, respectively ($p<0.0001$).

Conclusions: PVI in unselected AF-patients is a palliative strategy with high recurrence rates obtained by close monitoring. Grading of diastolic function can identify AF-patients who benefit most from PVI.

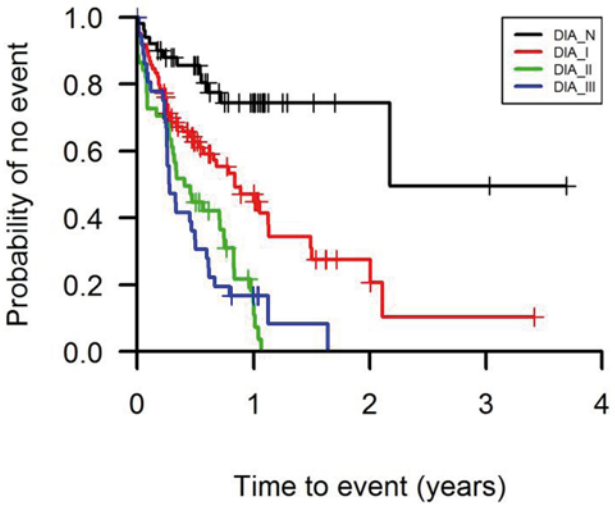

Fig. 1 Best long-term benefit from pulmonary vein isolation (PVI)

XXII-5

Safety and efficacy outcome of a single-centre ventricular tachycardia 24/7 ablation program

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Introduction: Ventricular tachycardia (VT) ablation is an evolving technology with a controversial risk-benefit ratio. The purpose of our study was to assess safety and feasibility of a single centre 24/7 VT ablation program.

Methods: All patients with a previously documented VT who underwent mapping and ablation from 10/2009 to 12/2012 were analysed retrospectively. Patients who underwent ablation of an outflow tract tachycardia or of ventricular premature beats were excluded. 3D CARTO mapping was used in all, since 2012 additionally the SmartTouch™ catheter. Full history of all patients together with prospective ICD follow-up data was available for analysis.

Results: A total of 46 consecutive patients were analysed. The median age was 67 years and 80.4% were male. 60.9% were affected by ischemic cardiomyopathy, 19.6% had non-ischemic cardiomyopathy, 4.3% had arrhythmogenic right ventricular dysplasia, and 15.2% of the patients had no structural heart disease. In 42.2% the left ventricular ejection fraction was below 30%. 97.8% had monomorphic VT, whereas one patient had torsades de pointes. Indications for ablation were electrical storm in 34.1%, appropriate shocks on ICD in 27.3%, recurrent slow VT below ICD therapy threshold in 11.4% and clinical VT in patients without ICD in 27.3%. In 38 patients a VT ablation was performed, in the other 8 patients ablation was not attempted due to not inducible VT in the absence of an endocardial substrate. Procedural success was achieved in 35 patients, defined as no VT inducible and/or elimination of all late potentials (80.0%) or clinical VT not inducible (20%). One procedure failed due to hemodynamical instability of the patient, two because of a non mappable VT. A procedure related complication occurred in three patients, among two pericardial effusions and one retroperitoneal hematoma. The 30 day mortality was 2.2%, two additional patients died within 1 year. During 3–37 months follow-up, VT recurred in 9/35 patients and could be terminated by antitachycardic pacing in seven and by amiodarone in one patient. Fatal slow VT recurred in one patient. No shock on ICD occured and there was no need for further ICD implantation after successful ablation in patients without ICD. In not attempted patients VT reoccurred in one patient.

Conclusion: VT ablation is a safe and effective intervention, even in patients in extremis. Recurrence rate of electrical storm, ICD discharge as well as the need for consecutive ICD implantation is low. Furthermore, patients without an ablation target have a good outcome.

XXII-6

Arterial hypertension accelerates rhythm instability and atrial remodeling in a porcine model of atrial fibrillation

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Introduction: Arterial hypertension is a risk factor for the development of atrial fibrillation (AFib). However, no animal model has been established to investigate effects of arterial hypertension on atrial remodeling and susceptibility to AFib.

