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BEST ABSTRACTS SITZUNG 1

BA I - 1

The right heart in HFpEF, insights from a cardiac magnetic resonance study

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Background: Cardiovascular magnetic resonance imaging (CMR) is the gold-standard technique for the assessment of right ventricular function. Recent data indicate that right ventricular ejection fraction (RVEF) < 45 % by CMR is a strong predictor of outcome in patients with dilated cardiomyopathy. However, the prognostic significance of RVEF in heart failure with preserved ejection fraction (HFpEF) is unknown.

Methods and results: Between December 2010 and September 2013 we prospectively enrolled 105 HFpEF patients. At baseline, all patients underwent CMR imaging in addition to invasive and non-invasive testing. Right ventricular systolic dysfunction (RVSD), defined by RV ejection fraction < 45 %, was present in 27 (25.71 %) patients.

Patients were followed for 434 ± 325 days, during which 31 had a cardiac event (hospitalization for heart failure and/or death for cardiac reason).

By univariate Cox analysis RVSD ($p = 0.007$), NYHA functional class ($p = 0.006$), 6-minute- walking-distance ($p < 0.001$), diabetes ($p < 0.001$), and invasively measured systolic ($p < 0.001$) and mean pulmonary artery pressures ($p < 0.001$) were significantly associated with outcome. By multivariable analysis only RVSD (HR 4.852, CI 1.97–11.92, $p = 0.001$) and diabetes (HR 3.99, CI 1.65–9.65 $p = 0.002$) remained significant predictors of cardiac events. In addition, patients with RVSD presented with significantly higher resting heart rate ($p = 0.022$), more advanced NYHA functional class ($p = 0.016$) and shorter 6-minute-walking-distance (t-test $p = 0.016$). By Kaplan Meier analysis, outcome was significantly worse in patients with RVSD (log rank, $p = 0.0052$).

Conclusions: Although HFpEF is considered a disease of the left ventricle, respective parameters are not related with outcome. In contrast, RVSD has a significant impact on outcome and clinical status in HFpEF patients. Assessment of RVSD by CMR is important for risk-stratification in this patient population.

BA I - 2

Dissecting mechanisms underlying murine neonatal cardiac regeneration

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Background: Cardiac remodeling and subsequent heart failure remain critical issues after myocardial infarction despite improved treatment and reperfusion strategies. Recently, we demonstrated complete cardiac regeneration in a neonatal mouse model of myocardial infarction. This regenerative potential of the heart is lost within the first week of life. The key mechanisms that promote regeneration at the perinatal stage remained entirely unclear.

Methods: Therefore, we used our protocol of left anterior descending artery (LAD) ligation in combination with consecutive FACS analysis 36 h and 5 days later to analyze the inflammatory response in neonatal vs. one-week old mice. Moreover, we performed an in-depth analysis of the transcriptome of sham versus myocardial infarction treated hearts.

Results: LAD ligation induced a robust inflammatory resoponse within the first 36 h irrespective of the timepoint of myocardial infarction. There was no marked difference in the myeloid compartment between one and seven-day-old mice. However, a significant difference was found in the lymphoid compartment. Whereas newborn mice presented a significant increase of γδT-cells upon LAD ligation, no change was evidenced in the one-week-old animals. Remarkably, 5 days after the initial ischemic injury, we observed complete clearance of the leukocyte infiltrate in the neonatal heart. In contrast, hearts that were LAD ligated on postnatal day 7 showed prolonged cardiac inflammation beyond the fifth day post injury. Furthermore, RNA-sequencing and KEGG pathway analyses of neonatal hearts imply pathways in cancer, MAPK signaling, and focal adhesion as mechanistic players.

Conclusion: In summary, neonatal hearts demonstrate rapid clearance of the ischemia induced infiltrate and their transcriptome is enriched in genes of mitosis and DNA replication. Together, these differences support the fast recovery of newborn mice following a complex ischemic cardiac damage.

BA I - 3

Association of aortic pulse wave velocity with NT-proBNP levels 12 months after acute STEMI

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Objectives: We have previously shown that aortic pulse wave velocity (PWV) is associated with biomarkers of myocardial wall stress measured 4 months after acute STEMI. We speculated that vascular-ventricular coupling might be responsible for these results. In the present study, we prospectively investigated the relationship of increased aortic stiffness with N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels 12 months after STEMI.

Materials and methods: 50 STEMI patients who were treated with primary coronary angioplasty underwent cardiovascular magnetic resonance (CMR) at baseline and at 12-month follow-up. Aortic PWV was determined by velocity-encoded, phase-contrast CMR. Blood samples were routinely drawn at baseline and follow-up to determine NT-proBNP levels. PWV and NT-proBNP levels were log-transformed for correlation analysis to achieve normal distribution.

Results: The mean age of the study population was 57 ± 12 years and median baseline PWV was 7.0 m/s (IQR: 5.8–8.4). After 12 months mean infarct size was 11 ± 6 % of left ventricular mass and mean ejection fraction was 53 ± 11 %. The median NT-proBNP level after 12 months was 169 ng/L (IQR: 97–335).

In univariate analysis NT-proBNP levels after 12 months correlated with PWV (r: 0.415, $p = 0.003$), age (r: 0.427, $p = 0.002$), end-systolic volume (r: 0.291, $p = 0.040$) and infarct size (r: 0.460, $p = 0.001$). After multivariate analysis PWV remained an independent predictor of NT-proBNP levels 12 months after STEMI (model: r: 0.742, $p < 0.001$).

Conclusion: Aortic stiffness, as determined by PWV, is associated with NT-proBNP levels 12 months after reperfused STEMI. This association remains significant after correction for infarct size, age and end-systolic volume. Our data suggests a role for aortic stiffness in chronic left ventricular remodeling after STEMI.

BA I - 4

Institutional experience with the HeartWare Ventricular Assist System in 100 patients

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Background: The implantation of a left ventricular assist device has become a standard treatment option for terminal heart failure. We present our institutional experience with the HeartWare Ventricular Assist System (HVAD) in 100 patients.

Methods: We retrospectively reviewed data of 100 patients receiving an HVAD between March 2006 and August 2013, regarding patient demographics, incidence of adverse events, length of support and outcomes, such as mortality or successful bridging.

Results: Mean age was 55 ± 13 years, ranging from 13 to 75 years. 82 % of the patients were male, 43 % suffered from ischemic cardiomyopathy. At the time of implantation, 30 % of the patients were in INTERMACS level 1, 12 % in INTERMACS level 2, 26 % in INTERMACS level 3 and 26 % in level 4–7. Duration of support ranged from 1 to 1631 days with a mean of 409±319 days (Median 348.5 days). 28 patients (28 %) were successfully bridged to transplantation, explant for recovery occurred in one patient (1 %), 27 died on LVAD support (27 %) and 44 remain still on the device (44 %). 28 patients (28 %) experienced at least one major bleeding event, including surgical bleedings in 43 %, gastrointestinal bleedings in 33 %, and intracranial bleedings in 24 %. One or more thromboembolic complications occurred in 18 patients (18 %) (50 % pump thrombus, 50 % ischemic strokes) and right heart failure in seven patients (7 %). 13 % of the adverse events had fatal consequences. 30-day and in-hospital mortality were low with 8 and 15 %, respectively. One-year survival was 80 %.

Conclusion: In our patient cohort, the HVAD has been demonstrated to efficiently support patients in terminal heart failure, providing excellent clinical outcomes.

BA I - 5

Immunosuppressive therapy in virus-negative inflammatory lymphocytic cardiomyopathy—who benefits most?

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Introduction: Immunosuppressive therapy appears to be beneficial in patients with virus-negative lymphocytic inflammatory cardiomyopathy. It was the aim of this single-center study to identify potential baseline characteristics that may predict positive response to therapy.

Methods: Virus-negative inflammatory cardiomyopathy was diagnosed in endomyocardial biopsies of 93 patients. Cortison and azathioprin for 6 months in addition to standard heart failure therapy was started in 79 patients. Endomyocardial biopsy and hemodynamic evaluation was repeated at six-months follow-up. Patients were classified as responders if NYHA class improved by at least one class or remained stable in class I and serum NT-proBNP dropped by ≥ 30 %.

Results: At this stage complete 6-months follow-up is available in 61 patients (age: 46 ± 11.3, female: 34 %, median disease duration: 3 months [0.25–42]). Compared to baseline we observed a significant improvement in NYHA class (I/II 59 %, III/IV 41 % before vs I/II 98 %, III/IV 2 % after therapy, $p < 0.001$) and NT-proBNP (852 ng/l [49–6118] vs 276 ng/l [45–8099], $p < 0.001$) in the entire cohort. Also left ventricular ejection fraction (LV-EF) (29 ± 12 vs 44 ± 12 %, $p < 0.001$) and left ventricular enddiastolic volume index (LVEDVI) (121±39 vs 107±36 ml/m2, $p < 0.001$) improved, as did cardiac index (2 ± 0.6 vs 2.4 ± 0.6 L min/m2, $p < 0.001$) and pulmonary capillary wedge pressure (15 mmHg [4–42] vs 11 mmHg [6–26], $p = 0.001$).

Responders ($n = 35$, 57 %) were characterized by higher NYHA class (III/IV 54 vs 23 %, $p = 0.014$), higher NT-proBNP levels (1387 ng/l [53–6118] vs 406 ng/l [49–5329], $p = 0.018$), lower LV-EF (26 ± 11 vs 34 ± 13 %, $p < 0.001$) and higher leucocytes (7.7 G/l [4.4–15.4] vs 6.4 G/l [4.2–12.6], $p = 0.007$) at baseline. Interestingly, no significant differences were found between groups with regard to hemodynamics, LVEDVI and the extent of myocardial inflammation/fibrosis. Standard heart failure therapy was comparable between groups at baseline and 6-months follow-up. Multivariate logistic regression analyses including disease duration, LV-EF, CI, leucocytes, CD14 positive lymphocytes/mm^2 revealed high leucocytes and low LV-EF at baseline as independent predictors of positive response to therapy.

Conclusion: From our data it appears that a positive response to immunosuppressive therapy in virus- negative lymphocytic inflammatory cardiomyopathy is more likely in patients with higher leucocytes and low LV-EF at baseline.

BA I - 6

Clinical efficacy and cardiac reverse remodelling in patients with severe mitral regurgitation and left ventricular dysfunction after percutaneous mitral Valve repair with the MitraClip system

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Background: Chronic severe mitral regurgitation (MR) leads to significant structural cardiac changes due to volume overload. It causes left atrial (LA) and left ventricular (LV) dilation, deterioration of LV contractile function and pulmonary hypertension. Surgical mitral valve repair is the therapy of choice when severe MR is associated with symptoms or LV- dysfunction. Percutaneous mitral valve repair with the MitraClip system evolved as a promising interventional tool in high risk patients. We report the clinical efficacy and echocardiographic findings in patients with symptomatic severe MR and reduced LVEF, 6 and 12 months after MitraClip implantation.

Methods: We included patients with heart failure (LVEF < 35 %) and significant MR > 3, who were declined for surgery. Transthoracic echocardiography was performed before, 6 and 12 months after the procedure. Differences in 6-min-walk test (6-MWT), NT-proBNP, New York Heart Association (NYHA) functional class were established. The evaluated parameters by echocardiography were LV end-diastolic and endsystolic volume, LVEF, LA-Index and systolic pulmonary artery pressure (sPAP)

Results: The MitraClip procedure was performed in 29 patients. 25 patients (86, 2 %) had functional MR and 4 patients (13, 8 %) had a mixed genesis of MR.

At 6 and 12 months, MR < 2 was present in 21 (96.6 %) and 17 (85 %) patients. Neither LVEF (from 26.2 + 6.4 % at baseline to 26.9 + 9.4 % at 6 months and 27.6 + 9.8 % at 12 months) nor left

ventricular enddiastolic volume (from 264.4 + 81.1 to 246.0 + 62.5 ml and 260.4 + 79.1 ml) changed significantly. A decrease of LA-Index (from 97.9 + 32.9 to 75.3 + 20.9 ml/m^2 and 79.4 + 22.5 ml/m^2) and sPAP (from 60.8 + 18.8 mmHg to 48.0 + 12.2 mmHg and 49.8 mmHg) was observed.

6-MWT distance and NYHA-class improved significantly. The Kansas City Cardiomyopathy Questionaire Score (KCCQ) revealed an improvement in life quality. However, NT-proBNP levels decreased significantly after 6 months but increased after 12 months.

Conclusion: Percutaneous edge-to-edge valve repair reduces severe MR in high surgical- risk patients with marked LV-dysfunction, leading to an improvement in functional capacity after 12 months. In addition, distinct decrease of LA-Index and sPAP was noticed. However, in contrast to other studies no significant reverse remodelling of the left ventricle was observed in our study population.

BEST ABSTRACTS SITZUNG II

BA II - 1

Comparison of cardiac magnetic resonance imaging and M-mode echocardiography data of longitudinal systolic ventricular interaction in pediatric and young adult patients with TOF

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Purpose: Aim of this prospective study was to evaluate longitudinal systolic left ventricular (LV)—right ventricular (RV) interaction using M-mode compared to magnetic resonance imaging (MRI) data in 146 pediatric and adults with operated tetralogy of Fallot (TOF).

Methods: We determined biventricular measures of longitudinal M-Mode echocardiography (i.e. tricuspid annular plane systolic excursion (TAPSE); the mitral annular plane systolic excursion (MAPSE)) compared to longitudinal function parameters using MRI. M-Mode data were compared to established normal z-score values.

Results: We found a good correlation between MAPSE and LVEF values (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 the LVEF was normal in patients with a normal RVEF, the LVEF was decreased in patients with significantly reduced RVEF. Patients with a significantly dilated RV (RVEDVi > 150 ml/m^2) showed a significantly reduced mean MAPSE of 1.30 ± 0.26 cm. LV longitudinal function decreases below – 2 SD of normal MAPSE z-score values after a mean of 22 postoperative years.

Conclusions: Our data confirm progressive adverse RV-LV interaction in the long-term follow-up of TOF. We show that simple M-mode measurement of the longitudinal LV function (i.e. MAPSE) is a sufficient surrogate for estimation of LVEF. Therefore determination of the MAPSE is a helpful additional tool for LV systolic function assessment late after TOF repair.

BA II - 2

Diffuse late gadolinium enhancement in carriers of duchenne muscular dystrophy is associated with clinical and morphometric signs of incipient heart failure

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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 early myocardial fibrosis as an early sign of heart involvement which might be associated with 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 (6MWT), blood sampling, ECG, echocardiography, and CMR was 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). T1-mapping was performed in order to determine extracellular volume.

Results: Twenty-two carriers were screened; however, three withdrew their consent due to claustrophobia. The remaining nineteen carriers (age 39.54 + 11.44 years, range 21–62 years) underwent complete examination. Seventeen of the included carriers (89.5 %) 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 6MWT was 479.79 + 93.91 m. Mean CK levels were 416.7 + 299.7 U/l, proBNP was 118.3 + 78.06 ng/l. Mean left ventricular ejection fraction (LVEF) was 61 + 7 %. Eight patients (42.1 %) had evidence of a diffuse LGE, which was predominantly distributed in the posterolateral and inferior wall. In general, mean extracellular volume was elevated in carriers (33.14 + 13.27 %, normal range < 30 %). Those presenting LGE had significantly lower LVEF, higher septum thickness, performed poorer in the 6MWT and had a trend towards a higher proBNP (Table 1)

Discussion: Myocardial involvement shown as LGE in CMR may occur in a substantial part of DMD carriers who are clinically asymptomatic. Nevertheless, they present with clinical and morphometric signs of incipient heart failure. Careful cardiologic examination and follow-up may be warranted in this cohort.

Table 1 LGE is associated with clinical and morphometric signs of incipient heart failure

	LGE –	LGE +	p
6MWT (m)	514.91 + 66.80	425.00 + 108.6	0.044
CK (U/l)	252.40 + 114.24	622.13 + 338.5	0.005
CK-MB (U/l)	11.88 + 2.23	22.71 + 5.4	< 0.001
Trop T (ng/l)	0.0125 + 0.017	0.017 + 0.01	0.72
proBNP (ng/l)	83.00 + 37.86	153.63 + 93.66	0.068
IVS (mm)	8.95 + 0.96	10.57 + 1.27	0.007
3D LVEF (%)	64.36 + 5.78	56.75 + 7.36	0.022

BA II - 3

First-in-man experience with a minimally invasive transcatheter pacemaker

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Introduction: A novel Transcatheter Pacing System (TPS) has been developed for pacing the right ventricle (RV). The device is delivered percutaneously and implanted at the RV apex where the steroid-eluting pacing cathode is fixed by 4 self-expanding metallic tines. The TPS has a VVIR pacing capacity with an estimated battery life ranging from 7–15 years. We report on the feasibility, safety and one-month follow-up of the first in vivo implantations of this novel TPS in humans.

Materials and methods: Percutaneous implantation of the TPS (Micra TPS, Medtronic Inc.) was performed via a right femoral access using a 23 F sheath. The TPS was directed with a deflectable delivery system to the apex of the RV under fluoroscopic guidance. For fixation of the TPS at the endocardium of the target region, the tines were deployed by pulling a feeder on the handle of the delivery system. Sufficient fixation was checked by performing a tug test via the delivery system under fluoroscopic guidance. Electrical performance of the system was assessed non-invasively before definite release of the TPS, pre-discharge and one month after the implantation, respectively.

Results: A TPS was successfully implanted at the RV apex of six patients (ages 74–86 years, 3 females/3 males) with an indication for VVIR pacing and preserved left ventricular ejection fraction. There were no unsuccessful implants. The mean total procedure time was 43 (73–26) min. The mean R-wave amplitude, pacing threshold and impedance at implantation were 13.72 mV, 0.48 V at 0.24 msec and 708 Ohms, respectively. During the first month after implantation, no major complications occurred. Electrical parameters, as assessed during the one-month-follow-up either remained stable or improved to a mean R-wave of 16.73 mV, pacing threshold of 0.44 V at 0.24 msec and impedance of 747 Ohms, respectively.

Discussion: This first experience in humans demonstrates the feasibility, safety and early efficacy of the novel Micra TPS cardiac pacemaker. Safety and efficacy of the TPS is currently being evaluated in the ongoing clinical study.

BA II - 4

Right ventricular dysfunction but not tricuspid regurgitation is associated with outcome in patients after left-sided valve surgery

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Background: Significant tricuspid regurgitation (TR) after previous left-heart valve surgery is frequent and associated with increased morbidity. Mortality rates for re-operation are high, while the impact of TR on survival in these patients remains unclear.

Methods: 571 consecutive patients 49 ± 29 months after left heart valve surgery were prospectively followed for 53 ± 15 months. Significant TR was defined as TR ≥ moderate by echocardiography.

Results: Significant TR was present in 123 (21.5 %) patients (64 % female, $p = 0.002$). Patients with significant TR more often had atrial fibrillation (46 vs. 20 %, $p < 0.001$), they were more symptomatic (NYHA≥II 56 vs. 31 %, $p < 0.001$), presented with larger right ventricles (RV; 37.5 ± 7.0 vs. 33.1 ± 4.7 mm, $p < 0.001$), larger left and right atria (66.8 ± 12.5 vs. 57.7 ± 7.8 mm and 64.9 ± 12.4 vs. 55.6 ± 7.3 mm; both $p < 0.001$), lower glomerular filtration rates (61 ± 17 vs. 68 ± 18 ml/min), worse left ventricular (LVEF < 50 %: 19 vs.11 %; $p = 0.032$) and RV systolic function (17 vs. 3 %, $p < 0.001$). 127 (22.2 %) patients died during follow-up: 84 patients with significant TR vs. 43 without ($p < 0.001$). By Kaplan-Meier analysis, overall survival was worse in patients with significant TR (log rank $p < 0.001$). However, by multivariable Cox analysis, age ($p < 0.001$), left atrial size ($p < 0.001$) coronary artery disease ($p = 0.011$), chronic obstructive pulmonary disease ($p = 0.047$) and RV dysfunction ($p = 0.032$) but not TR were significantly associated with mortality.

Conclusion: RV dysfunction but not TR late after left-sided valve surgery is significantly associated with survival. Thus isolated surgery of TR in this setting has to be scrutinized. Further studies are needed to define specific patient groups that would clearly benefit from such a procedure.

BA II - 5

Left ventricular global function index: relation with infarct characteristics and left ventricular ejection fraction after ST-segment elevation myocardial infarction

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Objectives: The left ventricular global function index (LVGFI) is a novel indicator of cardiac performance. In healthy individuals, decreased values are strongly associated with adverse cardiovascular events. Its role in patients after acute myocardial infarction is unknown. We sought to investigate the relationship between the LVGFI and infarct characteristics as well as left ventricular ejection fraction in patients after acute ST-segment elevation myocardial infarction (STEMI).

Materials and methods: 226 patients with first STEMI (mean age 57 ± 11 years) were enrolled in this observational study. All patients underwent cardiac magnetic resonance (CMR) imaging within the first week after STEMI. Infarct characteristics were determined with the use of late gadolinium enhanced images. Left ventricular dimensions and function were measured by cine true-FISP sequences.

Results: The mean LVGFI was 32 ± 8 %. Female patients displayed a higher LVGFI than male patients ($p = 0.032$). LVGFI was inversely related with peak creatine kinase ($r = -0.46$), peak cardiac troponin T ($r = -0.45$) and CMR-determined infarct size ($r = -0.42$, all $p < 0.001$). Significantly decreased LVGFI values were also observed in patients with microvascular obstruction and anterior STEMI (all $p < 0.001$). In addition, there was a strong correlation between LVGFI and left ventricular ejection fraction ($r = 0.91$, $p < 0.001$).