Materials and methods: AFib was induced in landrace pigs by 6 weeks of rapid atrial pacing at 600 bpm (RAP, $n=11$). Further pigs received an additional subcutaneous DOCA depot (100 mg/kg, an aldosterone analogon) together with high-salt feeding to induce arterial hypertension 2 weeks before and during RAP (RAP + DOCA, $n=5$). Three times per week, RAP was interrupted for up to 1 h to monitor the atrial rhythm telemetrically in unsedated pigs. Echocardiography was performed before DOCA-implantation, at the onset of RAP, and after 2, 4 and 6 weeks of RAP. Data were compared to untreated control animals ($n=41$) to account for animal growth. Digoxin (5 µg/kg/d p.o.) was administered to slow atrio-ventricular conduction during RAP.

Results: In RAP + DOCA, 3/5 pigs died within the fourth week of RAP, while all animals survived in RAP without DOCA. At 2 weeks of RAP, when all pigs were still alive, systolic blood pressure (tail-cuff) was 152±7 mmHg in RAP + DOCA vs 89±3 mmHg in RAP without

DOCA ($p<0.05$). RAP + DOCA resulted in left ventricular concentric hypertrophy (relative wall thickness at 2 weeks of RAP: 0.71±0.02 vs 0.56±0.02, $p<0.05$). Sustained AFib >1 h within 2 weeks occurred in 4/5 (80%) of RAP + DOCA vs 2/11 (18%) in RAP without DOCA ($p<0.05$). RAP resulted in left atrial (LA) enlargement, which was potentiated by DOCA (see graph).

Conclusion: DOCA-induced arterial hypertension resulted in an earlier onset of sustained AFib together with pronounced LA dilatation. This model will serve to characterize the impact of hypertension on atrial electrical and structural remodeling.

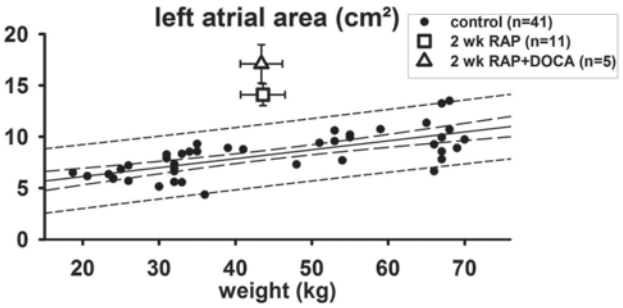

Fig. 1 RAP resulted in left atrial (LA) enlargement potentiated by DOCA

XXII-7

COOLLOOP first: eine first-in-man Studie zur Testung eines neuen zirkulären Kryoablationssystems bei Patienten mit paroxysmalem Vorhofflimmern

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Einleitung: Die Isolation der Pulmonalvenen (PV) mittels Radiofrequenz- und Kryoablation hat sich in den letzten Jahren zu einer wichtigen Methode in der Behandlung von Vorhofflimmern (VHF) entwickelt. Für ein optimales Ergebnis sind weite und komplette lineare Läsionen um die PV-Ostien mit nachgewiesener PV-Isolation (PVI) notwendig. Rekonnektionen der PV, die wiederum VHF auslösen, sind allerdings häufig. Aus diesem Grund wurde das COOLLOOP Katheterablationssystem (AFreeze; Innsbruck/Österreich) mit einem neuartigen zirkulären Kryoablationskatheter entwickelt. In dieser Studie wurde die Anwendung und Sicherheit des neuen Ablationssystems erstmals im Menschen getestet.

Methodik: 10 Patienten (6M/4F; 61,3±9,5J) mit symptomatischem, paroxysmalem VHF refraktär auf zumindest 1 Antiarrhythmikum und ohne zugrundeliegende strukturelle Herzerkrankung wurden in 2 österreichischen Zentren in die Studie eingeschlossen. Nach Ausschluss von linksatrialen Thromben mittels transösophagealer Echokardiographie wurde der COOLLOOP Katheter an jedem PV Antrum unter intrakardialer Echokardiographie (ICE) positioniert. Danach wurden an jeder PV 4–8 Kryoablationen (KA) über je 5 min durchgeführt. Entrance- und Exit-Block wurden anschließend mit einem zirkulären Mapping-Katheter überprüft. Während der der Ablationen in den rechten PVs wurde eine Phrenikus-Stimulation in der V. cava superior zur Überwachung der Funktion des N. phrenicus durchgeführt. Die Sicherheit des Eingriffs und das Wiederauftreten von VHF wurden in klinischen Kontrollen nach 2, 4, 8, und 12 Wochen getestet.

Ergebnisse: Der COOLLOOP Katheter konnte an allen PV Antra von allen Patienten mit ICE visualisiert und positioniert werden. Im Mittel wurden 5,6±1,8 KA in der LSPV, 5,6±1,6 in der LIPV, 6,3±2,5 in der RSPV und 5,4±1,6 in der RIPV durchgeführt. Die mittlere Prozedurzeit war 231,7±48,4 min und die mittlere Durchleuchtungszeit 39,3±13,3 min 6/10 LSPV, 6/10 LIPV, 5/10 RSPV and 6/10 RIPV konnten mit dem neuartigen Kryoablationssystem alleine isoliert werden. Zur Komplettierung der PVI wurden noch in 3 LSPV, 3 LIPV, 4 RSPV und 3 RIPV Kryotip oder Kryoballoon Touchup-Läsionen (Freezor Max oder Arctic Front; Cryocath Medtronic/USA) angewandt. 1 Patientin entwickelte ein Leistenhämatom, das eine operative Sanierung benötigte, und 1 kurze Episode einer transienten ST-Hebung durch eine Luftembolie (Restitution ohne Interventionen) wurde in einem anderen Patienten nach Einführen des Ablationskatheters in den linken Vorhof beobachtet. Andere klinische Komplikationen, insbesondere Katheter-bezogene Zwischenfälle oder Phrenikusparesen traten nicht auf. Nach einem Follow-up von 3 Monaten trat in 7/10 Patienten wieder VHF auf, 1/10 Patienten wurde wegen VHF hospitalisiert und kardiovertiert.

Diskussion: Die Kryoablation mit dem neuartigen COOLLOOP Ablationssystem ist bei Patienten mit paroxysmalem Vorhofflimmern durchführbar und sicher. Der mittel- und langfristige klinische Erfolg muss allerdings prospektiv evaluiert und mit anderen Katheterablationssystemen verglichen werden.

Abb. 1 COOLLOOP Katheter

Postersitzung XXIII: Risikofaktoren/ Stoffwechsel/Lipide 2

XXIII-1

Evolving biomarkers improve prediction of long-term mortality in patients with stable CAD: the BIO-VILCAD score

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Background: Algorithms to predict the future long-term risk of patients with stable coronary artery disease (CAD) are rare. The VIenna and Ludwigshafen CAD (VILCAD) risk score was one of the first scores specifically tailored for this clinically important patient

population. We aimed to refine risk prediction in stable CAD creating a new prediction model encompassing various pathophysiologic pathways. We therefore assessed 135 novel biomarkers for long-term mortality in stable CAD patients.

Methods: We included 1,275 stable CAD patients of the LUdwigshafen RIsk and Cardiovascular health (LURIC) study with a median follow-up of 9.8 years to investigate whether the predictive power of the VILCAD score could be improved by the addition of novel biomarkers. Additional biomarkers were selected in a bootstrapping procedure based on Cox regression to determine the most informative predictors for mortality.

Results: The final multivariable model encompassed nine clinical and biochemical markers: age, sex, left ventricular ejection fraction (LVEF), heart rate, NT-proBNP, cystatin C, renin, 25OH-vitamin D3 and HbA1c. The extended VILCAD biomarker score achieved a significantly improved C-statistic (0.78 vs. 0.73;$P=0.035$) and net reclassification index (14.9 %; $P<0.001$) compared to the original VILCAD score. Omitting LVEF, which might not be readily available, slightly reduced the accuracy of the new BIO-VILCAD score but still significantly improved risk classification (NRI: 12.5 %; $P<0.001$).

Conclusion: The VILCAD biomarker score based on routine parameters complemented by novel biomarkers outperforms previous risk algorithms and allows more accurate classification of stable CAD patients enabling physicians to choose more personalized treatment regimens for their patients.