Conclusion: This study demonstrates that the LVGFI is strongly associated with infarct characteristics and left ventricular ejection fraction in patients after acute STEMI. LVGFI might be a useful functional parameter of the left ventricle, but its definitive role as a prognostic marker needs to be determined in large outcome trials.

BA II - 6

Long-term predictive value of copeptin after acute myocardial infarction: a cardiac magnetic resonance study

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Objectives: Copeptin levels are associated with cardiac remodeling and adverse outcome after ST-segment elevation myocardial infarction (STEMI). We sought to assess the relation of copeptin determined on day 2 after acute STEMI with infarct size and functional parameters assessed by cardiac magnetic resonance (CMR) imaging 12 months after the index event.

Materials and methods: Participants ($n=41$) underwent contrast-enhanced cardiac magnetic resonance imaging at baseline and 12 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 12 months. Plasma copeptin values were determined by an established immunofluorescent assay.

Results: Copeptin levels were positively correlated to baseline (r = 0.42, $p=0.006$) and 12 months infarct size (r = 0.40, $p=0.011$). There were also significant correlations for copeptin with baseline stroke volumes (r = −0.48, $p=0.002$) and 12 months end-systolic volumes (r = 0.32, $p=0.039$), but not with baseline end-systolic volumes and end-diastolic volumes or 12 months end-diastolic volumes and stroke volume (all $p>0.05$). Copeptin was significantly related to acute and 12 months LVEF (r = −0.49, $p=0.001$, baseline; r = −0.36, $p=0.022$, 12 months follow-up). Furthermore, we made a distinction between patients with ($n=5$) and without ($n=36$) adverse remodeling 12 months after the acute event. The area under the ROC curve of copeptin (0.67, 95 % CI 0.47 to 0.86), with the optimal cut-off level of 11.8 pmol/l, showed 60 % sensitivity and 69 % specificity for the prediction of remodeling at 12 months follow-up.

Conclusions: Plasma copeptin was significantly associated with 12 months myocardial infarct size and LVEF after acute STEMI. Copeptin might be a useful biomarker for prediction of long-term myocardial function and thus potentially outcome.

BA II - 7

Long-term clinical outcomes of patients with atrial fibrillation undergoing percutaneous coronary intervention with stent implantation for acute and stable coronary artery disease

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Background: Patients with atrial fibrillation (AFib) are of increased risk for ischemic complications, and particularly in patients undergoing coronary stenting an excess in bleeding events may occur due to aggressive antithrombotic therapy. However, "real-world" clinical data on long-term mortality are scarce.

Methods: We analyzed 3,574 consecutive patients of a prospective single-center registry undergoing coronary stenting between 2003 and 2012, of whom 1,795 patients had stable coronary artery disease, while 1,779 patients presented with acute coronary syndromes (ACS). Cardiovascular risk factors, angiographic characteristics, co-morbidities and medical therapy were evaluated. As primary endpoint, we compared long-term all-cause mortality between patients with a history for, or new-onset of AFib and patients in permanent sinus rhythm (SR).

Results: History or presence of AFib was found in 167 (9.3 %) stable coronary artery disease (CAD) patients and 107 (6 %) ACS patients. The mean CHA2DS2-Vasc score was similar between stable CAD and ACS patients (3.6 ± 1.6, $p=0.969$). Patients with AFib were more likely to be older, to have renal dysfunction, a prior stroke or transient ischemic attack, peripheral artery disease, hypertension, hyperlipidemia, diabetes or heart failure, respectively. Bare metal stents were implanted in 73.6 % of patients with AFib as opposed to 48.6 % of patients in permanent SR. At hospital discharge, 33.1 % of AFib patients received "triple" antithrombotic therapy (including aspirin, clopidogrel and a vitamin K antagonist, VKA), whilst 65 % received dual antiplatelet therapy. In Stable CAD patients, duration of "triple" and dual antithrombotic therapy (followed by VKA monotherapy) was 2.8 ± 3.3 months and 5.7 ± 4.5 months, respectively, while treatment duration was longer in patients with ACS (3.7 ± 4.4 and 8.0 ± 4.3 month, $p=0.01$ for stable CAD vs. ACS). After a mean follow-up of 61 ± 27 month, long-term all-cause mortality was 37.1 and 11.2 % for stable CAD patients with AFib or with SR, whereas it was 34.6 and 13.2 % for ACS patients with AFib or SR, respectively.

Upon adjustment for confounders in the Cox proportional-hazards model, AFib was associated with a 1.8-fold hazard of long-term all-cause mortality in stable CAD patients (HR 1.80, 95 % CI 1.17;2.77, $p=0.008$), while in ACS patients AFib was tendentially, but not significantly associated with adjusted clinical outcome (HR 1.39, 95 % CI 0.91;2.13, $p=0.132$).

Conclusion: In a "real-world" setting, AFib patients were at higher cardiovascular risk than patients in SR, which translated into significantly increased adjusted long-term all-cause mortality for stable CAD, but not for ACS patients. Accordingly, patients with AFib and stable CAD undergoing invasive revascularization require accurate treatment for secondary prevention as well as optimal antithrombotic therapy in order to improve prognosis.

Postersitzung I: Akutes Koronarsyndrom I

I-1

Butyrylcholinesterase predicts cardiac mortality in young patients with acute coronary syndrome

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Background: The number of acute coronary syndrome (ACS) in young people (≤65 years) is continuously rising. While a large quantity of prognostic factors in ACS are already established less attention has been paid to their age-dependent prognostic value and their relevance in younger patients so far. The aim of our study was to assess the age-dependent prognostic impact of butyrylcholinesterase, which has been shown to be inversely associated with cardiac mortality.

Methods: We retrospectively included 624 patients with ACS into our cohort study. Patients were randomized and stratified into equal groups ($n=208$ per group) according to age "45–64 years", "65–84 years" and "over 85 years". Cox regression hazard analysis was used to assess the influence of butyrylcholinesterase on survival. The multivariate model was adjusted for clinical confounders and variables with a significant association with butyrylcholinesterase.

Results: After a mean follow-up time of 5 years, 154 (24.7 %) patients died due to cardiac causes including 11 patients (5.3 %)

between 45–64 years, 44 patients (21.2%) between 65–84 years and 99 patients (47.6%) >85 years. Median butyrylcholinesterase concentrations significantly differed between age groups with 7.20 kU/l (IQR = 5.90–8.63) in young patients (45–64 years), 6.71 kU/l (IQR = 5.70–8.00) in middle-aged patients (65–84 years) and 5.97 kU/l (IQR = 5.04–6.90) in very old patients (>85 years, $p < 0.001$). Butyrylcholinesterase showed a protective effect on survival free of cardiac mortality in the entire study cohort with an adjusted HR per one standard deviation (1-SD) of 0.70 (95% CI 0.53 – 0.93, $p = 0.01$). A significant interaction between butyrylcholinesterase and age groups was found ($p = 0.008$). Analysis of the age strata showed the strongest protective effect in the age group 45–64 years with an adjusted HR per 1-SD of 0.28 (95% CI 0.12 – 0.64, $p = 0.003$), and a decreasing association with mortality with increasing age (65–84 years: adjusted HR per 1-S. 0.66 [95% CI: 0.41 – 1.06], $p = 0.087$; >85 years: adjusted HR per 1-S. 0.89 [95% CI: 0.58 – 1.38], $p = 0.613$).

Conclusion: Butyrylcholinesterase is a specific predictor for cardiac mortality in younger patients with ACS with an age between 45 and 64 years, while no significant association could be detected in all other age classes. The exact pathophysiological mechanisms and the age-dependent effect of butyrylcholinesterase on cardiac mortality need to be elucidated in future studies.

I-2

Clinical characteristics and mean platelet volume in patients with Type-1 and Type-2 myocardial infarction

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Background: Type-1 myocardial infarction (MI) is defined as spontaneous MI due to intraluminal thrombus, whereas type-2 MI refers to a condition other than coronary artery diseases that contributes to an imbalance between myocardial oxygen supply and/or demand. Mean platelet volume (MPV), a simple, inexpensive and widely available marker of platelet activation was shown to be elevated in patients with MI. However, it remains unclear whether MPV differs between Type-1 and Type-2 MI. Therefore we compared clinical characteristics and MPV in patients with Type-1 and Type-2 non-ST-Elevation MI (NSTEMI).

Methods: Patients with NSTEMI who underwent coronary angiography were classified as Type-1 or Type-2 NSTEMI according to clinical and angiographic findings. Baseline characteristics and laboratory findings, including MPV were recorded.

Results: From 379 consecutive patients presenting with NSTEMI, 41 (10,8%) were diagnosed to have Type-2 NSTEMI in opposite to 338 (89,2%) patients who were classified to have Type-1 NSTEMI, respectively. The most common causes of Type-2 MI were tachycardia and hypertensive crisis ($n = 9$ (22%) each). Type-2 patients tended to be younger (median 63,4 (51,9–72,8) vs. 67,1 (56,5–77, 1) years, $p = 0$, 05), had significantly lower GRACE scores at admission (123,2 ±36,6 vs. 138,4 ±42,6, $p = 0{,}039$), and were less likely to have a history of hypertension (21 (51,2%) vs. 248 (73,4%) mmHg, $p = 0{,}003$) or MI (3 (7,3%) vs. 82 (24,3%), $p = 0{,}016$). Type-2 patients had higher LVEF (median 68 (58–77) vs. 61 (45–70) %, $p = 0{,}007$), and presence of ST-depression on admission electrocardiogram was less frequent (11 (26,8%) vs. 181 (53,6%), $p = 0$, 001). MPV (10,1 ± 0,9 vs. 10,6 ± 1,1 fl, $p = 0{,}033$) and platelet distribution width (12,0 ± 1,4 vs. 12,9 ± 2,3%, $p = 0{,}023$) was significantly lower. In an univariate logistic regression model low MPV was predictive of Type-2 NSTEMI (OR 0,61, 95% CI 0,38; 0,97, $p = 0{,}037$). Upon adjustment for GRACE score, MPV was tendentially, but not significantly associated with the type of MI (OR 0,63, 95% CI 0, 378; 1,036, $p = 0{,}068$).

Conclusion: In addition to differences in clinical parameters, patients with Type-2 NSTEMI presented with lower values of MPV compared to patients with Type-1 NSTEMI, pointing towards less platelet activation in Type-2 MI.

I-3

Coronary NET burden and DNase activity in ST-elevation acute coronary syndrome are predictors of infarct size

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Background: Mechanisms of coronary occlusion in ST-elevation acute coronary syndrome (STE-ACS) are poorly understood. We have previously reported accumulation of neutrophils (polymorphonuclear cells [PMNs]) in culprit lesion site thrombi. The goal of the present study was to quantify PMNs, their formation of neutrophil extracellular traps (NETs), and to examine the relationships of extracellular DNA, DNase and clinical outcomes.

Methods and results: We analyzed coronary thrombectomy aspirates from 112 patients undergoing primary percutaneous coronary intervention. Compared to systemic PMNs, coronary thrombus PMNs were characterized by high expression of activation markers and by the formation of aggregates with platelets. Nucleosomes, neutrophil elastase, myeloperoxidase and myeloid-related protein 8/14 were increased in coronary plasma, and NETs significantly contributed to the scaffolds of particulate coronary thrombi. Thrombus NET burden was directly correlated with infarct size, while culprit site DNase activity showed a reverse correlation with infarct size. Recombinant DNase accelerated lysis of coronary thrombi ex vivo.

Conclusion: PMNs are highly activated in STE-ACS and undergo NETosis at the culprit lesion site. Coronary NET burden and DNase activity are predictors of myocardial infarct size.

I-4

Fibrocytes accumulate at the coronary culprit lesion site and display enhanced migratory and reparative activity in STE-ACS

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Introduction: ST-elevation acute coronary syndrome (STE-ACS) is a major cause of death. Fibrocytes, a Collagen-I + CD34 + CD45 + progenitor cell population, are increased in cardiac tissue in ischemia. In ACS patients, circulating fibrocytes were shown to be decreased compared to stable angina and healthy controls. We hypothesized that fibrocytes are increased, more active and more susceptible to mitogenic signals within the coronary vessels, contributing to occlusion and consecutive reparative processes by production of Collagen-I.

Methods: Coronary (cor) blood samples from STE-ACS patients ($n = 15$, male = 87%, mean age = 65 ± 8.8 years) drawn at primary percutaneous coronary intervention were analyzed. Blood from the femoral artery served as a peripheral control (per). Flow cytometry was employed to characterize fibrocytes based on their expression of Collagen-I, BMPRII, CD34, CD11b, CXCR4 and CD45.

Results: Fibrocyte count is increased at the coronary site compared to peripheral blood (cor 1155 ± 1273/106 CD45+ cells, per 505 ± 559/106 CD45+ cells, $p = 0.031$). Furthermore, coronary fibrocytes display significantly increased expression of CD11b (cor MFI = 79860 ± 38830, per MFI = 52383 ± 23669, $p = 0.001$) and Collagen-I (cor 20551 ± 11817, per 13451 ± 10599, $p = 0.021$). Conversely, CXCR4 expression is significantly decreased in coronary fibrocytes (cor 51664 ± 24462, per 97302 ± 68827, $p = 0.023$). No difference in BMPRII, CD34 and CD45 expression was observed.

Conclusions: The two-fold increase of coronary fibrocyte count compared to peripheral blood is possibly due to homing to the coronary vessels in STE-ACS. Increased coronary CD11b and increased Collagen-I expression might reflect enhanced migratory and reparative activity of fibrocytes within the coronary vessels. The decreased CXCR4 expression of coronary fibrocytes could indicate that in the periphery, fibrocytes are stimulated to express CXCR4, a chemokine receptor considered to be important in the pathogenesis of fibrotic diseases of the heart and lung, with the expression being lost at the target site. Further experiments will clarify the contribution of fibrocytes to STE-ACS.

I-5

Expression of selected genes in aspirated coronary thrombi in patients with acute myocardial infarction

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Background: Acute myocardial infarction is a major cause of mortality worldwide. Although data about the clinical benefit of thrombus aspiration have shown controversial results, the knowledge of thrombus composition, particularly with respect to genetics, is of increasing interest as reports on the content of aspirated coronary thrombi until now mainly have focused on the structural and cellular components. We aimed to investigate the genetic expression of selected mediators and proteases actively involved in plaque rupture, platelet and neutrophil cell activation, coagulation, fibrinolysis and inflammation in aspirated coronary thrombi.

Methods: Coronary thrombi from 67 patients with acute myocardial infarction were investigated. RNA from aspirated coronary thrombi was isolated and gene expression arrays of selected markers were performed by a RT-PCR based method with relative quantification.

Results: Twenty of the 22 markers (not CRP and IL12) were expressed in > 50 % of the samples. The relative quantification of P-selectin correlated negatively to the ischemic time ($p = 0.01$), while genes related to fibrinolysis (t-PA, u-PA, PAI-1), inflammation (PTX3, CXCL9, MCP-1, IL18, TNF-alfa) and to plaque instability (MMP-2 and TIMP-1) correlated positively to the ischemic time (all < 0.05) (See Table). When dichotomizing ischemic time into ≤ median (4.0h) and > median, the relative reduction of P-selectin was 0.7-fold, while the relative increase in t-PA was 2.2-fold, u-PA 5.8-fold, PAI-1 8.7-fold, PTX3 1.7-fold, CXCL9 3-fold, MCP-1 2.6-fold, IL18 2.3-fold, TNF-alfa 2-fold, MMP-9 2.8-fold and TIMP-1 3.2-fold. The presence of type 2 diabetes increased PAI-1 expression 3.2-fold, while the presence of hypertension reduced IL-8 and TIMP-1 to about half-fold. Smoking and overweight did not affect any markers.

Conclusions: Gene expression of several pro-inflammatory markers could be detected in aspirated coronary thrombi. The genetic expression profile changed according to the ischemic time with a decrease in expression of genes related to platelets and an increase in expression of genes related to fibrinolysis, inflammation and plaque instability, respectively. Expression of PAI-1 was significantly higher in patients with type 2 diabetes, possibly confirming the particular role of impaired fibrinolysis in type 2 diabetes. The presence of hypertension seemed to be associated with markers of plaque instability.

Table Spearman correlations between biomarkers and ischemic time (n = 67), and absolute RQ-values of biomarkers in relation to median ischemic time

	Ischemic time			RQ-values[a]	*p*-value
	r	*p*-value			
MMP-2	0.480	*0.001*	–	1.1 (0.0–18.6)	*0.011*
			+	3.1 (0.3–32.4)	
MMP-9	−0.248	0.054			
TIMP-1	0.521	*< 0.001*	–	1.4 (0.3–8.7)	*< 0.001*
			+	4.5 (0.3–71.7)	
CD40L	−0.157	0.316			
PAR-1	−0.169	0.218			
P-selectin	−0.330	*0.010*	–	1.3 (0.1–6.1)	0.087
			+	0.9 (0.0–3.1)	
TF	0.186	0.301			
TFPI	0.186	0.147			
t-PA	0.444	*0.003*	–	1.3 (0.1–7.3)	*0.016*
			+	2.8 (0.1–36.8)	
u-PA	0.527	*< 0.001*	–	6.8 (0.2–194.0)	*0.003*
			+	39.1 (1.0–232.9)	
PAI-1	0.552	*< 0.001*	–	0.3 (0.0–4.1)	*< 0.001*
			+	2.6 (0.1–26.8)	
MPO	0.090	0.612			
PTX3	0.371	*0.020*	–	0.6 (0.1–2.6)	0.247
			+	1.0 (0.1–29.0)	
CRP	–	–			
CXCL9	0.507	*0.003*	–	0.2 (0.0–4.4)	*0.004*
			+	0.6 (0.2–8.5)	
Fractalkine	0.32	0.050			
MCP-1	0.489	*< 0.001*	–	0.9 (0.0–66.7)	*0.006*
			+	2.3 (0.0–31.2)	
IL-18	0.509	*0.001*	–	4.6 (0.8–70.1)	*0.008*
			+	10.7 (0.8–89.2)	
Il1β	0.069	0.603			
IL-8	0.225	0.076			
TNFα	0.418	*0.014*	–	0.9 (0.1–4.4)	0.187
			+	1.8 (0.2–9.3)	
IL-12	–	–			

– referes to ischemic time ≤ median (4.0 h), + refers to ischemic time > median (4.0 h)
[a]Medians and ranges are given

I-6

Prasugrel versus Ticagrelor in der klinischen Praxis bei Primär-PCI Erfahrungen aus dem Österreichischen Akut-PCI Register

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Hintergrund: Die ESC empfiehlt in ihren aktuellen Richtlinien zum ST-Hebungsinfarkt Prasugrel oder Ticagrelor bei Primär-PCI. Sowohl Prasugrel (TRITON-TIMI 38) als auch Ticagrelor (PLATO) wurde in der Zulassungsstudie mit Clopidogrel verglichen.

Es gibt keine Daten aus großen RCTs, die Prasugrel (Pra.) und Ticagrelor (Tic.) gegenübergestellt haben.

Methoden: Für die vorliegende Analyse wurden 875 konsekutive Patienten aus dem Österreichischen Akut-PCI Register, die zwischen Jänner 2012 und Februar 2013 eine Primär-PCI erhalten haben und vor Eintreffen im Katheterlabor entweder mit Pras. oder Tic. behandelt wurden, berücksichtigt. Die Patienten wurden hinsichtlich ihrer klinischen Charakteristika, Therapie und dem klinischen Outcome bis zur Entlassung verglichen.

Ergebnisse: Von den 875 eingeschlossenen Patienten erhielten 550 (62,9 %) Pra. und 325 (37,1 %) Tic. Die Patienten mit Tic. waren älter [63 (53–75) vs. 58 (51–66) Jahre; $p<0,01$, Median, IQR), seltener Raucher (44,9 vs. 56,2 %; $p<0,01$) und hatten eine länger Gesamtischämiezeit [1,44 (1,00–2,35) vs. 1,40 (1,00–1,92) h; $p=0,01$, Median, IQR], wohingegen die Rate stattgehabter Schlaganfälle in beiden Gruppen gleich war (Pra. vs. Tic., 3,0 vs. 4,8 %; $p=0,19$). Die Patienten mit Pra. erhielten häufiger vorab Clopidogrel (6,0 vs. 2,2 %; $p<0$, 01) und peri-interventionell häufiger Bivalirudin (11,3 vs. 3,7 %; $p<0,01$) darüber hinaus bestand ein starker Trend zu mehr Heparin bei Patienten mit Pra. (89,5 vs. 85,2 %; $p=0,06$) und die Patienten unter Pra. wurden letztlich seltener interveniert (93,1 vs. 96,4 %; $p=0,048$).

Die Krankenhausmortalität (Pra. vs. Tic., 1,5 vs. 2,8 %; $p=0,17$) und die Re-Infarktrate (Pra. vs. Tic., 0,9 vs. 0,6 %; $p=0,64$) war ebenso wie die Raten an TIMI major Blutungen (Pra. vs. Tic. 1,3 vs. 0,6; $p=0,35$) und ischämischen Schlaganfällen (Pra. vs. Tic, 0,2 vs. 0,6 %; $p=0,29$) niedrig und nicht unterschiedlich.

Conclusio: Sowohl Ticagrelor als auch Prasugrel ist in der täglichen klinischen Praxis mit einer niedrigen Mortalität bei Primär-PCI verbunden und, wenn unter ärztlicher Abschätzung des individuellen Komplikationsrisikos eingesetzt, im in-hospitalen Verlauf sicher.