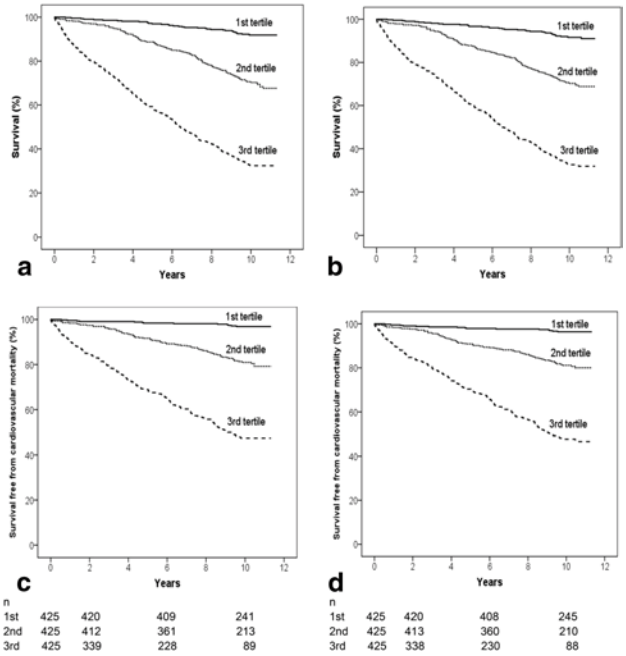

Abb. 1 VILCAD score could be improved by the addition of novel biomarkers

XXIII-2

Endostatin and physical exercise in young female and male athletes and controls

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Background: Physical inactivity is widely known to be an independent and avoidable risk factor for the development of cardiovascular disease by affecting endothelial function, which plays a key role in atherosclerosis. Endostatin, a mediator of angiogenesis with angiostatic effects, was suggested to be influenced by physical exercise. However, recent knowledge is based on few studies with small populations and data of women are missing.

Material and methods: We took routine laboratory parameter and performed a graded bicycle stress test in 88 healthy non-smoking individuals, divided into 25 female and 24 male athletes (endurance sport > 135 min/week) and 20 female and 19 male non-athletes (endurance sport max. 45 min/week). Venous serum endostatin levels were measured at rest before the stress test, after reaching maximum workload and 20 min after the procedure.

Results: Mean age and BMI were comparable in both groups (athletes: 24.82 ± 4.65 years, 21.77 ± 2.05 kg/m^2; controls: 23.10 ± 3.88 years, 22.14 ± 2.66 kg/m^2). At baseline, female controls had significantly lower levels than female athletes (89.28 ± 15.32 vs. 128.81 ± 20.84 ng/mL, $p<0.001$) and same holds true for male controls compared to male athletes (93.39 ± 15.00 vs. 147.53 ± 27.72 ng/mL, $p<0.001$). The bicycle stress test was associated with an increase in serum endostatin levels in both groups and sexes (p for all groups <0.001). The extent of endostatin increase was comparable in both groups and sexes and varied between 23–27 %. However, significance gets lost when the performance is plugged in as covariate. After 20 min. of relaxation, endostatin levels decreased in all participants whereby the drop was more pronounced in controls (16–18 %) compared to athletes (7–9 %). Baseline endostatin levels positively correlated with haemoglobin, haematicrit, thrombocytes, erythrocytes, sodium and blood glucose but only in athletes, except for a correlation of endostatin and erythrocytes which was also observable in non-athletes.

Discussion: Acutely induced physical strain leads to an increase in serum endostatin levels in both female and male athletes and controls whereas the extent of increase depends on the extent of workload. A sporty lifestyle with >135 min. of endurance training per week increases the circulating long-term endostatin amount. The correlation between endostatin and several blood parameter in athletes suggest a connection between sport, endostatin, angiogenesis and blood viscosity.