Postersitzung II: Basic Science I

II-1

CD4+CD28null T-cells are enriched at the culprit lesion site in STE-ACS and promote NET production

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Background: ST-elevation acute coronary syndrome (STE-ACS) is among the leading causes of death. Acute coronary atherothrombosis as the underlying event is still poorly understood. We hypothesized that circulating leukocytes adhere to atherosclerotic plaques and mediate thrombotic occlusion. It has been shown that circulating CD4+CD28null T-cells, which release high levels of granzyme B and perforin, are increased in STE-ACS, especially in patients suffering from diabetes and/or recurrent cardiovascular events. Neutrophil extracellular traps (NETs) released by activated polymorphonuclear neutrophils (PMNs) have been shown to be a crucial component in thrombogenesis. We characterized CD4+CD28null cells at the culprit lesion site in STE-ACS patients and tested their impact on NET formation.

Methods: We included 150 STE-ACS patients who underwent primary percutaneous coronary intervention (PCI) at the Vienna General Hospital. Culprit site blood and solid thrombus material were collected during thrombectomy. In parallel, a blood sample from the femoral arterial sheath was collected. Flow cytometry was employed to measure CD4+CD28null T-cells in whole blood and solid thrombus specimens. Granzyme B and perforin levels were determined in plasma by ELISA technique. Isolated PMNs were stimulated with granzyme B and/or PMA, and NET formation was assessed by immunohistochemistry.

Results: CD4+CD28null T-cells were increased at the culprit lesion site both in coronary whole blood and the solid thrombus, compared with peripheral blood ($n=106$, $p<0.0001$, 7.79 ± 9.68 vs. 9.92 ± 11.44 % of CD4+ cells; $n=20$, $p<0.01$, 8.14 ± 10.08 vs. 13.6 ± 14.12 % of CD4+ cells). Perforin and granzyme B were decreased in coronary CD4+CD28null T-cells and correlated inversely with granzyme B levels in culprit site plasma. Granzyme B induced netosis of PMNs *in vitro*.

Conclusion: Granzyme B/Perforin-releasing CD4+CD28 null T-cells accumulate at the culprit lesion site in STE-ACS, and may directly induce netosis. Further experiments will evaluate the significance of this finding in the pathogenesis of acute coronary syndromes.

No conflicts of interest.

II-2

Effects of Interleukin-33 on tissue factor in human endothelial cells in vitro

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Background: Interleukin (IL)-33 is a member of the IL-1 cytokine family. IL-33 was previously shown to induce angiogenesis and the expression of inflammatory cytokines and adhesion molecules in endothelial cells. Tissue factor (TF) is a primary trigger of coagulation. Elevated levels of TF are found in atherosclerotic plaques, and TF leads to thrombus formation, when released upon plaque rupture.

Aim: Here we investigated the impact of IL-33 on TF expression in human endothelial cells, as a new possible mechanism for IL-33 to regulate their thrombotic potential.

Methods and results: Human umbilical vein endothelial cells (HUVEC) and human coronary artery endothelial cells (HCAEC) were treated with 1, 10 or 100 ng/ml recombinant human IL-33 for 3, 6, 9 and 24 hours (h). Expression of mRNA specific for TF was determined by RT-PCR. TF protein and activity levels were measured by specific enzyme-linked immunosorbent assays (ELISAs). We found that IL-33 significantly ($p<0,001$) induced TF mRNA and protein expression in HUVEC an HCAEC in a time- and concentration-dependent manner. Stimulation with 100 ng/ml IL-33 for 3 and 6 h has also increased ($p<0,001$) cell surface TF activity level in HUVEC. Seite 2$6-siRNA-mediated gene knockdown inhibited

IL-33-induced TF expression, suggesting that this effect of IL-33 is facilitated through its receptor S. 2. Preincubation of HUVEC with 100 μM NFkB-inhibitor dimethyl-fumarate, abrogated IL-33-induced TF protein synthesis. IL-1 receptor antagonist (IL-1RA) had no effect on IL-33-induced increase of TF expression. In human carotid atherosclerotic plaques ($n=16$), TF mRNA positively correlated with IL-33 mRNA expression ($r=0,86$, $p<0,001$).

Conclusion: Our results showed that IL-33 increases TF expression and activity in human endothelial cells, and that this effect is S. 2/NFkB-dependent, but IL-1-independent. Furthermore, we supported our in vitro data in human atherosclerotic tissue where we found a strong positive correlation of IL-33 and TF expression. Thus, IL-33-induced changes in TF expression could affect the thrombotic potential of endothelial cells, as well as potentiate thrombotic events in the setting of ruptured human atherosclerotic plaque.

II-3

Elaboration of an experimental model of left ventricular hypertrophy and chronic diastolic dysfunction for translational research

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Background: Small animal models of myocardial hypertrophy using knock-out mice are widely used to understand the underlying pathophysiology and to improve the treatment of left ventricular hypertrophy (LVH), diastolic dysfunction and diastolic heart failure. Surgical partial occlusion of the ascendent aorta of pigs results in abrupt hemodynamic changes, therefore this method is not optimal for developing of a chronic LVH with diastolic dysfunction. The aim of our experiments was to elaborate LVH and chronic diastolic dysfunction using less invasive method and more translatable for human conditions. We have created artificial aortic isthmus stenosis by percutaneous implantation of undersized peripheral bare metal stents (BMS) in the descending aorta of juvenile pigs as the constant size of stent in growing pigs results in an antegrade partial obstruction of the aortic flow with gradual increase in afterload, which were controlled by serial non-invasive imaging.

Methods: Domestic pigs (male, 15 kg) underwent BMS (12 mm of diameter and 30 mm of length) implantation of the descending aorta below the aortic arch. At 1 and 3 months follow-up (FUP) aortography (computer tomography, CT) and transthoracic echocardiography (TTE) were performed to measure the aortic diameter and grade of stenosis, as well as LV systolic and diastolic function, respectively. By catheterization left ventricular haemodynamics and the right ventricular and atrial pressures were measured at the final 3-month FUP. In addition, histological examination of left ventricular myocardial tissue was performed using PicroSirius Red and compared to normal pig myocardium. Levels of fibrosis (red-stained collagen) of this myocardial hypertrophy model were quantified using ImageJ software.

Results: Aortography by CT showed a mild stenosis of the descendent aorta (31 ± 6 % diameter stenosis) at 3-month. TTE revealed moderate degree concentric LV hypertrophy at the final FUP (mean end-diastolic wall thickness 13.6 ± 2.8 mm). The global LV EF was 73 ± 8 % (area-length method). E/A ratio was 0.92 ± 0.56, the E/E`ratio 8.4 ± 1.5. Invasive pressure measurements at the final FUP resulted in a systolic pressure gradient of 21 ± 8 mmHg between LV and aorta descendent distal to stent, increased LV end-diastolic pressure (10 ± 9 mmHg) and mild elevation of pressures in the right atrium (mean 9.0 ± 1.4 mmHg) and right ventricle (systolic pressure 31 ± 4 mmHg, end-diastolic pressure 8 ± 2 mmHg). Picrosirius red staining showed a marked increase in fibrosis in the myocardial tissue (3.6 ± 0.8 vs 0.36 ± 0.1 % of the LV) in the treated vs normal pigs.

Conclusion: Our preliminary results confirmed that percutaneous artificial aortic isthmus stenosis in pigs is a useful method for translation research of LV hypertrophy and diastolic dysfunction, with enhanced myocardial fibrosis, and increase in right ventricular and atrial pressures during the first 3 months FUP. Refinement of this method aims to develop a preclinical model of diastolic heart failure with preserved LV systolic function. (These experiments were sponsored by the FIBROTARGET EU project).

II-4

Evaluation of diagnostic value of new biomarkers S100A12 Protein and adrenomedullin in acute coronary syndrome

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Background: It has been shown that adrenomedullin (ADM) (cardiovascular-regulatory peptide) and the neutrophil activation marker and pro-inflammatory cytokine S100A12 is a predictive marker of severity of coronary atherosclerosis and worse outcome in patients with coronary artery disease (CAD). The purpose of the study was to investigate the diagnostic role of these two biomarkers in patients with acute coronary syndromes, such as STEMI or NSTEMI.

Methods: Sixty-one patients ($n=31$ stable CAD; $n=14$ STEMI, $n=16$ NSTEMI) were prospectively included in the study. Plasma levels of ADM and S100A12 were determined immediately after diagnosis of STEMI, NSTEMI (according to relevant guidelines) or in patients with stable coronary artery disease. Clinical history (presence of cerebral or peripheral atherosclerosis, previous myocardial infarction, coronary intervention or bypass operation) and atherosclerotic risk factors were recorded. Plasma troponinT, creatine kinase and its MB fractions and NT-proBNP were determined. Exclusion criteria were chronic renal insufficiency (known factor influencing both new biomarkers), systematic diseases (eg. malignancy, haematologic or autoimmune disorders) or severe valve disease. Plasma levels of ADM and S100A12 were measured using ELISA.

Results: No baseline differences between the groups were documented, regarding clinical parameters. Table 1 shows the laboratory parameters.

Although a trend towards elevated levels of ADM and S100A12 was found in patients with STEMI, no significant difference could be proven. Presence of diabetes mellitus, hypertension, hypercholesterolaemia, smoking, previous clinical history was not associated with elevated levels of new biomarkers either in the entire cohort or in subgroups. The plasma levels of ADM and S100A12 did not correlated with plasma levels of troponinT or CK, or CK-MB, and even the highest interquartile range of ADM and S100A12 did not show correlation between the presence of STEMI or NSTEMI.

Conclusions: In a small consecutive patient cohort, ADM and S100A12 proved not to be a diagnostic marker of acute coronary syndrome, but it might be a valuable additional parameter for diagnosis of atherosclerotic disease.

Table 1 Laboratory parameters

	Group stable CAD	Group STEMI	Group NSTEMI
	n = 31	*n* = 14	*n* = 16
S100A12 (median with IQR) (pg/mL)	694 (0; 7445)	7405 (0; 13026)	5755 (0; 16092)
Adrenomedullin (median with IQR) (ng/L)	194 (160; 220)	216 (185; 353)	192 (173; 218)
NT-proBNP (median with IQR) (pg/mL)	212 (143; 298)	359 (120; 926)	732 (84; 3019)
Troponin T (mean ± SD) (mg/mL)	0.01 ± 0.01	*2.75 ± 2.92**	*1.29 ± 2.77**+*
Creatine kinase (mean ± SD) (U/L)	135 ± 88	*2519 ± 5044**	*478 ± 955**+*
Creatine kinase MB fraction (mean ± SD) (U/L)	5.9 ± 11.8	*149 ± 206**	*36 ± 84**+*

IQR Interquartile range
*$p < 0.05$ between Group stable CAD and Group STEMI
**$p < 0.05$ between Group stable CAD and Group NSTEMI
+$p < 0.05$ Group stable CAD and Group NSTEMI

II-5

Gene expression profiling of porcine myocardium after repetitive ischemia/reperfusion

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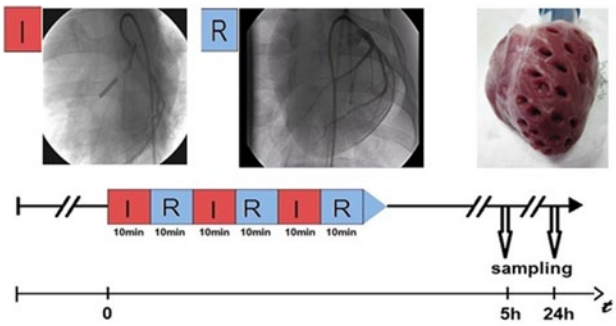
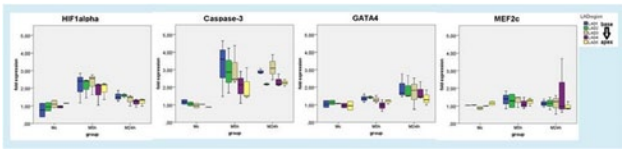
Background: We have analysed the gene expression profile of the myocardium after repetitive ischemia/reperfusion aiming to simulate human pre-infarction angina pectoris in an animal model ready to translate.

Methods: Under general anaesthesia domestic pigs underwent closed chest repetitive (3 × 10 cycle) ischemia/reperfusion by percutaneous balloon occlusion/deflation of the mid left anterior descending coronary artery. Sham balloon occlusion/deflation was performed in control pigs ($n = 3$). After 5 h ($n = 3$) and 24 h ($n = 3$) follow-up, five myocardial samples were harvested from the heart basis (LAD1) to apex (LAD5) including the border zone of the ischemia (LAD3) localized by using anatomical landmarks (below the origin of the 2nd diagonal branch). The hypoxia inducible factor-1 (HIF1alpha), caspase-3, GATA4 and myocyte enhancer factor 2 C (MEFC2) gene expression patterns of the corresponding regions were analysed by using quantitative real-time PCR (rtPCR). (Studydesign)



Results: Repetitive ischemia/reperfusion resulted in a rapid increase in HIF1alpha and caspase-3 expression in the ischemic area and border zone, while increase in MEF2c expression was moderate. GATA4 expression was more pronounced 24 h after the ischemic attack (Figure).



Conclusions: Short periods of repetitive ischemia/reperfusion without infarction cause alteration in gene expression profile of the myocardium, which might be responsible for the protective effect against subsequent infarction and necrosis.

II-6

Isolation of porcine cardiomyocytes: comparison of two methods

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Background: Cardiomyocyte culture represent an excellent in vitro model to study cardiac cell pathophysiology and biology. Porcine pre-clinical experiments are used for translational research due to the anatomical and physiological similarity of porcine heart to the human heart. In spite of extensive research on cardiac regeneration, up to now, there is no standardized method for isolating porcine cardiomyocytes.

Methods: Porcine cardiomyocytes were harvested from juvenile domestic pigs and were isolated with two different methods: enzymatic digestion and primary explant culture. Enzymatic digestion of heart tissue was performed with a digestion solution (Earl's Balanced Salt Solution, collagenase, BSA, Penicillin/Streptomycin). Pieces of heart tissue (~ 2mm^2) were incubated at 37 °C for 40 min in digestion solution. Harvested cells were resuspended in M199 media and seeded in 75cm^2 tissue flasks (320.000 cells/flask). For primary explants cultured Petri dishes were scratched with a scalpel to provide a suitable surface for cardiomyocytes to adhere. Pieces of heart tissue (~ 2mm^2) were placed on the scratches. Dishes were afterwards filled with M199 media and incubated at 37 °C and 5 % CO_2. Cell number and viability of isolated cells were monitored at day 6, day 12, and day 18. After 21 days of cultivation cardiomyocytes from both isolation methods were examined and stained with Picrosirius red stain to differ between fibrocytes and cardiomyocytes. Purity and phenotype of isolated cardiomyocytes were analyzed by immunofluorescent microscopy using cardiomyocyte markers TroponinT and α-sarcomeric actin.

Results: Cardiomyocytes from the primary explant culture started migrating out of the tissue after 8 days. On day 21 the total number of cells was 4.6*105 cells, in contrast with the number of cells obtained by the enzymatic digestion method (2.2*105 cells, $p < 0.05$). The cell viability of the myocyte cell culture was relatively low at day 21 (14 vs 12 % by enzymatic digestion method vs primary explant method). Troponin T and α-sarcomeric actin fluorescent staining confirmed the presence of living cardiomyocytes. Microscopic examination of cells obtained from primary explant culture showed round and rod-shaped cells. Some of the cells were spindle-shaped suggesting presence of fibrocytes. In contrast, cells obtained with enzymatic digestion method were rod-shaped like cardiomyocytes and had constantly similar granulation. The Picrosirius red staining confirmed that cells from the explant culture were a mixed population of cells. Cells isolated through enzymatic digestion showed to be a more homogeneous population of cardiomyocytes.

Conclusions: Using both (enzymatic digestion and primary explant culture) methods porcine cardiomyocytes could be successfully isolated and cultured. The enzymatic digestion method resulted in higher purity of the cells. The low rate viability of the cells requires further refinement of this method.

II-7

Reduced cardiotoxicity by liposome-encapsulation of doxorubicin via higher expression level of metabolic and oxidative gens compared with doxorubicin under experimental condition

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Background: The objective of the present experimental study was to compare the cardiotoxic effect of doxorubicine (DOX) with liposome-encapsulated doxorubicin-citrate complex (Myocet® MYO) exploring gene expression profile differences in pig hearts.

Materials and methods: Fifteen domestic pigs received either DOX ($n=6$) or MYO ($n=9$) in 3 cycles of cytostatic treatment of human dose. Cardiac magnetic resonance imaging (cMRI) with gadolinium late enhancement (LE) were performed at baseline and after the last dose application. Routine blood parameter such as number of leukocytes, red blood cells and thrombocytes were counted and liver, kidney parameter and electrolytes were controlled during the treatment. The left (LV) and right (RV) ventricular systolic (ejection fraction, EF), and diastolic (peak filling rate, PFR) function and myocardial fibrosis was assessed by LE-cMRI images. Plasma proBNP, troponinI and creatine kinase (CK) were measured using ELISA. Gene expression profile of the LV, RV and left atrium was analyzed by next generation sequencing (NGS).

Results: Animals receiving MYO showed significantly better LV EF (56.4 ± 5.6 vs 41.9 ± 13.5 %, $p=0.039$) and RV EF (42.1 ± 2.8 vs 28.9 ± 8.9 %, $p=0.009$) as compared with DOX, with better LV diastolic function in MYO group (PFR: 10.7 +/− 4.8 vs 7.9 +/− 2.5 ml/s, $p<0.1$). Trend towards less myocardial fibrosis was observed in MYO-treated animals vs DOX, confirmed by cMRI (LV: 5.8 +/− 4.1 vs 6.6 +/− 2.9 %; RV: 6.2 +/− 1.9 vs 8.6 +/− 3.9 %). Trend towards less proBNP (184 ± 96 vs 342 ± 299 pg/ml) was measured with similar CK and troponinI values at the final follow-up. NGS revealed 16 and 21 significantly ($p<0.05$) up-regulated metabolic and cell cycle and energy gene (eg. respiratory chain, mitochondrial genes, oxidative phosphorylation, NADH activity) in MYO LV and RV myocytes, respectively, as compared to DOX, while no difference in gene expression profile was observed in the left atrium between the groups.

Conclusions: The liposomal-encapsulated doxorubicin-citrat (MYO) proved to be less cardiotoxic as compared with DOX, resulting in better LV and RV systolic and LV diastolic function in association with higher level of oxidative, cell cycle and energy gene expression in an experimental model of cardiotoxic cytostatic therapy.

II-8

Extracellular adherence protein of staphylococcus aureus inhibits atherosclerosis in ApoE-deficient mice

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Background: Recruitment of monocytes and T-cells into the intima plays a crucial role in initiation and progression of atherosclerotic disease. Extracellular adherence protein (Eap) is an anti-inflammatory protein secreted by Staphylococcus aureus that was previously shown to inhibit ICAM-1-mediated interactions between leukocytes and lymphocytes with the vascular endothelium and to block leukocyte extravasation in various inflammatory disease models. We therefore aimed to investigate a possible influence of Eap on the development and progression of atherosclerotic lesions in ApoE-deficient mice.

Methods: Ten ApoE-/- mice (C57BL/6, age 8 weeks, weight 25 ± 2.3 g) were put on a high fat diet for 6 weeks. Afterwards, five mice in the control group were intraperitoneally injected daily with 200 µL sterile phosphate buffered saline (PBS). In the treatment group, 5 mice received a daily intraperitoneal injection of 50 µg Eap (strain Newman) in 200 µl sterile PBS. At day 28 of treatment, mice were sacrificed and the aortic root was HE-stained and plaque size was determined.

Results: Mice treated with Eap showed significantly smaller atherosclerotic plaques than mice treated with PBS only. The mean total plaque area was 0.66 ± 0.35mm² in the treated group as compared to 1.21 ± 0.66mm² in the control group ($p<0.05$).

Conclusion: We could show that intraperitoneal injection of Eap significantly reduced the size of atherosclerotic lesions in ApoE-/- mice within the aortic root. Thus, by interfering with extravasation of inflammatory cells, Eap could represent a therapeutic option in stable atherosclerotic disease.

II-9

Extracellular adherence protein of staphylococcus aureus inhibits thrombus resolution

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Background: Venous thromboembolism is the third most common cardiovascular disease with an overall annual incidence of 1–2 per 1000. We have previously shown that bacterial infection is associated with thrombus persistence, and with complicated thrombosis such as chronic thromboembolic pulmonary hypertension. Staphylococcal extracellular adherence protein (Eap) is a broad-spectrum adhesin that inhibits host leukocyte recruitment and angiogenesis. Both processes are involved in thrombus resolution, therefore we hypothesized that Eap may be a key mediator of vascular remodeling subsequent to thrombus infection.

Methods: We induced thrombus in the infrarenal vena cava (IVC) of an established murine model of stagnant-flow venous thrombosis. One day after IVC ligation we tail-vein-injected mice with wild-type Eap-competent Staphylococcus (S.) aureus or Eap-deficient S. aureus. To investigate the influence of Eap without infection, repeated intraperitoneal injections of isolated Eap were performed, and compared with saline injections. Thrombi were harvested at 3, 7, 14 and 28 days after IVC ligation, and (immuno)-histological analyses and real-time PCR were performed.

Results: Thrombus cross-sectional areas and volumes (Fig. 1) of Eap-competent S. aureus-infected mice were significantly larger than those of Eap-deficient S. aureus-infected mice on day 7 ($n=8$, $p<0.05$). Furthermore, between days 3 and 7, thrombus cross-sectional areas and volumes illustrated significantly delayed thrombus resolution in mice infected with Eap-competent S. aureus compared with mice infected with Eap-deficient S. aureus ($n=8$, $p<0.05$).

Conclusion: Our data confirm that infection with wild-type S. aureus delays thrombus resolution. This effect was significantly attenuated when mice were infected with an isogenic Eap-deficient strain. Eap is one of the S. aureus proteins that are responsible for thrombus persistence and vascular occlusion.

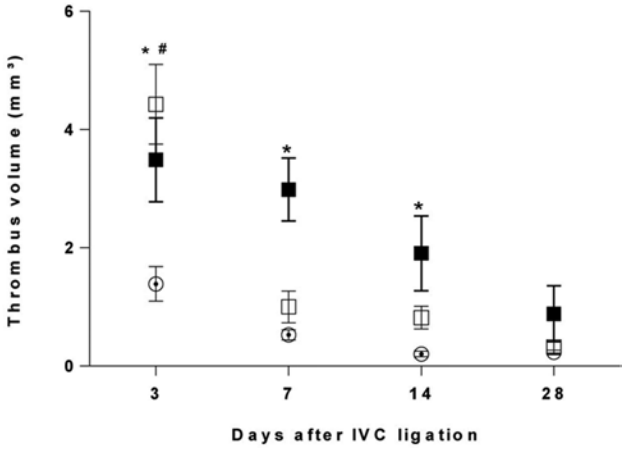

Fig. 1 Absolute thrombus volumes: Thrombi infected with Eap-competent staphylococci (■) had significantly larger volumes than the control group (⊙) on day 3, 7 and 14. Thrombi infected with Eap-deficient staphylococci (□) had significantly larger volumes than the control group (⊙) on day 3 (P = 0.005)

Postersitzung III: Bildgebung I

III-1

Anwendung der Stressechokardiographie in Österreich

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Hintergrund: Unter den nichtinvasiven diagnostischen Untersuchungsmethoden in der Kardiologie ist die Stressechokardiographie (SE) ein kostengünstiges, sensitives Verfahren ohne Strahlenbelastung. Ziel dieser Studie war es, die Anwendung der SE in Österreich zu erfassen.

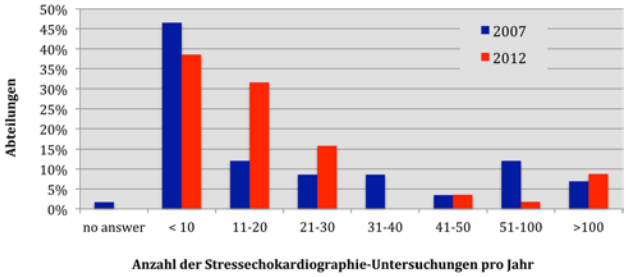
Methodik: In den Jahren 2013 und 2008 wurde per E-Mail ein Link zu einem webbasierten Fragebogen an 117 österreichische kardiologische oder allgemein internistische Abteilungen geschickt. Erhoben wurden die Häufigkeit der SE-Untersuchung, die Anzahl der Untersucher pro Abteilung, die Indikation und die angewandten Techniken für die Jahre 2012 und 2007.

Ergebnisse: Es wurden die Daten aller Krankenanstalten mit kardiologischen bzw. internistischen Abteilungen erfasst. Die SE wurde im Jahr 2007 von 58 (49,6 %) und im Jahr 2012 von 57 (48,7 %) Abteilungen durchgeführt. Mehr als 100 SEs wurden im Jahr 2007 von vier (6,9 %) und im Jahr 2012 von fünf (8,7 %) Abteilungen durchgeführt.

Im Jahr 2012 wurden zur Stressinduktion die physikalische Belastung, Dobutamin, sowie Dipyridamol von 15 (26,6 %), 52 (91, 20%) und 5 (8,7 %) der Abteilungen genutzt. Adenosin und Pacing wurden von je einer (1,75 %) der Abteilungen angewendet.

Kontrastmittel kam im Jahr 2012 in 26 (45,6 %) und Strain Rate Imaging in 11 (19,3 %) Abteilungen zum Einsatz. Transösophagale SE wurde in sechs (10,5 %) und 3D-Bildgebung in vier (7 %) Abteilungen angewendet.

Diskussion: Obwohl die SE international als Standardmethode in vielen Bereichen der kardiologische Diagnostik gilt und viele Vorteile (hohe Spezifität, hohe Sensitivität, fehlende Strahlenbelastung, kostengünstig) mit sich bringt, ist ihr nationaler Stellenwert äußerst gering. So wurde die SE sowohl im Jahr 2012 als auch im Jahr 2007 sehr selten angewandt. In den meisten Abteilungen konnten die Qualitätsstandards nicht eingehalten werden. Ob dies nur an der inadäquaten Verrechenbarkeit liegt, kann an dieser Stelle nicht beantwortet werden. Ohne großer Veränderungen der Rahmenbedingen, wie z. B. durch Änderung der Verrechnung oder durch Kursangebote, wird die SE in Österreich wohl auch in Zukunft in der Schublade bleiben.



Jahr	2012	2007
Anzahl der Abteilungen mit SE	57	58
Anzahl der UntersucherInnen	123	179
Maximale Anzahl an SEs	1800	2110
Indikationen für SE		
Ischämiediagnostik	34	43
Vitalitätsdiagnotik	24	30
Low-flow, low-gradient Aortenstenose	42	44
Symptomatische Mitralinsuffizienz	6	10
Evaluierung einer Hypertrophen Kardiomyopathie	15	7

III-2

Myocardial biopsy for the validation of cardiac magnetic resonance T1 mapping for quantification of extracellular matrix

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Universitätsklinik für Innere Medizin II, Klinische Abteilung für Kardiologie, Wien

Background: Diffuse myocardial fibrosis/extracellular matrix expansion is a landmark feature of various cardiac diseases and is associated with an unfavorable prognosis. Recently, cardiac magnetic resonance (CMR) T1-mapping has been proposed for the quantification of extracellular matrix.

Published series mainly used two T1 mapping sequences: 1. Modified Look-Locker Inversion recovery (MOLLI) T1 mapping, allowing the calculation of extracellular volume (ECV), 2. Post-contrast multiple breath-hold T1 mapping. In addition, native (pre-contrast) T1 mapping has gained increasing interest.

Although CMR T1 mapping is a very promising technique and has been advertised as the new "non-invasive myocardial biopsy", validation data, particularly in heart failure patients, are sparse.

Methods: 22 heart failure patients underwent CMR T1 mapping on a 1.5-T scanner (Avanto, Siemens Medical Solutions, Erlangen,

Germany) and left ventricular biopsy within 4 weeks. The population consisted of 16 HFpEF (heart failure with preserved ejection fraction) patients, 3 patients suffering from dilated cardiomyopathy and 3 amyloidosis patients. In all patients the 3 T1 mapping sequences were applied.

Left ventricular biopsies were stained with modified Trichrome and Congo-red. Extracellular matrix was quantified with TissueFAXS and HistoQuest© analysis.

Results: Extracellular matrix by TissueFAXS was 43.8 ± 20.8 % of the region of interest, ECV as determined by MOLLI was 33.6 ± 9.9 %. The average post-contrast T1 time by the multiple breath-hold sequence was 407 ± 85 ms and native T1 times were 1000 ± 61 ms.

The amount of extracellular matrix by TissueFAXS correlated significantly with MOLLI ECV ($r = 0.583$, $p = 0.011$) and with multiple breath-hold post-contrast T1 times ($r = -0.459$, $p = 0.042$), but not with native T1 times ($r = 0.375$, $p = 0.114$).

Conclusion: In the present series, MOLLI ECV appears to be the most accurate method for the quantification of extracellular matrix expansion when validated against myocardial biopsies. Although multiple breath-hold post-contrast T1 mapping may be influenced by renal function, heart rate, and time of acquisition, it also appears useful for non-invasive measurement of extracellular matrix. Native T1 mapping showed the weakest correlation with extracellular matrix by TissueFAXS, but there was a tendency towards a significant relationship (r = 0.375, p = 0.114).

III-3

Patterns of cardiac late enhancement by magnetic resonance imaging in patients with pulmonary sarcoidosis

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Background: Cardiac involvement in pulmonary sarcoidosis is associated with adverse prognosis. The frequency and pattern of cardiac involvement in sarcoidosis patients without cardiac symptoms, however, is unclear. The aim of the present study was to screen patients with proven pulmonary sarcoidosis for potential cardiac involvement by cardiac magnetic resonance imaging (CMR) including late gadolinium enhancement (LGE) and to describe frequency and pattern of abnormalities.

Materials and methods: We prospectively studied 76 patients with biopsy-proven pulmonary sarcoidosis (48.7 % female, age 48.0 ± 12.7 years, time since diagnosis of pulmonary sarcoidosis 6.7 ± 6.2 years). Patients were followed for 21 ± 10 months. Endpoints were defined as death and ventricular tachycardia (VT).

Results: All patients had normal systolic left and right ventricular functions. CMR revealed positive LGE in 62 patients (81.6 %). Only 14 patients (18.4 %) hat no LGE at all. 26 patients (34.2 %) had minimal lesions < 2 % LGE mass of left ventricular mass (LVM). These 26 patients were also considered LGE negative. Two patterns of LGE were found. Type A: midmyocardial LGE in the left ventricular free wall (7 patients, 9.2 %, LGE mass 3.5 ± 2.7 % of total left ventricular mass). Type B: LGE at the septal insertion of the right ventricle (29 patients, 38.2 %, LGE mass 3.2 ± 0.9 % of total left ventricular mass). During follow-up 2 patients had documented a non-sustained VT (2.6 %, both with type A lesions), but no sustained VT or death occurred.

Conclusions: The present prospective study shows that positive LGE is frequent in patients with systemic sarcoidosis and normal left ventricular function. However, LGE mass was limited (3.3 ± 1.4 % of LVM on average). The value of the small amount of LGE in patients with systemic sarcoidosis, who are otherwise healthy, remains to be determined, but mid-term prognosis appears to be good.

III-4

A novel algorithm for determining variability of 2D speckle-tracking data obtained in clinical settings

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KH der Elisabethinen Linz

Background: There is limited information regarding analytical tools that can be used in clinical settings for assessing the quality of deformation curves and identifying potential sources of error and uncertainty in two-dimensional speckle tracking imaging (2DTI) estimates of myocardial deformation. We sought to test the feasibility of a novel mathematical algorithm that assesses the variance in 2DTI curves by (1) performing multiple repetitions of 2DTI curves from each grayscale loop of parasternal short axis (PSAX) view, (2) building designated groups of superimposed component curves and (3) measuring variability between each group of curves by using Curves Dispersion Index (CDI).

Methods: We retrospectively analyzed 44 patients without structural heart disease—thereby achieving 2, 640 datasets of component curves (four different datasets of 2DTI component curves 15 times for each patient). After building of designatet groups of superimposed component-curves a total number of 1, 056 CDI measures were evaluated for the following variables: age, gender, heart rate, level of PSAX plain, 2D frame rate, 2D image quality, component type of myocardial motion and anatomical segment location.

Results: The reproducibility of the various indices of cardiac motion varies with 2D image quality, component of myocardial motion, 2D frame rate, and the location of anatomical segment.

Best reproducibility was seen for radial displacement, whereas variability was higher in lateral or posterior LV segments and with the presence of LV rotation. Use of analytical approaches with 2DTI datasets in clinical settings could help apriori detection of high intrinsic curve variability for excluding datasets from impacting clinical decision making.

III-5

Assessment of myocardial ischemia during dobutamine stress echocardiography by 2D speckle tracking in patients with suspect coronary artery disease

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KH Elisabethinen Linz, Kardiologie

Background: Stress echocardiography is useful in assessment of flow-limiting coronary artery disease (CAD) in clinical practice. However, the interpretation of regional wall motion abnormalities during stress is operator-dependend and requires experience. Quantification of left ventricular longitudinal strain using two dimensional speckle tracking echocardiography (2D-STE) was shown to be a sensitive method for identifying significant CAD. The aim of our study was to assess if use of 2D speckle tracking at rest and during dobutamine stress echocardiography can improve the prediction of significant CAD in stable patients referred for coronary angiography (CAG).

Methods: We performed a dobutamine stress echocardiography according to a standard protocol in patients with no history of CAD before coronary angiography. Aquired images were analysed

using 2D STE at rest and at peak stress including regional and global longitudinal strain. Furthermore wall motion was analysed using a 16 segment wall motion index (WMSI). The indication for coronary angiography in the study subjects was determined by the clinical judgement of the referring providers.

The patients were then divided in 3 groups. Group 1 consisted of patients with normal wall motion (WM) and normal strain values at stress. Group 2 consisted of patients with reduced WM and reduced strain values and Group 3 consisted of patients with normal WM and reduced strain values. Coronary angiography was performed one day after stress echocardiography. After CAG, knowing the morphology of coronary arteries, we analysed the accuracy of WM and strain values.

Results: 29 consecutive patients were included in our study. In Group 1 ($n=17$) a stenosis > 70 % in any artery in was seen in 0 patients. In Group 2 ($n=4$) a significant stenosis was present in 3 patients and in Group 3 ($n=8$) significant coronary artery stenosis was seen in 6 patients.

Conclusion: Stress echocardiography using 2D STE is feasable but technically challenging. However, this method has the potential to increase the sensitivity of stress echocardiography in prediction of significant coronary artery disease.

Postersitzung IV: Diverses

IV-1

Blutungsrisiko bei Stürzen unter Gerinnungstherapie

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Einleitung: Sturzereignisse können zu Blutungsereignissen führen und beeinflussen häufig die Indikation für orale Antikoagulantien und Plättcheninhibitoren. In dieser Arbeit wurde der Einfluss verschiedener gerinnungswirksamer Medikamente auf Blutungsereignisse und Sturzfolgen bei Patienten mit dokumentierten Sturzereignissen untersucht.

Material und Methode: Seit 2004 werden im Krankenhaus der Bramherzigen Schwestern Linz alle Sturzvorfälle mittels Sturzprotokoll dokumentiert. In diesem Protokoll werden Sturzhergang, Sturzfolgen, Sturzort, Datum und Uhrzeit erfasst. Auf Basis der Sturzprotokolle und der elektronischen Patientenakten wurde eine retrospektive Datenanalyse durchgeführt. Neben der gerinnungshemmenden Medikation, wurde der Hämoglobingehalt vor und nach dem Sturz, die Verabreichung von Erythrozyten-Konzentraten, die Thrombozytenzahl und der INR-Wert vor dem Sturz sowie alle klinischen Blutungsereignisse und Sturzfolgen ausgewertet.

Resultate: Insgesamt wurden 4046 Stürze von 3374 Patienten dokumentiert. 235 Patienten wurden zum Zeitpunkt des Sturzes mit Vitamin-K-Antagonisten (VKA), 924 Patienten mit Acetylsalicylsäure (ASS), 254 Patienten mit Clopidogrel und 2087 Patienten mit Heparin bzw. Heparin-Analoga (meist in Prophylaxedosis) behandelt. Weitere 1204 Patienten erhielten zum Zeitpunkt des Sturzes keine Gerinnungsmedikation. Der Abfall des Hämoglobin-Gehaltes nach dem Sturz betrug unter VKA 0,24 ± 1,12 g/dl, unter ASS 0,24 ± 1,14 g/dl, unter Clopidogrel 0,24 ± 1,09 g/dl, unter Heparin 0,26 ± 1,13 g/dl und in der Gruppe ohne Gerinnungshemmer 0,31 ± 1,23 g/dl ($P=0,894$). Blutungsereignisse nach der TIMI-Klassifikation (minor und major) traten in der VKA-Gruppe bei 2 (0,9 %), in der ASS-Gruppe bei 11 (1,2 %), in der Clopidogrel-Gruppe bei 4 (1,6 %), in der Heparin-Gruppe bei 24 (1,1 %) und in der Gruppe ohne Gerinnungshemmer bei 22 (1,8 %) Patienten auf ($P=0,379$). Schwere und mittlere Sturzfolgen traten unter VKA bei 10 (4,3 %), unter ASS bei 52 (5,6 %), unter Clopidogrel bei 18 (7,1 %), unter Heparin bei 113 (5,4 %) und in der Gruppe ohne Gerinnungsmedikamente bei 59 Pat. (4,9 %) auf ($P=0,802$). Die Verabreichung von Erythrozyten-Konzentraten im Zeitraum 0–3 Tage nach dem Sturz erfolgte in der VKA-Gruppe in 4 (1,7 %), in der ASS-Gruppe in 24 (2,6 %), in der Clopidogrel-Gruppe in 9 (3,5 %), in der Heparin-Gruppe bei 57 (2,7 %) und in der Gruppe der Patienten ohne Gerinnungstherapie in 34 (2,8 %) der Fälle ($P=0,795$). Die Indikation zur Verabreichung von Blutkonserven erfolgte stets bei vorbestehender Anämie und nicht aufgrund einer durch den Sturz ausgelösten Abnahme des HB-Gehaltes.

Diskussion: Stürze von Patienten unter Antikoagulantien und Plättchenhemmern sind nicht mit häufigeren Blutungsereignissen und schweren Sturzfolgen assoziiert als Stürze von Patienten, die nicht mit Gerinnungshemmern behandelt werden. Pat. mit Stürzen sollte bei gegebener Indikation die gerinnungshemmende Therapie nicht vorenthalten werden.

IV-2

Fehlender Effekt einer Renalen Denervation bei therapierefraktärer arterieller Hypertonie nach 6 Monaten in einem Single-Center Register

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Hintergrund: Die katheterbasierte Radiofrequenz-Ablation des renalen Sympatikus [Renale Denervation (RDN)] gilt als neue Therapieoption bei therapierefraktärer arterieller Hypertonie. Rezente randomisierte, kontrollierte Studien lassen jedoch diesbezügliche Zweifel aufkommen.

Methoden: Prospektives Single-Center Register konsekutiver RDN Patienten im Zeitraum von März 2012 bis November 2013. RDN wurde unter Intubationsnarkose mittels Symplicity-Katheter (Medtronic) nach standardisiertem Protokoll in beiden Nierenarterien durchgeführt. Einschlusskriterien: 3 od. mehr Antihypertensiva, Office Blutdruck > 150 mmHg systolisch und Nierenarteriendiameter > 4 mm. Eine 24 h Blutdruckmessung erfolgte vor, sowie 1, 3 und 6 Monate nach der Intervention.

Ergebnisse: Nach Screening konnten lediglich zwölf Patienten (5 Frauen, 7 Männer) in 18 Monaten mit RDN behandelt werden (4,4 ± 0,8 Ablationspunkte/Nierenarterie; Range 2–5). Der mittlere systolische und diastolische 24 h Blutdruck vor der Intervention (149 ± 21/80 ± 14 mmHg) zeigte keine signifikante Änderung nach 1, 3 oder 6 Monaten (151 ± 17/82 ± 14, 154 ± 24/83 ± 15, 153 ± 17/82 ± 9 mmHg; $p=0,919$ systolisch, $p=0,958$ diastolisch). Die antihypertensive Medikation konnte von 4,9 ± 1,3 (Range 3–8) nicht reduziert werden (5,2 ± 1,2; Range 4–7; $p=0,169$). Auch nach post-hoc Exklusion von 4 Patienten mit normalem mittlerem 24 h Blutdruck (< 135/85 mmHg) vor RDN (trotz korrekter Einschlusskriterien), zeigte sich kein signifikanter andauender Effekt (162 ± 11/85 ± 13 vs. 152±13/80 ± 13 mmHg, 165 ± 18/87 ± 16, 158 ± 17/85 ± 9 mmHg; $p=0,372$ systolisch, $p=0,755$ diastolisch). Zwei Patienten (16 %) erfüllten die Kriterien eines „RDN Responders“ (Reduktion des mittleren systolischen 24 h Blutdruckes > 5 mmHg) jedoch ohne statistische Signifikanz nach 6 Monaten (163 ± 14 vs. 141 ± 4 mmHg, 152 ± 16, 149 ± 9 mmHg; $p=0.438$).

Diskussion: Mit den derzeitigen klinischen Einschlusskriterien und methodischen Möglichkeiten der RDN zeigt sich in unserem prospektiven Single-Center Register mit 12 Patienten kein signifikanter Blutdruck-senkender Effekt nach 6 Monaten. Die Kriterien der Patientenselektion und auch die Ablations-Methodik müssen daher überdacht werden. Diesbezüglich sollen die Ergebnisse laufender randomisierter Multicenter Studien abgewartet werden.

IV-3

Integrierte sektorenübergreifende Gesundheitsversorgung von Patienten nach einem kardialen Ereignis für das Bundesland Vorarlberg – Verbesserung der Effektivität und Effizienz der kardiologischen Rehabilitation mittels Case Management

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Einleitung: Die Wirksamkeit der kardiologischen Rehabilitation ist durch randomisierte, kontrollierte Studien und Metaanalysen gesichert. Trotzdem werden in Österreich nur etwa 30 % aller Patienten nach einem kardialen Ereignis in ein Rehabilitationszentrum aufgenommen und dann oft erst sehr spät. Somit besteht auf diesem Gebiet der Kardiologie ein erhebliches therapeutisches Defizit mit ernstzunehmenden gesundheitlichen und ökonomischen Folgen sowohl für das Individuum als auch für die Gesellschaft. Ziel dieses Projektes ist es, die Gründe für dieses Defizit anhand einer Problemanalyse darzulegen und evidenzbasierte Maßnahmen zur Verbesserung der Gesundheitsversorgung dieses Patientenkollektivs zu entwickeln.

Methodik: Zur Erfassung der Ist-Situation wurden zuerst eine Medline-gestützte Literaturrecherche und eine Problemanalyse vorgenommen. Aufbauend auf den Ergebnissen wurde eine retrospektive Analyse von an unserem Institut bereits vorhandenen Reha-Daten durchgeführt. Diese Analyse diente dem Vergleich zwischen der bisher geübten Praxis und der aufgrund der vorliegenden Evidenz zu setzenden Maßnahmen. Es wurden die Daten von 351 Patienten nach Koronarintervention (PCI) retrospektiv ausgewertet. Gruppe I umfasste 144 Patienten im Alter von 52,3 ± 7,7 Jahren, die bereits übliche Behandlungsstufen nach PCI ohne weitere spezielle, die Rehabilitation koordinierende Maßnahmen durchliefen. Gruppe II umfasste 207 Patienten im Alter von 53,0 ± 6,8 Jahren, bei denen die Rehabilitation durch eine Case Management Servicestelle vermittelt wurde.