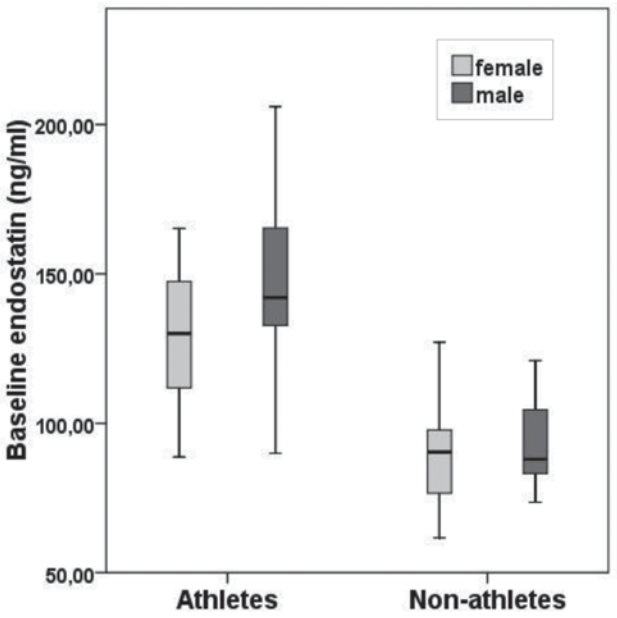

Fig. 1 Increase in serum endostatin levels depends on the extent of workload

XXIII-3

Wie häufig sind fehlerhafte anamnestische Angaben zum Tabakkonsum? Analyse von anamnestisch und biochemisch bestimmtem Raucherstatus bei Patienten der LURIC-Studie

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Einleitung: Zigarettenrauchen stellt einen wichtigen Risikofaktor kardiovaskulärer Erkrankungen dar. Die Erhebung des individuellen Raucherstatus ist daher wichtiger Bestandteil kardiovaskulärer Studien. Als Methoden stehen eine Selbstangabe der Studienteilnehmer über Fragebögen und eine Bestimmung biochemischer Parameter (Cotinin) des Tabakkonsums zur Verfügung. Erstere ist unabhängig von einer Probennahme, kostengünstig und leicht in großer Zahl durchführbar, weist aber eine Abhängigkeit der Ergebnisse von der Mitarbeit der Studienteilnehmer auf. Letztere erfordert eine Probennahme (Plasma, Urin) und ist teurer, jedoch unabhängig von den Angaben seitens des Patienten. In unserer Studie erfolgte ein Vergleich der mit beiden Verfahren erhaltenen Ergebnisse zum Raucherstatus bei Patienten der Ludwigshafen Risk and Cardiovascular Health Study (LURIC).

Material und Methode: Eingeschlossen wurden 3316 zur Durchführung einer Koronarangiographie hospitalisierte Patienten. Die Erhebung des Raucherstatus erfolgte durch Selbstangabe der Patienten in einem Fragebogen bzw. Bestimmung der Konzentration von Cotinin im Serum mittels Radioimmunoassay und einem Cut-off Level von 15 µg/l (Nikotin-Metabolit RIA, DPC Biermann GmbH, Bad Nauheim, Deutschland).

Ergebnisse: In ihrer Selbstangabe beurteilten sich 1194 (36,0 %) Studienteilnehmer als Nie-Raucher, 1468 (44,3 %) als Ex-Raucher und 654 (19,7 %) als Raucher. Cotininkonzentrationen unterhalb des Cut-offs fanden sich bei 2819 (85,0 %) Studienteilnehmern, während 497 (15,0 %) Werte oberhalb des Cut-offs aufwiesen. In 123 Fällen (3,7 %), davon 16 Nie-Raucher und 107 Ex-Raucher fand sich eine Diskrepanz zwischen den Ergebnissen der Selbstangabe im Fragebogen und der Cotininbestimmung. Die logistische Regressionsanalyse mit schrittweisem Einschluss von Geschlecht, Alter, koronarvaskulärer Erkrankung, vorangegangenem Myokardinfarkt und Bildungsniveau zeigte, dass nur männliches Geschlecht (Odds ratio männlich/weiblich: 2,00, 95 % Konfidenzintervall (CI): 1,22–3,33, $p=0{,}007$) und Alter (Odds ratio pro Jahr: 0,79, 95 % CI: 0,66–0,94, $p=0{,}008$) mit dem Auftreten einer derartigen Diskrepanz assoziiert waren.

Diskussion: Die Daten unserer Studie zeigten bei 3,7 % der Studienteilnehmer eine Diskrepanz zwischen den Selbstangaben im Fragebogen und den Ergebnissen der biochemischen Analytik mit der Folge einer möglichen Fehlklassifikation bei ausschließlicher Erhebung des individuellen Raucherstatus basierend auf den Angaben des Fragebogens. Auffälligerweise neigen unterschiedliche Gruppen (Geschlecht, Alter) verschieden stark zu Fehlklassifikationen, was auf Unterschiede im Gesundheitsbewusstsein zwischen Männern und Frauen und in verschiedenen Altersgruppen hinweist. Die Häufigkeit der Fehlklassifikationen in Höhe von 3,7 % liegt im Vergleich zu anderen Studien im unteren Bereich (Häufigkeiten bis 20 %). Zu berücksichtigen ist hierbei jedoch, dass die Häufigkeit von Fehlkassifikationen auch von der Art der Studie (höhere Häufigkeit in klinischen Studien als in Populationsstudien) und von der Höhe des gewählten Cut-off Levels abhängt. Bei einem wichtigen Risikofaktor wie Rauchen kann bereits eine geringe Rate von Fehlklassifikationen zu einer deutlichen Verzerrung der Studienergebnisse hin zu falsch-negativen Ergebnissen führen. Daher sollte in Studien eine biochemische Bestimmung des individuellen Raucherstatus gegenüber einer Selbstangabe seitens des Patienten mittels Fragebogen vorgezogen werden.

XXIII-4

Awareness of cardiovascular risk factors in Austrian female and male civil and military servants of the Ministry of Defence and Sports

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Background: Much research work is performed in investigating the broad field of cardiovascular risk factors such as hypertension, diabetes, dyslipidaemia or physical inactivity. However, much of this serious progress might not filter down to (concerned) population. The aim of this study was to investigate the knowledge of Austrian population about cardiovascular risk factors.

Material and methods: The survey was done in 520 female and 822 male government employees in Austria (86.26 % Eastern, 5.02 % Northern, 5.02 % Southern and 3.69 % Western Austria) by means of a questionnaire (sent and received per mail) with more than 50 questions inquiring anthropometric data, lifestyle factors (smoking, alcohol, physical activity…) and knowledge about cardiovascular risk factors.

Results: Mean age and BMI in males was higher than in females (48.19±7.54 vs. 41.69±10.55 years resp. 27.05±4.01 vs. 24.54±4.89 kg/m^2). BMI correlated positively in both sexes with age and negatively with educational level. Female population believed that the number one cause of death for females is cancer (59.9 %) and for males cardiovascular disease (CVD) (74.4 %). Similar results were received when asking male participants about female number one cause of death (53.2 % cancer) and male number one cause of death (80.8 %). The presence of the following risk factors was affirmed for (in % of participants, female/male): smoking: 30.2/27.6 %, hypercholesterolaemia: 12.2/17.5 %, hypertension: 12.4/22.2 %, diabetes: 1.8/3.6 % and myocardial infarction or stroke in family: 49.8/46.3 %. The term “coronary artery disease” was known by 43.3 % of women and 51.1 % of men. Main cardiovascular risk factors were correctly identified as follows (in % of participants, female/male): hypertension: 81.0/77.5 %, smoking: 76.3/77.1 %, overweight: 82.9/80.5 %, physical inactivity: 65.5/64.2 %, hypercholesterolaemia: 55.8/52.3 %, alcohol: 48.4/51.8 %, diabetes: 21.6/23.2 % and positive family history: 11.8/8.1 %. About 53 % of women and 60 % of men stated to have taken preventive actions in the past year mostly because they wanted to do something for their health and to feel better/healthier. The most frequent reasons preventing people from taking preventive actions is that they do not consider themselves as person at risk (about 39 %), followed by having too less time because of the job (about 29 %).

Discussion: The prevalence of hypertension, overweight, diabetes and hypercholesterolaemia seems to be higher in male population whereas more females are smokers. Only about one in two is familiar with the term coronary artery disease. The level of awareness of hypertension smoking and overweight is much better than

of physical inactivity and hypercholesterolaemia. Only every fourth to fifth associated diabetes with cardiovascular disease. The principle "men die from MI and women from cancer" still seems to be widely spread. The results of this study show that people are not sufficiently informed about cardiovascular risk factors making it difficult to take individual prevention, which is based on knowledge.