Ergebnisse: In der Patientengruppe I ohne Case Management (CM) fanden wir 34 von 144 (24 %) Patienten, die eine Rehabilitation abschlossen. Die Aufnahme erfolgte in einem Zeitintervall von 33 ± 17 Tagen ab PCI. In der Patientengruppe II mit CM fanden wir 90 von 207 (43 %) Patienten mit abgeschlossener Rehabilitation. Die Aufnahme erfolgte in einem Zeitintervall von 30 ± 15 Tage ab PCI. Mit Hilfe des CM konnte die Rehabilitationsrate bei Patienten nach PCI somit um 19 % erhöht werden (Unterschied: Gruppe I 24 % Reha; Gruppe II 43 % Reha; $p < 0.01$). Das Zeitintervall von PCI bis zur Rehabilitation konnte durch CM nicht signifikant verkürzt werden. Als Gründe für eine niedrige Rehabilitationsrate und einen verzögerten Rehabilitationsantritt in der derzeit geübten klinischen Praxis im Land Vorarlberg wurden folgende Faktoren identifiziert: a) zu wenig Zeit für das Arztgespräch, b) unzureichende Kenntnisse der Ärzte über Indikation und therapeutischen Stellenwert der Rehabilitation, c) unkoordinierte medizinische Versorgung der Patienten durch verschiedene, eigenständig agierende Leistungsträger und d) unzureichende Rehabilitationswilligkeit der Patienten.

Diskussion: Unsere Analyse zeigt, dass die Rehabilitationsrate bei Patienten nach PCI durch die Einrichtung einer Case Management-Servicestelle signifikant erhöht werden kann. Basierend auf den aus der Literatur abgeleiteten evidenzbasierten Lösungsstrategien, auf einer umfassenden Problemanalyse vor Ort sowie auf den Erkenntnissen aus der vorliegenden Pilotstudie, wurde ein prospektives randomisiertes und kontrolliertes Studiendesign entwickelt, das auf die Überprüfung wirksamer Maßnahmen für eine integrierte sektorenübergreifende Gesundheitsversorgung von Patienten nach einem kardialen Ereignis im Bundesland Vorarlberg abzielt. Eine abschließende ökonomische Evaluation ist vorgesehen. Erste Ergebnisse sind 2015 zu erwarten.

IV-4

Mitral annular plane systolic excursion (MAPSE) as a parameter of left ventricular long-axis function: Reference values and calculation of z-score values in healthy children

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Background: Longitudinal myocardial function has gained more interest in the last years. The mitral annular plane systolic excursion (MAPSE) is an echocardiographic measurement to assess left ventricular (LV) long-axis function in adults. Aim of this study was to evaluate MAPSE values in a healthy pediatric population and to propose reference values.

Methods: A prospective study was conducted in a group of 558 healthy children and adolescents (age: day 1 to 18 years), (BSA: 0.18 to 2.21 m^2). We determined the effects of age and body surface area (BSA) on MAPSE values and a possible correlation of MAPSE values with LV ejection fraction (EF) values.

Results: The MAPSE ranged from a mean of 0.57 cm (Z-score ± 2: 0.38–0.76 cm) in neonates to 1.63 cm (Z-score ± 2: 1.31–1.95 cm) in 18 year old adolescents. The MAPSE values showed a positive correlation with age ($r = 0.87$, $p < 0.001$) and BSA ($r = 0.89$; $p < 0.001$) with a non-linear course. There was no significant difference in MAPSE values between females or males. A positive correlation was found between MAPSE values and LVEF values ($r = 0.28$; $p < 0.001$).

Conclusions: Z-scores of MAPSE values were calculated and percentile charts were established to serve as reference data in patients with congenital heart disease (CHD) or heart failure in the future.

IV-5

Perioperative beta-blockers for preventing surgery-related mortality and morbidity

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Background: Randomized controlled trials (RCTs) yielded conflicting results regarding the ability of beta-blockers (BB) to influence perioperative cardiovascular morbidity and mortality.

Methods: We conducted a meta-analysis by searching the following databases from the date of their inception until June 2013: MEDLINE, EMBASE, CENTRAL, Biosis Previews, CAB Abstracts, CINAHL, Derwent Drug File, Science Citation Index Expanded, Life Sciences Collection, Global Health and PASCAL. We included RCTs if their participants were randomized into a BB group or a control group (either standard care or placebo). Surgery (any type) had to be performed under general anaesthesia in all or at least in a significant proportion of patients. Subgroup analyses for various potential effect modifiers were performed.

Results: We included 89 RCTs with 19211 participants. Outcomes were evaluated separately for cardiac (CS) and non cardiac surgery (NCS). In CS (53 trials) BBs did not influence all-cause mor-

tality (ACM) (RR 0.73, 95 % CI: 0.35 – 1.52, $p = 0.40$) or the incidence of acute myocardial infarction (AMI) (RR 1.04, 95 % CI: 0.71 – 1.51, $p = 0.85$). BBs did not affect the incidence of cerebrovascular events (CVE) (RR 1.52, 95 % CI: 0.58 – 4.02, $p = 0.40$), whereas a protective effect against ventricular (VA) (RR 0.37, 95 % CI: 0.24 – 0.58, $p < 0.0001$, NNT: 29) and supraventricular arrhythmias (SVA) could be shown (RR 0.46, 95 % CI: 0.37 – 0.56, $p < 0.00001$, NNT: 6). Hypotension (HY) (RR1.54, 95 % CI: 0.67 – 3.51, $p = 0.31$), bradycardia (BR) (RR 1.61, 95 % CI: 0.97 – 2.66, $p = 0.06$) and congestive heart failure (CHF) (RR 0.22, 95 % CI: 0.04 – 1.34, $p = 0.10$) were not increased with the use of beta-blockers. BBs reduced length of hospital stay (LOS) on average by 0.54 days (95 % CI: – 0.90 to – 0.19, $p = 0.003$). In NCS (36 trials) BBs overall did not influence ACM (RR 1.24, 95 % CI: 0.99 – 1.54, $p = 0.06$). However, restricting the meta-analysis to low risk of bias studies revealed an increase of ACM with BBs (RR 1.26, 95 % CI: 1.02 – 1.57, $p = 0.04$, NNH: 185). BBs exhibited a significant protective effect in the prevention of AMI (RR 0.73, 95 % CI: 0.61 – 0.87, $p = 0.0005$, NNT: 71) and SVAs (RR 0.72, 95 % CI: 0.56 – 0.92, $p = 0.008$, NNT: 111). However, adverse events such as HY (1.49, 95 % CI: 1.37 – 1.62, $p < 0.00001$, NNH: 16) or BR (RR 2.30, 95 % CI: 1.58 – 3.37, $p < 0.0001$, NNH: 17) were significantly increased by BB treatment. Risk for CVEs was overall not influenced by BBs (RR 1.59, 95 % CI: 0.93 – 2.71, $p = 0.09$). Restricting the meta-analysis to low risk of bias studies again revealed an increase of CVEs with the use of BBs (RR 2.09, 95 % CI: 1.14 – 3.82, $p = 0.02$, NNH: 255). VAs (RR 0.64, 95 % CI: 0.30 – 1.33, $p = 0.23$), CHF (RR 1.17, 95 % CI: 0.93 – 1.47, $p = 0.18$) as well as LOS (mean difference – 0.27 days, 95 % CI: – 1.29 to 0.75, $p = 0.60$) were not affected by BB treatment.

Discussion: According to our findings the perioperative application of BBs still plays a pivotal role in CS, as they can substantially reduce the high burden of SVAs and VAs in the aftermath of surgery and reduce oxygen consumption in patients diagnosed with coronary heart disease. The role of BBs in preventing AMI and potentially causing CVE, HY, BR or death in this setting is still unclear. In NCS evidence indicates a reduction of SVAs and AMIs, whereas data from low risk of bias trials points to an increase in ACM and the incidence of CVEs with the use of BBs. As the quality of evidence is still low to moderate, more evidence is needed to draw a definite conclusion.

IV-6

Tissue engineering of artificial heart valve scaffold using different seeding methods with mesenchymal stem cells

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Background: Heart valve tissue engineering attracts increasing attention in paediatric cardiology due to the lack of living, non-immunogenic heart valve grafts with adaptive self-growing. The EU Project "LifeValve" aims to develop a tissue engineered living heart valve, with the capacity of growth that can be implanted without invasive open-heart surgery using percutaneous catheter-based technology. The objective of our study is to evolve an optimal method of seeding biodegradable tissue engineered heart valve constructs with porcine mesenchymal stem cells (pMSCs).

Materials and methods: Decellularized biodegradable scaffolds, were provided by the Technical University of Eindhoven. The scaffolds were pretreated using 4 different methods for MSC seeding. The constructs were either air dried (M1); air dried and stabbed with needles (M2); air dried, stabbed and pretreated with 2.5 µg/ml fibronectin (M3) or air dried and treated with fibronectin (M4; 2.5 µg/ml). Fibronectin, an extracellular matrix glycoprotein that acts like a "cell-glue" was used to promote cell adhesion and migration into the scaffolds. pMSCs were thawed and cultured for one week before seeding and seeded carefully (density 500.000 cells per well of a 6-plate) to the scaffolds. After 2 days of incubation and a media change, the scaffolds were processed to perform histology analysis including HE-staining and Höchst fluorescent cell nucleus staining. Proliferation and spreading of cells into the scaffolds was observed using light and fluorescence microscopy in combination with planimetric quantification using image.

Results: Conventional microscopically observation showed a pMSC proliferation only into the upper layers of the scaffold in all method groups. Comparing the seeding methods using fluorescent cell nucleus staining microscopy displayed a significant difference ($p < 0$, 05) in the percentage area of cell ingrowth between M1 [0.14 % +/– 0.29] and M2 [5.18 % +/– 3.5], and M3 [4.72 % +/– 3.88] and M4 [0.11 % +/- 0.09], due to the fact that the scaffolds used for M2 and M3 were used from another batch than M1 and M4. According to fibronectin seeding there was no significant difference in cell growth comparing both scaffolds batches (fibronectin [2.55 % +/– 3.64]; untreated [3.13 % +/– 3.70]). There was no significant cell growth difference between M1 and M4 as well as in M2 and M3.

Discussion: We showed that pMSCs successfully migrated into the upper layers of the cell scaffold either way using fibronectin pretreatment or not, which implies that our seeding procedure operates in general. To achieve a denser ingrowth to the deeper scaffold layers, a higher fibronectin concentration and longer cultivation time will be applied in our further experiments.

IV-7

Verwendung von Ventrikelschraubsonden in der intermittierenden Schrittmachertherapie

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Einleitung: Überlegungen, die Verlässlichkeit einer intermittierenden Schrittmachertherapie (ISM) zu erhöhen, haben an unserer Abteilung mit Beginn des transfemoralen Aortenklappenersatz-Programms (TAVI) zur Verwendung von Ventrikelschraubsonden anstatt von herkömmlichen ISM-Sonden geführt.

Material und Methode: Ventrikelschraubsonden unterschiedlicher Hersteller wurden über einen rechtsseitigen transjugulären Zugang mittels 7 F-Schleuse entweder in das interventrikuläre Septum oder in den rechtsventrikulären Apex geschraubt. Als Reizschwelle wurde eine Impulsamplitude von maximal 1,0 Volt akzeptiert. Anstatt eines externen Schrittmachers kamen 4 nicht implantierte Schrittmacheraggregate zum Einsatz, die im VVI-Modus mit einer Grundfrequenz von 50/Minute programmiert wurden. Nach Verankerung der Schrittmachersonde mit Hautnähten und Konnektion wurde das Schrittmacheraggregat mittels eines Verbandes rechts infraklavikulär an der äußeren Thoraxwand des Patienten fixiert. Die Durchführung eines Thoraxröntgen nach Implantation war obligat.

Ergebnisse: Im Beobachtungszeitraum zwischen November 2008 und Jänner 2014 wurden intermittierende Schrittmacher unter Verwendung von Ventrikelschraubsonden sowohl zum ‚rapid pacing' bei TAVI als auch bei herkömmlicher Indikation (vor allem totaler AV-Block) nach oben angeführter Methode implantiert. Von insgesamt 129 ISM erfolgten 83 im Rahmen eines transfemoralen Aortenklappenersatzes und 46 bei anderer Indikation. Bei 40 Patienten wurde die Ventrikelschraubsonde im interventrikulären Septum und bei 89 im rechtsventrikulären Apex platziert. Die typischen prozeduralen Komplikationen Pneumothorax oder Perforation traten bei keinem Patienten auf (0 %). Bei 2 Patienten kam es zu einer Sondendislokation (1,55 %). Verglichen mit der früher üblichen Verwendung herkömmlicher ISM-Sonden und externer Schrittmacher haben sich die Mobilisierung der Patienten auf der Intensivstation sowie das Handling für das Pflegepersonal als einfacher und sicherer gezeigt. Die verwendeten Ventrikelschraubson-

den wurden kostensparend im Set mit Schrittmacheraggregaten eingekauft. Durch die hohe Zahl an Generatortäuschen standen ausreichend Sonden für den Gebrauch im Rahmen einer intermittierenden Schrittmachertherapie zur Verfügung. Verglichen mit herkömmlichen ISM-Sonden resultierte eine Kostenersparnis von knapp 50 %.

Diskussion: Unsere Beobachtungen zeigen sowohl eine niedrige prozedurale Komplikationsrate als auch eine niedrige Dislokationsrate. Dazu kommen ein höherer Patientenkomfort und Erleichterungen im Zusammenhang mit pflegerischen Maßnahmen. Unter ökonomischen Gesichtspunkten ist auch eine deutliche Kostenreduktion gegeben. Die bisherigen Ergebnisse sprechen für eine sichere, patienten- und personalfreundliche sowie kosteneffektive Methode.

IV-8

Nachholbedarf bei Patienten mit Migrationshintergrund in der ambulanten kardiologischen Rehabilitation

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Patienten mit Migrationshintergrund stellen einen immer größer werdenden Anteil in kardiologischen Abteilungen Österreichs dar, im unmittelbaren Einzugsgebiet des Klinikums Wels leben immerhin knapp 24 % Menschen ohne Deutsch als Muttersprache.

In dieser systematischen, prospektiven Studie analysierten wir alle Patienten, die 2013 am ambulanten Phase II-Rehabilitationsprogramm des Instituts Cardio-Vital Wels teilnahmen, hinsichtlich ihrer demographischen Daten, der zugrundeliegenden Erkrankung, des Risikoprofils und der Veränderungen durch die Rehabilitation.

Von Jänner bis Dezember 2013 nahmen in 19 Gruppen 189 PatientInnen (75 % Männer, 59 ± 12 Jahre) an dem Programm teil. Die Indikationen waren wie folgt: akutes Koronarsyndrom 54 %, Stentimplantation bei KHK 18 %, Kardiomyopathie 7 %, aortokoronare Bypassoperation 5 %. Lediglich 13 Patienten (7 % des Kollektivs, davon 3 Frauen) wiesen einen Migrationshintergrund auf. Diese waren signifikant jünger als die übrigen Teilnehmer (52 vs. 60 Jahre, $p < 0{,}05$), unterschieden sich jedoch hinsichtlich weiterer anamnestischer und laborchemischer Risikofaktoren nicht signifikant. In der Fahrrad-Ergometrie am Beginn erbrachten diese eine signifikant geringere Leistung (65 ± 14 vs. 78 ± 17 % der errechneten Zielleistung). Die Leistungssteigerung nach 6 Wochen war jedoch in beiden Gruppen vergleichbar (11 ± 15 vs. 14 ± 14 %, p = n. s.). Auch die variablen Risikofaktoren wie Körpergewicht und das Lipidprofil veränderten sich ähnlich.

Obwohl unterrepräsentiert in der Population, profitieren die weniger fitten Patienten mit Migrationshintergrund vergleichbar von einer ambulanten kardiologischen Rehabilitation.

Postersitzung V: Herzinsuffizienz I

V-1

Outcome of conservative management versus surgery in patients with advanced refractory heart failure

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Background: In patients with advanced refractory heart failure (HF) besides cardiac transplantation (HTX), conservative medical management and the implantation of a ventricular assist device (VAD) represent valuable options. The determination of the best therapeutic destination strategy for the individual patient remains a challenge.

Aim: The aim of the present study was to assess clinical outcome in three groups of advanced refractory HF patients. The first group was managed conservatively receiving optimal contemporary medical therapy as well as intravenous prostaglandin E 1 ("conservative"). Additionally to optimal medical therapy, the second group underwent pulsatile flow VAD ("pVAD") implantation and the third group underwent continuous flow VAD ("cVAD") implantation.

Methods: 252 consecutive patients were included into this retrospective analysis. All-cause mortality at 12 and 24 months was assessed and compared between the three groups.

Results: 87 (35 %) patients were managed conservatively, 69 (27 %) received a pVAD and 96 (38 %) a cVAD. Predicted life expectancy based on the Seattle HF model were 48 ± 26, 41 ± 20 and 48 ± 26 months (overall $p = 0.138$). Death within one year occurred in 20 (29.0 %) patients of the conservatively managed group, 40 (59.7 %) patients who received a pVAD and 18 (19.6 %) patients who were treated with a cVAD (Fig. 1, Log-rank test $p < 0.001$). In destination therapy patients (in INTERMACS profile >1 at baseline, who died, or fully completed 24 month follow-up free from HTX), all-cause death occurred in 17 (34 %, conservative), 22 (88 %, pVAD) and 12 (43 %, cVAD) patients (Log-rank test $p < 0.001$). Conservatively managed patients spent 16.6 ± 9.0 months, pVAD 3.1 ± 5.7 and cVAD 13.1 ± 9.6 months out of hospital (conservative vs pVAD $p < 0.003$; conservative vs cVAD $p = 0.03$; pVAD vs cVAD $p < 0.003$).

Conclusion: cVAD resulted in a significantly better clinical outcome than pVAD implantation. Conservative management with current optimal medical therapy appears to remain a valuable option for patients with advanced HF.

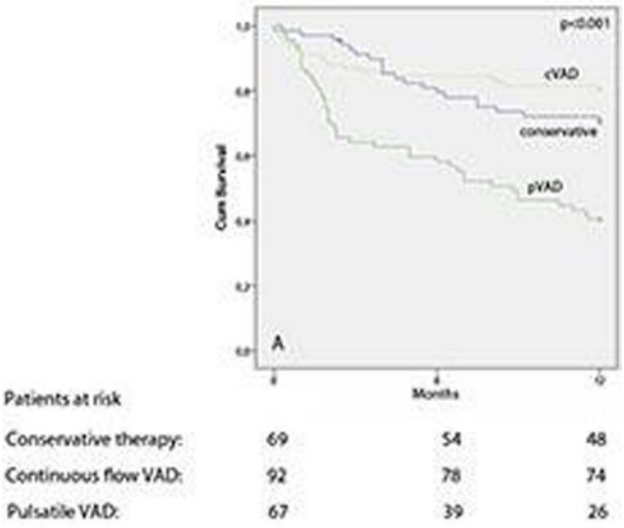

Fig. 1 Outcome of conservative management versus surgery in patients with advanced refractory heart failure

V-2

Prognostic significance and determinants of the 6-minute walk test in patients with pulmonary hypertension associated with heart failure and preserved ejection fraction

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Background: Symptoms of exertional fatigue and dyspnea, as well as a reduced exercise tolerance are cardinal features of pulmonary hypertension (PH) associated with heart failure with preserved ejection fraction (HFpEF). The underlying mechanisms limiting exercise capacity in this complex clinical syndrome remain incompletely understood. The aim of the present study was to define the prognostic significance and clinical determinants of the six-minute walking distance (6-MWD) in affected patients.

Methods: Consecutive patients with a definite diagnosis of PH-HFpEF, as confirmed by right heart catheter, were enrolled in our prospective, observational registry. Hospitalization for HF and/or death for cardiac reason were defined as the primary study endpoint. To establish determinants of the 6-MWD, four separate multiple regression models were constructed for TTE, hemodynamic, laboratory and pulmonary parameters. For quantification of left ventricular (LV) extracellular matrix (ECM) using the TissueFAXS and HistoQuest® software, myocardial biopsies were taken from 18 patients.

Results: Between December 2010 and July 2013, 142 PH-HFpEF patients (99 women and 43 men, mean age 71 ± 9 years) were included to the study. After a mean follow-up of 14.0 ± 10.0 months (range 0.5–34.0 months), 43 patients (30.3 %) reached the combined endpoint. Patients in the adverse outcome group had a significantly shorter 6-MWD (246.8 ± 115.6 versus 345 ± 110.2 m, $p < 0.001$) and a higher Borg dyspnea score (BDS; 5 ± 2 versus 3 ± 2, $p < 0.001$). The 6-MWD (hazard ratio [HR]: 0.992; 95 % confidence interval [CI]: 0.990; 0.995; $p = 0.013$) was found to be an independent predictor of outcome. Other clinical parameters associated with a worse prognosis were presence of atrial fibrillation (HR: 2.482; 95 %CI: 1.198; 5.139; $p = 0.014$) and COPD (HR: 2.048; 95 %CI: 1.084; 3.869; $p = 0.039$). The following parameters were found to be independent determinants of the 6-MWD: systolic and mean pulmonary artery pressures, transpulmonary gradient, pulmonary arterial compliance, hemoglobin, urea, partial pressure of oxygen in arterial blood and vital capacity. There was a significant inverse correlation between the 6-MWD and the amount of ECM ($R = -0.501$, $p = 0.034$) in the heart tissue samples.