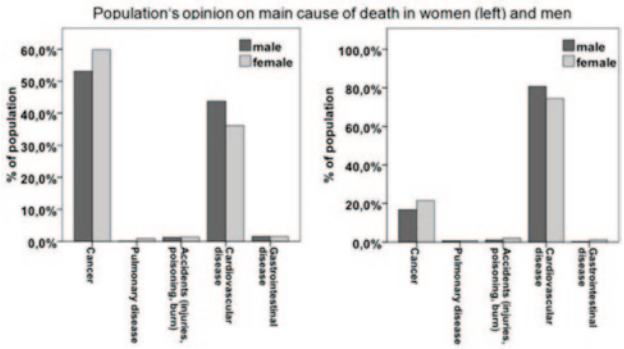

Fig. 1 Population's opinion on main cause of death in women (*left*) and men

XXIII-5

Veränderungen von Laborparametern des Gerinnungs- und des Fibrinolysesystems bei aktiven Rauchern der Ludwigshafen Risk and Cardiovascular Health Study (LURIC)

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Einleitung: Kardiovaskuläre Erkrankungen stellen vor allem in den Industrieländern eine wesentliche Ursache der Morbidität und Mortalität dar. Risikofaktoren für kardiovaskuläre Erkrankungen sind neben Parametern des Lipidstoffwechsels auch solche des Gerinnungs- bzw. des Fibrinolyse-Systems sowie Entzündungsparameter. Rauchen stellt einen wichtigen und vermeidbaren Risikofaktor kardiovaskulärer Erkrankungen dar. Ziel unserer Studie war die Analyse des Einflusses von Rauchen auf die Parameter von Gerinnung und Fibrinolyse.

Material und Methode: Die Plasmakonzentrationen bzw. -aktivitäten von Protein C, Faktor V, Protein S, Fibrinogen, Prothrombinfragment 1 und 2, D-Dimer, Plasminogenaktivator-Inhibitor 1 (PAI-1), Tissue Plasminogen Activator (t-PA), Tissue Factor Pathway Inhibitor (TFPI) und Endogenem Thrombinpotential (ETP) wurden bei 3316 Patienten mit Indikation zur Koronarangiographie, die in der Ludwigshafen Risk and Cardiovascular Health Study (LURIC) eingeschlossen waren, untersucht, davon 769 aktive Raucher (AR) und 1168 lebenslange Nichtraucher (NR). Während eines medianen Beobachtungszeitraums von 10 Jahren verstarben 995 Patienten, davon 221 AR und 302 NR.

Ergebnisse: AR wiesen im Vergleich zu NR signifikant höhere Werte von Fibrinogenkonzentration (AR vs. NR, 417,0±113,9 vs. 384,1±99.7 mg/dl, $p<0{,}001$), ETP (99,1±24,5 vs. 94,4±28,5, $p<0{,}001$), Protein S-Aktivität (120,2±35,7 vs. 114,4±32,8 %, $p=0{,}027$) und TFPI (1,30±0,37 vs. 1,23±0,37 µg/L, $p<0{,}001$) sowie signifikant niedrigere Werte der Protein C-Aktivität (106,7±25,3 vs. 112,1±25,1 %, $p=0{,}006$) auf. Keine signifikanten Unterschiede fanden sich hingegen für die Werte von Prothrombinfragment 1 und 2 (AR vs. NR, 0,82±0,61 vs. 0,82±0,76 nmol/L, $p=0{,}257$), D-Dimer (0,62±1,06 vs. 0,60±1,05 mg/L, $p=0{,}991$), PAI-1 (25,8±24,7 vs. 24,3±30,8 U/mL, $p=0{,}309$) und t-PA-Aktivität (0,80±0,74 vs. 0,81±0,66 U/L, $p=0{,}252$).

Diskussion: Die Daten zeigen, dass aktive Raucher im Vergleich zu Nichtrauchern deutliche Veränderungen einzelner Parameter des Gerinnungs- bzw. Fibrinolysesystems aufweisen. Ein Vergleich der betroffenen Parameter weist dabei auf ein bei Rauchern insgesamt erhöhtes thrombogenes Potential in Verbindung mit einer Verminderung der Thrombolyse hin. Daher sollte bei Rauchern neben einer Bestimmung der Plasmalipide zur Abschätzung des individuellen kardiovaskulären Risikos eine Analyse von Parametern des Gerinnungssystems bzw. des fibrinolytischen Systems erfolgen.