Discussion: The limited exercise capacity in PH-HFpEF patients can be explained by a variety of cardiac and non-cardiac factors that contribute to increased ECM deposition in the LV and consecutive hemodynamic alterations. We hypothesize that PH-HFpEF is a multifactorial systemic disease with end-organ damage of the heart.

V-3

Quality of medical therapy in heart failure patients undergoing coronary artery bypass grafting

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Background: Management of patients with coronary artery disease and reduced left ventricular ejection fraction (LVEF) remains a challenge for cardiologists and surgeons alike. The STICH landmark-trial showed that patients assigned to coronary artery bypass grafting (CABG), as compared with those assigned to medical therapy alone, had lower rates of important secondary endpoints. The STICH trial did not assess dosages of disease modifying drugs in this important patient population. Therefore, the aim of the present study was to assess the extent to which guideline-recommended optimal medical therapy (OMT) is currently prescribed in "real-world" patients with an LVEF ≤35 % undergoing CABG.

Methods: We included consecutive STICH-eligible patients (ischemic heart failure and LVEF < 35 %) undergoing elective CABG at a tertiary center between 2009 and 2013. Heart failure specific medical therapy was recorded at admission and at discharge. Patients were then grouped into quartiles according to the percentage of guideline-recommended target dosage received (1: none, 2: 1–49 %, 3: 50–99 %, 4: 100 %). OMT was defined as a target dose of 100 % for both beta blocker (BB) and either angiotensin-converting enzyme inhibitor (ACE-I) or angiotensin receptor blocker (ARB).

Results: Of the 128 patients included, 108 (83 %) were male. The median age at time of surgery was 65.5 years (IQR 58–72). At time of admission, the median LVEF was 26.5 % (25–30), the median predicted mortality using the logistic EuroSCORE was 7.52 % (4.1–14.9).

Discharge medication was suboptimal—only 4 patients (3 %) were on OMT.

Concerning BB, 17 patients (13 %) were in quartile 1.49 (38 %) in quartile 2.51(39 %) in quartile 3 and 10 (8 %) in quartile 4 and for ACE-I or ARB, 21(16 %) were in quartile 1.48 (38 %) in 2.33(26 %) in 3 and 25 (20 %) in 4 (Fig. 1).

Forty-nine patients (39 %) received a mineralocorticoid receptor antagonist and 90 patients (71 %) were on a statin.

Data on medication dosages at 6 month follow-up, survival and re-hospitalization is currently being gathered and will be presented at the meeting in 2014.

Conclusion: Patients suffering from ischemic heart failure with an LVEF ≤35 % undergoing CABG are frequently treated with dosages below the recommended levels. Clearly, up-titration of heart failure specific medication is a continuous process and awareness should be raised in surgeons and cardiologists treating these patients in order to schedule up-titration after discharge.

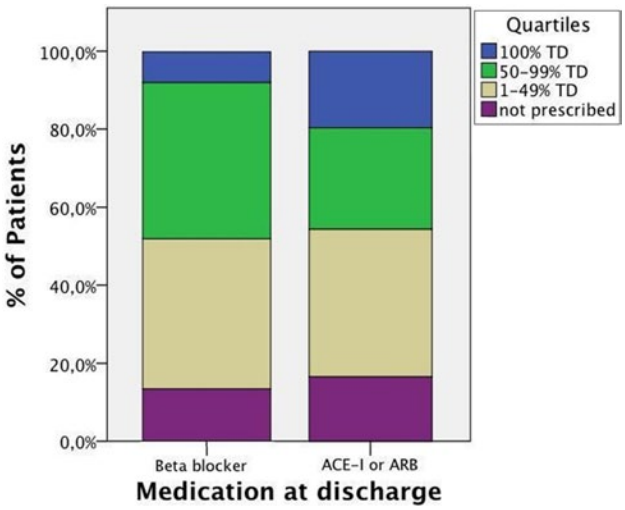

Fig. 1 Patients suffering from ischemic heart failure are frequently treated with dosages below the recommended levels

V-4

Outcome in heart failure with preserved ejection fraction strongly depends on right ventricular performance

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Medizinische Universität Wien

Background: Heart failure with preserved ejection fraction (HFpEF) is recognized as a major cause of cardiovascular morbidity and mortality. However, knowledge of risk factors in this specific patient population is scarce. Therefore, we aimed to improve risk prediction using a large variety of imaging modalities including hemodynamic, echocardiography and cardiac magnetic resonance (CMR) imaging.

Methods: We prospectively included 142 patients with a definite diagnosis of HFpEF into our observational, non-interventional registry. Echocardiography, cardiac magnetic resonance imaging and invasive hemodynamic assessments were performed in all patients. Hospitalization for heart failure and/or cardiac death was observed over a median follow up of 10 months.

Results: We did not detect a significant association between imaging or functional parameters of the left ventricle and outcome in our adjusted analysis. However, the strongest risk factors were reduced right ventricular function measured using echocardiography (adj. HR 6.53; 95 %CI 3.08–13.83; $p<0.001$) or CMR (adj. HR 6.67; 95 % CI 1.82 – 24.48; $p=0.004$) and systolic pulmonary arterial pressure using echocardiography (adj. HR per 1-S. 1.46; 95 % CI 1.07 – 2.00; $p=0.02$) and invasive measurements (HR per 1-S. 1.55; 95 % CI 1.15 – 2.09; $p=0.004$). Kaplan Meier analysis demonstrated a significant increase of the primary endpoint, hospitalization for heart failure and/or death for cardiac reason, in patients with significantly reduced right ventricular function (Fig. 1a; $p<0.001$), in patients with increased systolic pulmonary arterial pressure (Fig. 1b; cut-off = median; $p=0.001$), and increased pulmonary capillary wedge pressure (Fig. 1c; cut-off = median; $p=0.006$).

Conclusion: Outcome in patients with HFpEF does not correlate with left ventricular size or function but strongly depends on the performance of the right ventricle. For optimal clinical management thorough evaluation of the right ventricle is indispensable in affected patients.

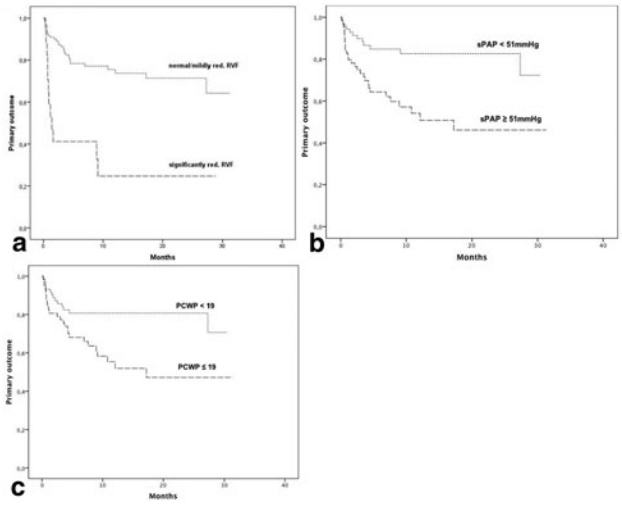

Fig. 1 Outcome in patients with HFpEF strongly depends on the performance of the right ventricle

V-5

Heart Failure in Hemodialysis Patients: An Interim Analysis of the DERAIL Study (Development and Regulation of Heart Failure with Preserved Ejection Fraction in Patients with Chronic Kidney Disease)

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Purpose: Premature cardiovascular death is extremely common in patients on maintenance hemodialysis (HD) with heart failure as the central cause of mortality. Since the majority of cardiovascular events cannot be attributed to systolic impairment, diastolic dysfunction has emerged as a possible independent mortality risk factor. This pathophysiologic abnormality is crucially connected to the clinical syndrome of heart failure with preserved ejection fraction (HFPEF). However, little is known about the applicability of diagnostic HFPEF criteria in HD patients, as ancillary laboratory parameters are categorically elevated. We determined both prevalence and association with clinical parameters in this unique cardiovascular high-risk cohort.

Methods: Patients underwent standardized pre-HD bioimpedance volume status assessment and post-HD transthoracic echocardiography ($n=51$). HFPEF was formally diagnosed according to the definition criteria of the European Society of Cardiology (1. signs/symptoms of heart failure, 2. left ventricular ejection fraction > 50 % and 3. evidence of abnormal left ventricular relaxation, filling or diastolic stiffness). Ejection fraction < 50 % led to classification as heart failure with reduced ejection fraction (HFREF). Associated clinical, demographic and laboratory parameters are provided.

Results: Diastolic dysfunction was present in all patients but one. By definition, 73 % had heart failure, of whom 81 % had HFPEF and 19 % had HFREF. All patients had elevated NT-proBNP levels. Compared to patients without HF (median 2851 ng/ml), those with HFPEF had similar but slightly higher values (median 4050 ng/ml), while they were significantly more elevated in patients with HFREF (median 35.000 ng/ml). Similarly, almost all patients had markedly enlarged left atrial diameters (mean 58 ± 10 mm) with the most extreme in HFREF patients (mean 74 ± 11 mm). No significant differences regarding dialysis-associated factors and fluid overload were observed.

Conclusion: While the formal definition of HFPEF remains challenging in HD patients, we demonstrate that HFPEF patients may constitute the majority of maintenance HD patients. NT-proBNP might solely aid to distinguish HFREF but not HFPEF. Future prospective studies including invasive hemodynamics are needed to determine the natural course of the disease and define the potential reversibility after kidney transplantation.

V-6

Differential cardiotoxic effects of Doxorubicin, Epirubicin and liposomal Myocet: an experimental study with echocardiography

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Introduction: Anthracycline chemotherapy allows effective treatment of malignancies such as breast cancer or lymphomas.

Cardiotoxicity with clinical or subclinical LV dysfunction is a major concern, leading to increased cardiovascular morbidity and mortality in cancer survival patients. Anthracyclines may cause clinical manifest heart failure either acutely or in a delayed, progressive fashion. Encapsulation of drugs with liposomes limits the cytostatic delivery to healthy tissues and is a recognized method to reduce drug toxicities.

Objectives: The aim of this pre-clinical experimental study was to investigate and compare the cardiotoxic effects of three anthracycline chemotherapeutics: Doxorubicin (DOX), Epirubicin (EPI) and a liposome–encapsulated doxorubicin–citrate complex (Myocet, MYO).

Methods: Twenty-four pigs were divided in 3 groups; each group received human dose-equivalent of either conventional DOX, or EPI, or MYO in 3 cycles. Transthoracic echocardiography was performed before treatment and 3 weeks after the last chemotherapy cycle and the left and right ventricular and atrial diameter, left ventricular (LV) systolic function with fractional shortening (FS) and ejection fraction (EF) and diastolic function in terms of mitral E/A and tissue Doppler E/E` ratio were measured. Blood levels of NT-proBNP were determined by using porcine-specific ELISA at baseline and at final follow-up.

Results: After 3 cycles a high mortality was observed, and due to low number of survivals (5/6 DOX, 6/9 MYO and 2/9 EPI), the EPI group was excluded from the final analysis. The baseline echocardiographic and laboratory parameter did not show differences between the groups. The final LV and RV end-diastolic, and left and right atrial diameter were similar in all groups. Trend towards smaller LV end-systolic diameter was measured in the MYO group. Animals in the MYO group had significantly better LV systolic function (fractional shortening FS 43.8 ± 5.7 vs 36.2 ± 4.5 %, $p = 0.039$; ejection fraction EF 74.3 ± 6.3 vs 66.0 ± 5.7 %, $p = 0.048$). The E/A ratio was non-significantly lower in the MYO group as compared with the DOX group (1.3 ± 0.3 vs 1.6 ± 0.3). However, the diastolic parameter average E/E` ratio was significantly lower in the MYO group (6.1 ± 1.3 vs 8.6 ± 1.6, $p = 0.02$) as compared with the DOX group, indicating better diastolic function in animals receiving the liposomal MYO. A trend towards lower level of NT-proBNP was measured in the MYO group as compared to DOX group (184 ± 96 vs 342 ± 299 ng/mL).

Conclusion: The encapsulation of doxorubicin in liposome resulted in less cardiotoxic adverse effects in terms of better LV systolic and diastolic function in an experimental model of cardiotoxicity.

Postersitzung VI: Interventionelle Kardiologie I

VI-1

Blutdrucksenkung nach renaler Sympathikusdenervierung: Erfahrungen eines großen Zentrums

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II. Interne Abteilung, Klinikum Wels-Grieskirchen

Einleitung: Die renale Sympathikusdenervierung (RSD) ist ein interventionelles Verfahren zur Behandlung der therapierefraktären arteriellen Hypertonie. Sie wird in unserem Zentrum seit 2011 durchgeführt, wobei die Patienten postinterventionell in engmaschigen Kontrollen stehen.

Material und Methode: Vor der Intervention (ambulant) sowie 3, 6 und 12 Monate nach der RSD werden sowohl Office-Blutdruckmessungen als auch ein ambulantes 24-Stunden Blutdruckmonitoring (24-h-BDM) durchgeführt. Die Ergebnisse werden präsentiert und mittels gepaartem t-Test verglichen. Zusätzlich werden die Patienten nach dem Ansprechen in Responder (Blutdrucksenkung in der Office-Messung um mindestens 10 mmHg bzw. im 24-h-BDM um mindestens 5 mm Hg) und Nicht-Responder kategorisiert.

Ergebnisse: Das Patientenkollektiv umfasst derzeit 53 Patienten (32 Männer, 21 Frauen, mittleres Alter 62 Jahre [Range 36–80 Jahre]; mittlerer Body-Mass-Index 32,1 kg/m^2). 43 % der Patienten hatten eine begleitende koronare Herzerkrankung, 45 % waren Diabetiker.

Die Intervention selbst verlief bei allen Patienten ohne wesentliche Komplikationen, einmal war aufgrund einer Dissektion am Nierenarterienostium eine Stentimplantation erforderlich, die problemlos durchgeführt wurde. Das 3-, 6-und 12-Monats-Follow-up ist bei 42, 44 und 37 Patienten verfügbar. Der Office-Blutdruck betrug initial 170/95 mmHg. Die systolische/diastolische Senkung des Office-Blutdrucks betrug nach 3, 6 und 12 Monaten 21/9, 16/5 und 23/8 mmHg (alle p-Werte < 0,01).

Der Durchschnittswert des 24-h-BDM betrug vor dem Eingriff 150/87 mmHg. Die systolisch/diastolische Senkung des 24-h-BD betrug nach 3, 6 und 12 Monaten 11/4, 7/4 und 10/6 mmHg (alle p-Werte < 0,01).

Die Responderrate laut Office-Messung betrug nach 3, 6 und 12 Monaten 80, 64 und 70 %. Die Responderrate laut 24-h-BDM betrug nach 3, 6 und 12 Monaten 67, 61 und 69 %.

Diskussion: Die RSD ermöglicht eine substantielle Blutdruckabsenkung bei einem großen Teil von Patienten mit therapierefraktärer arterieller Hypertonie.

VI-2

Korreliert die Katecholaminausscheidung im 24-Stunden Sammelharn mit der Blutdrucksenkung nach renaler Sympathikusdenervierung?

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Einleitung: Die renale Sympathikusdenervierung (RSD) ist ein interventionelles Verfahren zur Behandlung der therapierefraktären arteriellen Hypertonie. Sie wird in unserem Zentrum seit 2011 durchgeführt. Determinanten der Blutdrucksenkung nach RSD sind mit Ausnahme des Ausgangsblutdrucks bisher nicht bekannt. Als Mechanismus der Blutdrucksenkung nach RSD wird eine Senkung des Sympathikotonus postuliert.

Material und Methode: Im Rahmen der Abklärungen vor RSD erfolgt die Bestimmung der Katecholamine und Katecholamin-Metaboliten im 24h-Sammelharn mittels high pressure liquid chromatography zum Ausschluss eines Phäochromozytoms mit definierten Normwerten (Noradrenalin 20–105 µg/SZ, Adrenalin 4–20 µg/SZ, Dopamin 190–450 µg/SZ, Normetanephrin < 390 µg/SZ und Metanephrin < 320 µg/SZ). Vor der Intervention sowie 3, 6 und 12 Monate nach der RSD werden sowohl Office-RR-Messungen als auch eine 24h Blutdruckmessung durchgeführt. Der Zusammenhang zwischen Katecholaminwerten und Blutdruckänderung nach RSD wird mittels univariater Korrelationsanalysen (Pearson's r) bestimmt. Zusätzlich wird mittels t-Test und Mann-Whitney-U Test bestimmt, ob RSD-Responder (Blutdrucksenkung mindestens 10 mmHg in der Office-Messung oder mindestens 5 mmHg in der 24-Stunden-Messung) initial höhere Katecholaminwerte aufweisen.

Ergebnisse: Wir berichten von 53 Patienten (32 Männer, mittleres Alter 62 Jahre [Range 36–80 Jahre]; mittlerer Body-Mass-Index 32, 1 kg/m^2).

Der Office-Blutdruck betrug initial 170/95 mmHg, der 24-Stunden Blutdruck 150/87 mmHg.

Die systolische/diastolische Senkung des Office-Blutdrucks betrug nach 3, 6, und 12 Monaten 21/9, 16/5, und 23/8 mmHg (alle p-Werte < 0.01).

Die systolische/diastolische Senkung des 24-h-BD betrug nach 3, 6, und 12 Monaten 11/4, 7/4, und 10/6 mmHg (alle p-Werte < 0.01).

Die initiale Messung ergab eine mittlere Ausscheidung von 112 µg Metanephrin, 342 µg Normetanephrin, 6 µg Adrenalin, 51 µg Noradrenalin sowie 200 µg Dopamin in 24 h.

Mit Ausnahme einer schwachen positiven Korrelation zwischen dem Office-DBP vor der Intervention und der Metanephrinausscheidung bestand kein statistisch signifikanter Zusammenhang zwischen dem Blutdruck vor der Intervention und der Katecholaminausscheidung.

Im Follow-up bestand keine signifikante Korrelation zwischen der Änderung des systolischen oder diastolischen Blutdrucks nach 3, 6, und 12 Monaten, wobei dies sowohl für die Office- als auch für die 24 Stunden-Blutdruckmessung gilt. Als Ausnahme fand sich hier ein Trend zu einer höheren Blutdrucksenkung (Office-SBP) nach einem Jahr und der Ausscheidung von Metanephrin vor der RSD.

RSD-Responder bezogen auf die Office-Messung oder bezogen auf die 24-Stunden-Messung wiesen keine signifikant unterschiedlichen Katecholaminwerte im Vergleich zu Non-Respondern auf. Es bestanden lediglich schwache, nicht-signifikante Trends zu höherer Katecholaminausscheidung bei Respondern.

Diskussion: Die im Rahmen des Screenings vor RSD bestimmten Katecholamine im Sammelharn eignen sich nicht zur Abschätzung des Erfolges der renalen Sympathikusdenervierung.

VI-3

Effects of renal denervation on ambulatory blood pressure measurements in patients with resistant hypertension

V. Gammer, T. Lambert, A. Nahler, H. Blessberger, J. Kammler, M. Grund, K. Kerschner, G. Buchmayr, K. Saleh, A. Kypta, S. Hönig, S. Schwarz, C. Steinwender

1st Medical Department—Cardiology, Linz General Hospital, Academic Teaching Hospital of the Universities of Vienna and Innsbruck

Background: Renal sympathetic denervation (RDN) can reduce office blood pressure (BP) values in patients suffering from resistant hypertension. Compared to office blood pressure (OBP) measurements, ambulatory blood pressure measurement (ABPM) is a better predictor of cardiovascular morbidity and mortality in patients with arterial hypertension. We have investigated the effects of RDN on ABPM.

Methods: Resistant hypertension was defined as mean systolic office BP > 160 mmHg (> 150 mmHg in patients with diabetes), despite at least 3 antihypertensive drugs. RDN was performed using sedoanalgesie via a right transfemoral approach with the Symplicity Catheter System (Medtronic).

OBP measurements and ABPM were performed in all patients before RDN and 3 and 6 months after the procedure, respectively. Patients with a mean systolic 24-hour-BP reduction of ≥ 5 mmHg in ABPM were classified as responders.

Results: A total of 86 patients were enrolled in the study and 5 patients had to be excluded from analysis because of less than 70 % valid ABPM recordings. Out of the 81 studied patients, we found 49 responders (60.5 %) with a mean systolic BP reduction of ≥ 5 mmHg in ABPM.

In these patients, ABPM decreased from 144.3/84.7 mmHg at baseline to 138.3/81.5 mmHg after 6 months ($p = 0.025/p = 0.045$). Mean day-time BP was reduced by –6.5/–0.2 mmHg ($p = 0.014/p$ = n. s.). The mean night-time BP was only reduced non-significantly by – 6.2/– 1.9 mmHg.

Conclusion: By the use of ABPM, we found a significant BP reduction in about two- thirds of patients with resistant hypertension 6 months after RDN. BP reduction was mainly driven by the significant reduction of day-time BP levels.

VI-4

Effects of renal denervation on ambulatory blood pressure measurements in elderly patients with resistant hypertension

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I. Interne Abteilung, AKH Linz

Background: Elderly patients suffering from hypertension have a higher risk of cardiovascular events and death. A high prevalence of co-morbidities often results in poly-pharmacy with the risk of pharmacological interaction and non-adherence. Therefore, renal denervation (RDN) as additional treatment option to medical antihypertensive treatment is a promise on better blood pressure (BP) control, especially in patients with resistant hypertension.

Methods: We systematically investigated the effects of RDN by the use of ambulatory blood pressure measurements (ABPM) in a consecutive series of patients with resistant hypertension (Office BP > 160 mmHg; > 150 mmHg in patients with diabetes). ABPM was performed in all patients at baseline and 6 months after RDN, respectively. Patients were separated in two groups, younger and older than 70 years (group A and B) and treatment success ("responders") was defined as a mean systolic BP reduction of more than 5 mmHg in ABPM. The primary endpoint was the mean systolic BP reduction in responders in both groups.

Results: We included 106 patients with 45 of them being older than 70 years (group B). The responder rate was 47.5 % in group A and 53.3 % in group B. In responders, the mean 24-hour-BP at baseline was 153 ± 16.8/95.7 ± 15.6 mmHg in group A and 151.3 ± 14.5/84.8 ± 13.6 mmHg in group B, respectively. After 6 months, the mean BP reduction in ABPM was – 17.6/–8.7 mmHg in group A ($p < 0.001/p < 0.001$) and – 19.2/– 9.4 mmHg in group B ($p < 0.001/p < 0.001$; p = n. s. between group A and B).

Considering only patients with a systolic 24-hour-BP of more than 135 mmHg the responder rate in all patients was 62.9 %.

Conclusions: y the use of ABPM, we found a significant BP reduction in almost two-third of patients with RDN for resistant hypertension. BP reductions in ABPM were comparable in patients younger and older than 70 years.

VI-5

Effects of renal sympathetic denervation on inflammatory parameters

D. Lang, T. Lambert, M. Grund, J. Auer, C. Steinwender

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Objective: Renal sympathetic denervation with radiofrequency ablation substantially reduces blood pressure in patients with treatment-resistant hypertension. We investigated changes of inflammatory parameters after renal sympathetic denervation and their association with ambulatory blood pressure changes.

Design and method: We conducted a retrospective analysis of inflammatory parameters among 78 patients treated with renal sympathetic denervation. Serum C-reactive protein concentration, interleukin-6 concentration and leukocyte count were assessed

before, 6 and 12 months after denervation. Separate analyses were conducted for responders (defined as decrease in ambulatory systolic blood pressure of 5 mm or more) and non-responders.

Results: There were no meaningful differences between baseline, 6 and 12 months CRP concentrations ($p=0.891$ and $p=0.434$, respectively). There was no significant interaction for responder status, for baseline ambulatory blood pressure (ABP) levels, and for ABP-changes at 6 months.

We observed a reduction in interleukin-6 concentrations at 6 and 12 months (−0.55 pg/ml ± 3.0; $p=0.042$ and −1.68 pg/ml ± 3.8; $p<0.001$, respectively). There was a significant interaction between changes in serum interleukin-6 concentrations and responder status at six months (−1.11 pg/ml versus +0.21 pg/ml for responder and non-responder, respectively; $p=0.028$). Baseline Il-6 concentrations significantly correlated with baseline ambulatory blood pressure ($r=0.255$; $p=0.027$) and with ambulatory blood pressure differences at 6 months ($r=0.295$; $p=0.020$).

White blood cell (WBC) counts were significantly decreased at 6 and 12 months after renal sympathetic denervation (−0.46 × 103/µl ± 1.39; $p=0.017$ and −0.78 × 103/µl ± 1.88; $p<0.001$). We did not find any interaction between WBC count and responder status. There was no significant correlation between changes in WBC counts and baseline ambulatory blood pressure (ABP) levels, and ABP changes at 6 months.

Conclusions: Renal sympathetic denervation may be associated with a substantial decrease of serum inflammatory marker concentrations. ABP and Il-6 appear to be closely related to each other, with baseline Il-6 concentration possibly predicting the degree of ABP reduction by renal sympathetic denervation.

VI-6

Metabolic and endocrinologic effects of renal sympathetic denervation

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Objective: Renal sympathetic denervation with radiofrequency ablation substantially reduces blood pressure in patients with treatment-resistant hypertension. We investigated the effects of renal sympathetic denervation on body weight, glucose- and lipid metabolism and thyroid function as well as their association with ambulatory blood pressure changes.

Design and method: We conducted a retrospective analysis of metabolic and endocrinologic parameters among 78 patients treated with renal sympathetic denervation. Body mass index, fasting glucose concentration, HbA1c fraction, low density lipoprotein, high density lipoprotein, cholesterol, non-HDL-cholesterol and triglyceride concentrations as well as free serum thyroxine (T4) and thyroid-stimulating hormone (TSH) concentrations were assessed before and 6 months after renal denervation.

Results: BMI significantly decreased by 0.5 kg/m^2 (±1.3; $p=0.004$) during 6 months of follow up, reduction in mean body weight was −1.4 kg (±3.7; $p=0.006$). BMI reduction was significantly correlated with the reduction of systolic ambulatory blood pressure at 6 months ($r=0.273$; $p=0.041$).

Fasting plasma glucose concentration and HbA1c fraction did not change significantly during 6 months follow up. Mean serum HDL concentrations (+1.1 mg/dl ± 7.2; $p=0.031$) and mean triglyceride levels (+14.4 mg/dl ± 46.6; $p=0.020$) increased significantly during follow up, the other lipid metabolism parameters remained unchanged. Concerning glucose and lipid metabolism parameters, we found no significant interaction for baseline ABP of ABP changes at 6 months.

Free serum thyroxine (T4) concentrations significantly decreased at 6 months follow up (−0.8 µg/dL ± 1.7; $p=0.029$), while there was a non-significant increase in serum TSH concentrations (+0.4 µU/mL ± 1.1; $p=0.140$). Baseline TSH concentrations were found to be significantly correlated with ABP changes at 6 months ($r=-0.399$; $p=0.038$).

Conclusions: Renal sympathetic denervation may be associated with a reduction in body weight and with changes in lipid metabolism. Our results also suggest changes in thyroid function after RSD. This analysis did not reveal any meaningful effects on in glucose metabolism.

VI-7

Effects of renal sympathetic denervation on office versus ambulatory blood pressure and renal function parameters

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Objective: Renal sympathetic denervation (RSD) with radiofrequency ablation substantially reduces blood pressure in patients with treatment-resistant hypertension. We investigated changes in office (OBP) and ambulatory blood pressure (ABP) as well as in renal function parameters after renal sympathetic denervation.

Design and methods: We conducted a retrospective analysis of ambulatory and office blood pressure and renal function parameter data among 78 patients treated with renal sympathetic denervation. ABP, OBP, serum creatinine concentration, GFR (MDRD) and Cystatin C concentration were assessed before, 6 and 12 months after the treatment.

Results: Office blood pressure among all patients was shown to be significantly reduced by −16.0/−6.4 mmHg (±25.8/16.8; $p<0.001/p=0.002$) at 6 months, but only and non-significantly by −0.4/+0.6 mmHg (±30.2/19.8; $p=0.928/0.824$) at 1 year.

Overall ambulatory blood pressure was non-significantly reduced by −2.6/−1.4 mmHg (±18.2/10.2; $p=0.067/0.087$) on average within 6 months and significantly by −8.2/−3.8 mmHg (±18.8/11.5; $p=0.001/0.005$) at 12 months.

We found no significant changes in creatinine concentration and glomerular filtration rate at 6 and at 12 months. Mean Cystatin C concentration significantly increased by an average of +0.04 mg/L ± 0.14 ($p=0.026$) at 6 months and by +0.14 mg/L ± 0.21 ($p<0.001$) at 12 months.

Conclusions: Our results suggest, that ABP may be a better parameter to assess RSD results than OBP, as we found, that renal sympathetic denervation significantly decreased ambulatory blood pressure up to 1 year, while office blood pressure reductions could not be sustained during follow up.

Although creatinine concentration and GFR remained without statistically significant changes up to one year, the significant changes in Cystatin C concentration may suggest, that impairment of renal function after RSD cannot be fully precluded.

VI-8

Removal of Active-Fixation Coronary Sinus Leads using a Mechanical Rotation Extraction Device (Cook Evolution©)

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AKH Linz, Abteilung Interne I

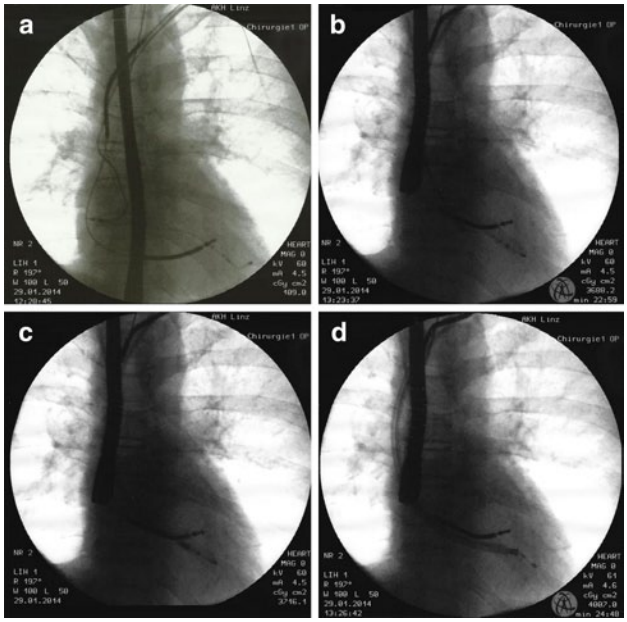
Background: Active fixation coronary sinus (CS) leads are widely used in patients with cardiac resynchronization therapy

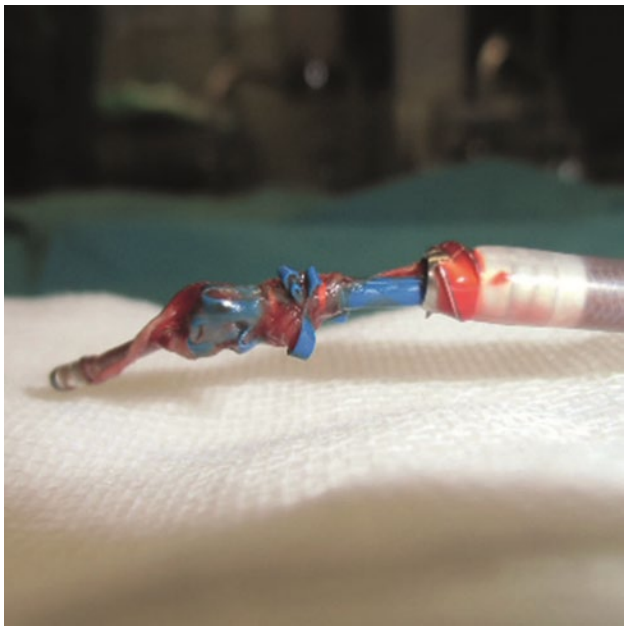
(CRT). Due to their very low dislodgement rates they are an attractive option for implanters. However, as compared to passive fixation CS leads—that are usually easy to remove—extraction of active fixation CS leads is a complex procedure that bears potential fatal risks for patients.

Methods: We performed a retrospective analysis of patients undergoing StarFix© lead extraction at our institution. The indication for lead extraction in all patients was severe device infection. Procedural outcomes as well as patient characteristics are reported. For removal of the StarFix® lead the Evolution® mechanical rotation extraction sheath was used in combination with a lead locking device.

Results: Between November 2011 and January 2014, six patients underwent trans-venous lead extraction of Medtronic StarFix® leads (Medtronic Inc., Minneapolis, MN, USA). Only one of these patients was a 47 year old female, whereas the others were males (mean age 64 ± 12 years). Patients had their StarFix® leads implanted for on average 46.5 ± 8.2 month. All leads could be successfully extracted with the Cook Medical Evolution© tool. A lead locking stylet was used for all procedures (2 patients with a Lead Locking Device from Spectranetics®, and 4 with the Cook® Liberator). All StarFix® leads could be extracted totally. In one patient (16.6 %) pericardial tamponade occurred as a major complication immediately after extraction requiring immediate surgical intervention (sternotomy). After establishment of an on-pump cardiopulmonary bypass a 5 mm long sharp cut in the lateral vein of the CS could be identified. The leak could be surgically fixed and the patient survived. No patient of our cohort died. On all extracted leads significant tissue growth between the fixation lobes could be observed.

Discussion: Attain StarFix® leads implanted years ago can be extracted with the help of a mechanical extraction sheath. However, this procedure bears potential risks and should only be performed by experienced operators with a cardiac surgery standby. We conclude that in young patients or those at higher risk for device infection, Attain StarFix® leads should only be implanted, if all other trans-venous left ventricular pacing devices are not suitable.





Postersitzung VII: Interventionelle Kardiologie II

VII-1

Reduced radial expansion of the everolimus-eluting bioresorbable vascular scaffold compared to the metallic everolimus-eluting stent

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Background: Everolimus-eluting bioresorbable vascular scaffolds (BVS) represent a novel treatment option for coronary artery disease. First clinical and angiographic results seem to be promising, however data on its handling and procedural performance are scarce. The aim of our study was to assess the radial strength of BVS by Optical Coherence Tomography (OCT) in clinical routine.

Methods: Post-implantation, OCT images of 40 BVS were evaluated and compared to 40 metallic everolimus-eluting stents (EES). Gross device under expansion was defined as an in-stent minimal lumen area (MLA) of less than 80 % of the average reference lumen area. The primary endpoint was the radial expansion at the site of the MLA defined by the diameter-ratio (Fig. 1).

Results: Patients receiving BVS were younger than those with EES (54.0 ± 11.2 versus 61.7 ± 11.4, $p = 0.012$), the remaining baseline, vessel and lesion characteristics were comparable between groups. Lesion preparation was more frequently performed and inflation time was longer in the ABSORB™ than in the XIENCE™ group, respectively ($n = 34$ versus $n = 23$, $p = 0.006$; 44.2 ± 12.8 versus 25.6 ± 8.4 s, $p < 0.001$). There were no significant differences in maximal inflation pressures and postdilation-frequencies with non-compliant balloons between groups. Although device under-expansion was not significantly different the diameter-ratio was significantly higher in the BVS compared to the EES group, respectively ($n = 11$ versus $n = 12$, $p = 1.000$; 1.46 ± 0.20 versus 1.32 ± 0.19, $p = 0.004$).

Conclusion: Our data show, that local radial expansion is significantly reduced in BVS compared to EES. Although the clinical

consequences of this finding are unclear, the reduced local radial expansion should be considered in the PCI strategy especially in calcified lesions.

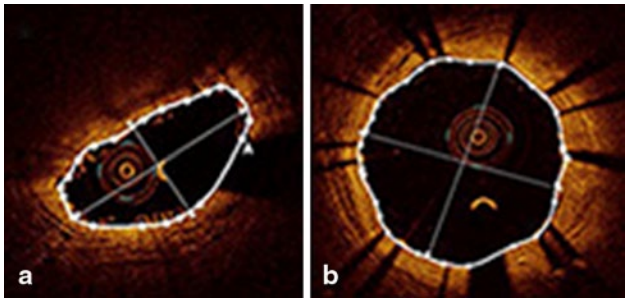

Fig. 1 Case example. Automatic measurements performed at site of minimal lumen area. Diameter ratio between maximal- and minimal diameter was calculated and compared between ABSORB™ scaffolds (a) and XIENCE™ stents (b)

VII-2

Relative survival of elderly patients who underwent an elective PCI—a multicenter retrospective study

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Background: Age is a strong predictor of survival in patients with coronary artery disease. Older patients often suffer from multiple co-morbidities and are consequently more fragile. Percutaneous coronary intervention (PCI) is associated with more complications and, therefore, worse outcome in these old patients. The calculation of relative survival rates adjusts for the "background" mortality in the general population by correcting for age and gender. We analyzed if older patients after elective PCI have a worse relative survival compared to younger patient groups.

Methods: A total of 8,342 patients who underwent elective PCI at two high volume centers (Medical University Hospital Vienna, LKH St. Pölten) between 1998 and 2009, were analyzed.

Results: The relative survival of all patients after PCI was slightly lower compared to the general population. In a multivariate Cox regression model age amongst others was a strong predictors of survival (Fig. 1—absolute survival according to age quartiles). Stratifying patients according to their age the relative survival of the younger population (Q1: <58 years—2,046 patients), the older population (Q3: 66–73 years—2,090 patients) and the very old population (Q4: >73a—2,307 patients) was similar. The relative survival of mid-aged patients (Q2: 58–65a—1899 patients) was significant better than that of all other patient groups (Fig. 2).

Conclusion: Old patients after elective PCI have a similar survival compared to younger patients. Mid-aged patients have a better relative survival compared to other patient groups and may benefit most from elective PCI.

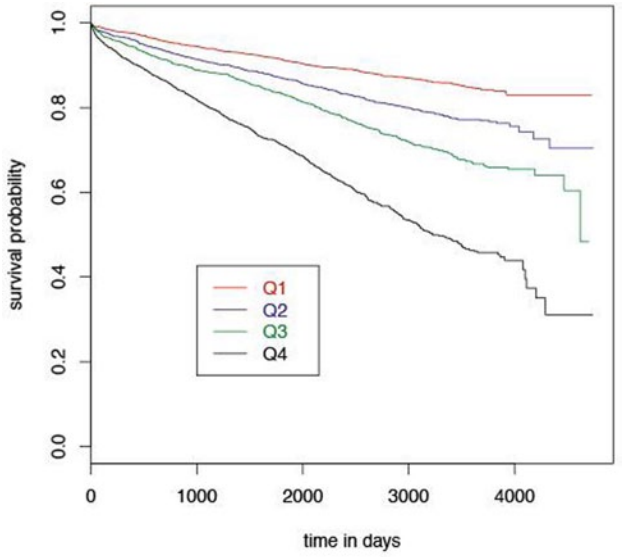

Fig. 1 Absolute survival

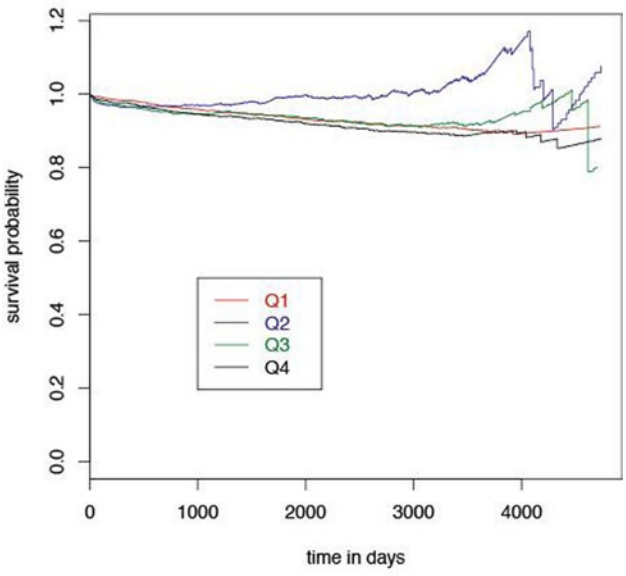

Fig. 2 Relative survival

VII-3

Malapposition, underexpansion and edge dissection in everolimus-eluting bioresorbable vascular scaffolds and metallic everolimus-eluting stents—a comparison based on Optical Coherence Tomography

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Background: The everolimus-eluting bioresorbable vascular scaffold (ABSORBTM) is characterized by a greater strut thickness (152 vs. 81 μm), but it has a greater flexibility compared to the metallic everolimus-eluting XIENCETM stent. Due to its fragility the inflating pressure of the ABSORB scaffold is limited and suitable lesions have to be well prepared. This study assesses the incidence of malapposed stent-struts, and the frequency of stent-underexpansion and edge dissection after ABSORBTM implantation compared to the XIENCETM stent.

Methods: Twenty-three patients after implantation of an ABSORBTM scaffold ($n=30$) were matched with 26 patients after implantation of a XIENCETM stent ($n=30$) according to gender, age, stent-diameter and length. Stent performance after implantation was assessed by Optical Coherence Tomography (OCT) were compared between groups.

Results: Pre-dilation was more frequently done in the ABSORBTM group (28 versus 19 times, $p=0.005$). Inflation time was longer in the ABSORBTM group (44 ± 14 versus 28 ± 9 s, $p<0.001$) and the inflation pressure of the stent-balloon was lower (11 ± 3 versus 14 ± 3 atmospheres, $p=0.005$). The frequency of post-dilatation with a non-compliance (NC) balloon (20 versus 15 times, $p=0.147$) and the inflating pressure (17 versus 16 atmospheres, $p=0.797$) were similar between groups. After the implantation less ABSORBTM-struts were malapposed (11 ± 23 versus 41 ± 59, $p=0.011$), and, in trend, less edge dissections occurred with the ABSORBTM scaffold (6 versus 12, $p=0.079$). The incidence of underexpansion was similar between groups (14 versus 12 times, $p=0.397$).

Conclusion: OCT assessment demonstrated a better performance of the ABSORBTM-scaffold than of the XIENCETM stent immediately after implantation.

VII-4

Incidence and predictors for late acquired stent malapposition of drug-eluting-stents with second-generation permanent and biodegradable polymer-coatings—a prospective, randomized comparison using Optical Coherence Tomography

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Background: The polymers releasing the drug of first-generation drug-eluting stents (DES) may induce allergic reactions and inflammation, resulting in late-acquired stent malapposition (LASM) with uncoverage of struts, and risk of stent thrombosis. The incidence and predictors of LASM in DES with different polymers designed to improve biocompatibility are unknown.

Methods: Fifty patients with 59 lesions of interest were randomized to elective treatment with Everolimus-eluting stents (EES; $n=17$, 20 lesions)], Zotarolimus-eluting stents (ZES; $n=15$, 19 lesions), and Biolimus-eluting stents (BES; $n=18$, 20 lesions) and underwent optical coherence tomography after implantation and after 1 year.