XXIII-6

Hochsensitives CRP (hsCRP) und lipoproteinassoziierte Phospholipase A2 (LpPLA2) bei Rauchern und Nichtrauchern der Ludwigshafen Risk and Cardiovascular Health Study (LURIC)

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Einleitung: Kardiovaskuläre Erkrankungen sind vor allem in westlichen Industrieländern eine wesentliche Ursache von Morbidität und Mortalität. Zigarettenrauchen stellt einen wichtigen und vermeidbaren Risikofaktor dieser Erkrankungen dar. Die Bestimmung prädiktiver Faktoren (z. B. Erhebung des Plasmalipidstatus, Blutdruck, Raucherstatus) erlaubt eine Abschätzung des individuellen Risikos. Von Bedeutung ist jedoch auch eine Aussage zu Entzündung und Plaquestabilität insbesondere bei Patienten mit erhöhtem Risiko, die durch eine Bestimmung von hochsensitivem CRP (hsCRP) und lipoproteinassoziierter Phospholipase A2 (LpPLA2) erfolgen kann. Ziel unserer Studie war die Untersuchung dieser Parameter bei Rauchern und Nichtrauchern der Ludwigshafen Risk and Cardiovascular Health Study (LURIC).

Material und Methode: In die Studie eingeschlossen wurden 3316 Patienten mit Indikation zur Koronarangiographie, die an der Ludwigshafen Risk and Cardiovascular Health Study (LURIC) teilnahmen, davon 769 aktive Raucher (AR) und 1168 lebenslange Nichtraucher (NR). Während eines medianen Beobachtungszeitraums von 10 Jahren verstarben 995 Patienten, davon 221 AR und 302 NR. Bei den Patienten erfolgte eine Bestimmung der Plasmakonzentrationen von hochsensitivem CRP (N High Sensitivity CRP,

Dade Behring, Marburg, Germany) und lipoproteinassoziierter Phospholipase (LpPLA2, diaDexus Inc., San Francisco, CA, USA).

Ergebnisse: Raucher wiesen im Vergleich zu Nichtrauchern eine signifikante Zunahme sowohl der Konzentration von LpPLA2 (AR vs. NR, 424,2 (293,7–630,2) vs. 383,8 (272,3–533,5) ng/mL, $p<0{,}001$) als auch der Konzentration von hsCRP (4,9 (1,8–10,3) vs. 2,7 (1,2–7,0) ng/mL, $p<0{,}001$) auf. Zwischen den Konzentrationen beider Parameter bestand dabei eine deutliche Korrelation ($rS=0{,}132$, $p<0{,}001$). Auffällig war jedoch, dass es sowohl bei Rauchern als auch bei Nichtrauchern isolierte Erhöhungen der Werte eines Parameters gab. So wiesen 125 (16,3 %) AR einen Wert der LpPLA2 oberhalb des Medians auf, während der Wert des hsCRP darunter lag. Umgekehrt fand sich bei 179 (23,3 %) AR ein Wert des hsCRP oberhalb des Medians wärend der Wert der LpPLA2 darunter lag. Die entsprechenden Werte bei NR betrugen 276 (23,6 %) bzw. 208 (17,8 %).

Diskussion: Die Daten bestätigen die Bedeutung insbesondere einer Bestimmung von LpPLA2 und hsCRP zur Abschätzung des individuellen Risikos einer Plaqueruptur. Aufgrund möglicher Diskrepanzen der zu erhaltenden diagnostischen Aussagen bei einer Einzelbestimmung erscheint trotz der bestehenden Korrelation zwischen LpPLA2 und hsCRP eine Bestimmung beider Parameter indiziert. Die bei Rauchern gegenüber Nichtrauchern erhöhten Werte weisen auf das vor allem bei Rauchern erhöhte Risiko einer Plaqueruptur und die Notwendigkeit einer entsprechenden Untersuchung in dieser Risikogruppe hin.