Results: After implantation 29 early stent malappositions (ESM) were documented in 29 lesions (49 % of lesions), distributed to 11 lesions treated with EES (55 %), 11 with ZES (58 %), and 7 with BES (35 %; n. s.). After one year 18 late stent malappositions (LSM) in 14 lesions (24 %) were detected; nine ESM persisted (EPSM) after one year (1 EES, 6 ZES, 2 BES), whereas 20 ESM resolved. In addition, 9 LASM were documented (5 LASM in early well-apposed Stents, 4 LASM in Stents which also have EPSM). LASM was present in 7 hydrophilic polymer-coated ZESs (37 %), in 2 fluoropolymer-coated EESs (10 %), and in none of the biodegradable polymer-coated BESs ($p=0.003$). Independent predictors of LASM were the vessel treated (RCA as vessel with high motion; $p<0.022$) and type of polymer (biodegradable or permanent; $p<0.035$).

Conclusion: The incidence of ESM and EPSM were similar, whereas the incidence of LASM was different in second-generation DES with different polymers. Biodegradable polymer prevented LASM, stent locations with significant vessel movement (RCA) enhanced LASM.

Table 1 Distribution of ESM, LSM and LASM

	EES	ZES	BES	Total
ESM	11	11	7	29
Resolved	10	5	5	20
Persisting	1	6	2	9
LASM	2	7	0	9
LASM only	2	3	0	5
LASM+ pers.	0	4	0	0
1y LSM Stents	3	9	2	14
LASM only	2	3	–	5
LASM + pers.	–	4	–	4
Persist. only	1	2	2	5

VII-5

Incidence of coronary stent fractures in patients at high risk—a systematic screening using Coronary Computered Tomography

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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 27 out of 102 patients (27 %) coronary CCT revealed a stent gap including 17 patients with a stent fracture (17 %) and 10 patients with an overlap failure (10 %). In the following CCA all stent gaps were confirmed by optical coherence tomography. A clinically relevant stent-related pathology could be detected in 8 out of 27 patients (30 %) with stent gaps (in-stent- restenosis in four patients, chronic total occlusion in two patients, coronary aneurysm and thrombus in one patient, respectively) including 6 out of 17 patients

(35 %) with a stent fracture and 2 out of 10 patients (20 %) with an overlap failure. Compared to the 6 out of 17 stent fracture patients (35 %) with a clinically relevant pathology, only two out of 22 controls (9 %) had a clinically relevant pathology (chi-square p = 0.044).

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.

VII-6

Incidence of Renal Artery Stenosis after Renal Denervation in Patients with Resistant Arterial Hypertension

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AKH Linz, I. Interne Abteilung

Background: The sympathetic nervous system is crucial in the development and maintenance of arterial hypertension. In patients with resistant hypertension, renal denervation (RDN) led to significant blood pressure (BP) reductions in various studies. In context of the discussion on the efficacy of RDN, systematic evaluations of the benefit/risk ratio are necessary. One important safety concern about RDN is the development of focal renal artery stenosis due to fibrotic scarring in the Intima after radiofrequency ablation.

Methods: We systematically evaluated the renal artery anatomy in a consecutive series of patients with resistant hypertension at baseline and 6 months after RDN. Resistant hypertension was defined as systolic office BP > 160 mmHg or > 150 mmHg in patients with diabetes. Treatment success was defined by a mean systolic BP reduction of more than 10 mmHg 6 months after RDN. In all patients, renal artery anatomy was evaluated by the use of MRI-angiography or CT-angiography. A renal artery stenosis > 70 % was considered hemodynamically significant.

Results: We enrolled 76 patients in our study. The mean age was 63.9 years and 43.4 % of the patients were female. The mean office BP at baseline was 165.1 ± 19.7/88.3 ± 13.5 mmHg. Six months after RDN, we found a treatment success in 45 patients (60 %). In these responders, mean office BP reduction was −30.2/−13.7 mmHg ($p < 0.001$/$p < 0.001$).

Renal artery imaging was obtained in all patients at baseline and 6 months after the procedure (MRI: $n = 66$; CT: $n = 10$) and no renal artery stenosis were detected.

Conclusions: In this study we found a significant BP reduction in almost two-third of our patients with resistant hypertension. Renal artery imaging 6 months after RDN revealed no renal artery stenosis in this consecutive series of patients.

VII-7

Biomarker NT-proBNP—a predictor of outcome in transfemoral aortic valve implantation?

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Background: Plasma NT-proBNP has been reported to predict survival in severe aortic stenosis (AS). Aim of this study was to examine the change in NT-proBNP levels over time and its value as predictor of outcome after treatment with transfemoral aortic valve implantation(TAVI).

Methods: From May 2007 until June 2013, 142 consecutive patients with severe AS (mean age 83 years (63–95), 56 male, AVA 0.58cm^2 (0.3 – 1.1) underwent TAVI in our department (23 CoreValve, 119 Edwards Sapien). Plasma NT-proBNP, NYHA functional class, hemoglobin and creatinine were analysed at baseline, 30 days, 6 months and 1 year after TAVI. Echocardiographic assessment of left ventricular function (LVF), degree of mitral regurgitation (MR) and paravalvular aortic regurgitation (AR) were performed. Overall survival data and the relation to NT-proBNP levels were analysed.

Results: Median baseline NT-proBNP before TAVI was 1912 pg/ml (IQR 1040.5–4750 pg/ml). Survival rate at 1 year after TAVI was 75.6 % (CI 0.67 – 0.82). At 30 days NT-proBNP showed a trend in reduction (1715 pg/ml, IQR 858 – 3455; $p = 0.055$). A significant decrease at 6 months was observed (1214 pg/ml; IQR 632 – 2806; $p = 0.0026$), as well as 1 year after TAVI (1271 pg/ml; IQR 654 – 2395; $p = 0.007$). There was a significant reduction of NYHA classification at all follow up visits ($p = 0.0001$). NYHA class was significantly related to NT-proBNP. Cox regression analysis of baseline NT-proBNP on survival after TAVI evidenced a significant effect (HR 1.339; $p = 0.0116$), with increased mortality in the upper quartiles of NT-proBNP. The cox model of the course of sequential NT-proBNP after TAVI illustrated a highly significant effect on survival (HR 1.58; $p = 0.0002$). Analysis of MR showed a trend in reduction after 6 months ($p = 0.095$), with significant reduction after 1 year ($p = 0.015$). Hemoglobin and creatinine significantly improved 6 months after TAVI compared to baseline ($p = 0.0001$ for both). Interestingly, paravalvular AR after TAVI decreased significantly between 30 days and 6 months after TAVI ($p = 0.001$).

Conclusion: Release of pressure overload after TAVI is reflected by a significant reduction of NT-proBNP accompanied by improval of NYHA stage. Higher BNP before TAVI is associated with lower survival. However, TAVI is a feasible option for elderly patients with high surgical risk and improves hemoglobin, renal function and degree of MR.

VII-8

The DISCOVER trial: 1-year-outcomes of the direct flow medical transcatheter aortic valve

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Introduction: The Direct Flow Medical transcatheter aortic valve (DFM) system is a non-metallic design with a pressurized support structure which allows precise positioning, retrieval and full hemodynamic assessment of valve performance prior to permanent implantation. The DISCOVER Trial was a prospective, multicenter evaluation of the safety and efficacy of the Direct Flow Medical Percutaneous Aortic Valve System for the treatment of severe symptomatic aortic stenosis in high and extreme risk patients.

Materials and methods: One hundred patients with a logistic EuroScore ≥ 20 or other high surgical risk comorbidities not reflected by the logistic EuroSCORE were enrolled at 10 centers in Europe. The primary endpoint of all cause mortality was assessed in these 100 patients. Secondary acute procedural and 1-year clinical and echocardiographic VARC defined outcomes were assessed in 75 patients after prespecified exclusion of the 25 roll-in patients. Patients were reviewed by an independent review committee con-

sisting of cardiac surgeons and interventional cardiologists. All echocardiographic and angiographic data were evaluated by an independent core laboratory (Medstar) and adverse events adjudicated by an independent clinical event committee using VARC definitions.

Results: Patients were 83.1 ± 6 years, logistic EuroSCORE 22.5 ± 11.3 % and STS scores 9.7 ± 8.7 %. Other comorbidities included coronary artery disease in 59 %, prior CABG 23 %, and chronic kidney disease (defined as GFR < 60) 24 % of cases. A 25 mm valve was implanted in 59 % and a 27 mm in 41 % of cases. Device success was obtained in 93 % of cases, 30-day freedom from death was 99 % and freedom from combined safety endpoint was 91 % at 30 days and 89 % at 6 months. Core lab echocardiographic assessment using ACC/AHA criteria demonstrated 74 % none or trace, 23 % mild and 3 % moderate aortic regurgitation at 30 days. The mean gradient was similar at 30 days and 6 months (12.5 ± 5.7 and 13.0 ± 7.5:mmHg) as well as effective orifice area (1.50 ± 0.50 and 1.50 ± 0.49 cm^2). 90 % of patients were in NYHA class 1 or 2 at 6 months.

Conclusions: The Direct Flow Medical Transcatheter Aortic Valve System provides excellent 30-day and 6-months clinical and hemodynamic outcomes in high and extreme surgical risk patients with severe aortic stenosis. One-year-outcomes will be available at the time of the meeting.

Postersitzung VIII: Rhythmologie I

VIII-1

Arterial stiffness is associated with increased left atrial volume in patients with atrial fibrillation

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Objective: Hypertension and increased left atrial volume are important predictors for the development and maintenance of atrial fibrillation. Previous echocardiographic studies suggest a relation between arterial stiffness and increased left atrial dimensions in hypertensive patients. We sought to examine the relation of arterial stiffness to left atrial volume in patients with symptomatic atrial fibrillation (AFib).

Design and methods: We enrolled 27 patients (mean age 59 ± 10.9 years, 16 males, 55.6 % hypertensives) with highly symptomatic AFib (85.2 % paroxysmal, 14.8 % persistent), referred for catheter ablation. In all patients electrocardiogram-gated, multi slice, computed tomography was performed. Left atrial volume (LAV) and left atrial appendage volume (LAAV) were calculated with EnSite™ Verismo™ Segmentation Tool. Carotid-femoral pulse wave velocity (cf-PWV), central blood pressure and wave reflections (pressure augmentation, augmentation index, central pulse pressure) were assessed non-invasively in stable sinus rhythm using a commercially available SphygmoCor©-System before or after catheter ablation.

Results: In univariate correlation analysis increased LAV was associated with higher cf-PWV ($R = 0.503$, $p = 0.007$) and age ($R = 0.426$, $p = 0.026$). LAAV was significantly and positively related to cf-PWV ($R = 0.562$, $p = 0.002$) but not with age. No significant association between LAV or LAAV and peripheral and central blood pressure levels or parameters of wave reflections were found. In multivariate regression analysis the relation of cf-PWV to LAV was not significant any more after correction for age (beta = 0.183, p = 0.33). Relation of LAAV and cf-PWV was independent of age in multivariate analysis (beta = 0.397, $p = 0.04$).

Conclusions: Arterial stiffness is associated with increased left atrial volume in patients with AFib. The relation of cf-PWV on LAV seems to be at least partly due to the effect of aging. Our findings suggest that arterial stiffness may be associated with left atrial structural remodeling and be a contributing factor to atrial fibrillation development and maintenance.

VIII-2

Echocardiographic predictors of left atrial fibrosis: the importance of the A-Wave

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Background: Pulmonary vein isolation (PVI) is the cornerstone of ablation of atrial fibrillation (AF).

The success of this procedure and eventual need for additional ablation is very much dependent on the occurrence of left atrial fibrosis. Different echocardiographic parameters may have the potential to predict left atrial fibrosis and therefore could help to predict ablation success and plan the ablation.

Methods and results: 84 consecutive patients with symptomatic AF (59 ± 10.6 years, 63 % male, 70 % paroxysmal AF) undergoing PVI were enrolled prospectively.

In all patients ecg-gated, multi slice computed tomography and echocardiography (transthoracic and transesophageal) were performed prior to the ablation procedure. 76 % of patients were in sinus rhythm at the time of echocardiography.

Measured echocardiographic parameters included left ventricular ejection fraction (LVEF), left atrial anterior posterior dimension (LAD), mitral inflow velocity profile (A-wave, E-wave, E/A ratio), tissue

Doppler imaging of septal mitral annulus (e` and E/e´ ratio) and left atrial appendage (LAA) flow velocity. Left atrial volume (LAV) was calculated by the use of a Segmentation Tool (EnSite™ Verismo™, St. Jude Medical, St. Paul, USA).

During the ablation procedure, left atrial endocardial bipolar voltage was measured on at least 50 different sites (133 ± 72 points). Areas below 0, 5 mV were defined as low voltage and were found in 24 % of the population.

In univariate calculation advanced age, persistent AF, congestive heart failure, increased body surface area, reduced glomerular filtration rate, reduced A-wave, reduced LAA flow velocity and increased indexed LAV showed a significant correlation with the occurrence of low voltage areas.

However, in a multivariate regression analysis only persistent AF (beta = 0.273; $p = 0.046$), reduced A-wave (beta = – 0.415; $p = 0.004$) and advanced age (beta = 0.473; $p = 0.001$) still showed a significant correlation with the occurrence of low voltage areas.

Conclusions: For patients in sinus rhythm, the A-wave can serve as an independent predictor of left atrial fibrosis and therefore can help to predict the success of PVI and to plan the eventual need for substrate modification in case of relevant low voltage areas.

VIII-3

About the association of arterial stiffness and left atrial fibrosis in patients with atrial fibrillation

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Background: Left atrial fibrosis is an important predictor for the maintenance of atrial fibrillation. Arterial stiffness, as measured noninvasively by wave reflection parameters, is known to be related with increased left atrial dimension. Therefore, these parameters may have the potential to predict left atrial fibrosis.

Methods and results: We enrolled 39 patients (mean age 60 ± 10.6 years, 67 % males) with symptomatic atrial fibrillation (77 % paroxysmal), referred for catheter ablation. Carotid-femoral pulse wave velocity (cf-PWV), central blood pressure and wave reflections (augmentation pressure, augmentation index, central pulse pressure) were assessed non-invasively in stable sinus rhythm using a commercially available SphygmoCor- System before or after catheter ablation. During ablation procedure left atrial endocardial bipolar voltage was measured on at least 50 different sites (141 ± 88). Areas below 0, 5 mV were defined as low voltage and were found in 21 % of the population.

In univariate correlation analysis increased augmentation pressure, advanced age, persistent AF, congestive heart failure and reduced ejection fraction showed a significant association with the occurrence of low voltage areas. However, in the multivariate regression analysis only increased augmentation pressure (beta = 0.253, $p = 0.026$) and type of atrial fibrillation (beta=0.503, $p < 0.001$) were independent and still correlatied with occurrence of low voltage areas.

Conclusion: Increased arterial stiffness as indicated by augmentation pressure is independently associated with left atrial fibrosis. Thus, arterial stiffness may serve as a risk factor for the development of left atrial fibrosis.

VIII-4

The effect of statin therapy on the recurrence of atrial fibrillation after cardioversion

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Background: Atrial fibrillation is one of the most common cardiac arrhythmias, which can be terminated by medical or electric cardioversion. Several studies have analyzed the effect of statin therapy on the rate of recurrence in atrial fibrillation with conflicting results. We sought to examine whether statin therapy has the potential to prevent recurrence after cardioversion in patients with persistent and paroxysmal atrial fibrillation.

Methods and Results: We retrospectively enrolled 436 patients (mean age 67 ± 10.6 years, 72 % males) with atrial fibrillation and flutter who underwent cardioversion in LK Mödling between January 2002 and January 2013. 39.9 % had paroxysmal, 37.2 % persistent atrial fibrillation and 22.2 % had atrial flutter. The population with statin therapy (39.4 %) did not differ in age from the population without statin therapy (60.6 %), but had a significantly higher rate of hypertension, cardiomyopathy, diabetes and coronary heart disease.

In univariate analysis the population with statin therapy had a significantly reduced rate of recurrence ($p < 0.001$). 55.3 % of patients with statin therapy and 22.8 % without had atrial fibrillation after electric cardioversion. Furthermore, medication with aldosterone antagonists ($p = 0.023$) and diuretics ($p = 0.025$) showed fewer relapses, as well as the presence of cardiomyopathy ($p = 0.033$), coronary heart disease ($p = 0.02$) and diabetes ($p = 0.049$). However, in multivariate regression analysis statin therapy was the only independent predictor for reduced recurrence. It was independent from age, sex, concomitant diseases (cardiomyopathy, coronary heart disease, hypertension and diabetes) and medication (antiarrhythmic medication, ß-blockers, ACE inhibitors, angiotensin II receptor antagonists, calcium antagonists, aldosterone antagonists and digitalis) (OR = 0.258, $p < 0.001$).

Conclusion: Patients on statin therapy had a significantly reduced rate of arrhythmia recurrence after being cardioverted for atrial fibrillation or flutter, even though this population had significantly more concomitant diseases. These results were independent from age, sex, concomitant diseases and medication. Our findings suggest that statin therapy may have the potential to prevent atrial fibrillation after cardioversion.

VIII-5

T-wave variability for the prediction of fatal ventricular arrhythmias—a prospective, single-blind study

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Background: T-wave variability (T-Var) is an ECG phenomenon defined as beat-to-beat alteration of the morphology, amplitude, and/or polarity of the T-wave. Besides left ventricular ejection fraction (LVEF) assessment of T-Var is suggested for risk stratification.

Methods: In this prospective, single-blind study, we performed three short-term (20 min) Holter ECG based T-Var measurements (I1 at baseline, I2 after 6.5 ± 1.6 months and I3 after 13.1 ± 2.0 months) in 121 patients (46 % preserved LVEF) with implanted devices capable of ventricular arrhythmia (VA) storage. T-Var was defined as the variability of the T-segment that maximizes an oscillation: T-Var = √ (variance of a segment) x maximum value of the oscillation. Primary endpoint was a potentially fatal VA (ventricular tachycardia > 240 bpm leading to syncope or ventricular fibrillation).

Results: During a follow-up period of 20 ± 4 months 20/121 patients (55 % ischemic heart disease, 15 % preserved LVEF) had fatal VA terminated by the implanted defibrillator or external cardioversion. Patients with fatal VA had higher T-Var values (I1: 10.7 ± 7.3 µV, I2: 14.0 ± 6.5 µV, I3: 17.0 ± 5.4 µV) as compared to those without (I1: 7.8 ± 4.1 µV, $p = 0.170$; I2: 8.2 ± 3.6 µV, $p = 0.030$; I3: 8.8 ± 4.6 µV, $p = 0.004$; p-values adjusted for multiple testing). Patients stratified according to the degree of left ventricular function had similar T-Var values ($p = 0.893$). ROC calculation revealed that the best cut-off was T-Var > 8.54 µV at I1 with 57 % sensitivity and 71 % specificity (AUC = 0.606) to predict fatal VA within the follow-up time in the study sample. At I2, T-Var > 10.06 µV was found to be the best cut-off with 89 % sensitivity and 73 % specificity (AUC = 0.828) for a fatal VA after I2. An increase in T-Var > 6.91 µV between I1 and I2 was estimated to predict fatal VA after I2 with 78 % sensitivity and 97 % specificity (AUC = 0.841). After adjustment for LVEF in a multiple logistic regression model, the odds for developing fatal VA were estimated to increase by a factor of 1.1 ($p = 0.056$) for each 1 µV increment in T-Var at I1, and by 1.4 ($p = 0.006$) for each 1 µV increment in T-Var at I2.

Conclusions: T-Var is elevated in patients developing fatal VA, and both, elevation of T-Var and increase in T-Var can complement LVEF as an independent tool for risk stratification.

VIII-6

High-degree atrioventricular block in patients with pre-existing bundle branch block or bundle branch block occurring during transcatheter aortic valve implantation

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Background and aims: In the recent years transcatheter aortic valve implantation (TAVI) has become the standard therapy for high-risk and non-operable patients with severe aortic stenosis. However, the procedure involves several adverse effects such as access site complications or acute kidney injury. In patients who are treated with the Medtronic CoreValve bioprosthesis, rhythm and conduction disturbances are among the most frequent complications. Patients with post-procedural left bundle branch block appear to have an increased mortality risk, whereas patients with pre-procedural right bundle branch block display a higher rate of bradyarrhythmias. At present, permanent pacemaker (PM) implantation is only recommended in case of symptomatic or high-degree atrioventricular block (AVB). We, therefore, investigated the occurrence of high-degree AVB in patients with pre-existing bundle branch block (BBB) or BBB occurring during TAVI.

Methods: In this prospective single centre study 50 consecutive patients undergoing TAVI were included. Patients with pre-existing BBB or BBB occurring during TAVI received a primary prophylactic permanent DDD-PM. All devices were programmed to the AAIsafeR-mode allowing intrinsic conduction and switch to DDD mode in case of AV-conduction abnormalities (first- and second-degree AVB, complete AVB and pauses > 2 s). Furthermore all devices featured dual channel event counters as well as stored intra-cardiac electrocardiograms (EGMs) of AVB episodes. PM readouts and intracardiac EGMs were analysed for the occurrence of high-degree AVB.

Results: Of the whole study population, 20 patients presented with permanent atrial fibrillation or already had a permanent PM implanted. Two patients died peri-procedurally. The occurrence of rhythm and conduction disturbances was studied in the remaining 28 patients. Out of these, 17 patients with pre-existing BBB or BBB occurring during TAVI received a primary prophylactic permanent PM. Ten of them (58.8 %) developed episodes of high-degree AVB that were immediately terminated due to switch into DDD backup pacing. Most importantly, in 5 (29.4 %) of the cases, episodes of high-degree AVB only occurred after hospital discharge. The mean period from hospital discharge until the first documented episode of high-degree AVB was 300.6 (± 285.0) days. The mean follow-up period was 578.1 (± 294.9) days.

Conclusion: Development of high-degree AVB is a common complication in patients with pre-existing BBB or BBB occurring during TAVI. Accordingly, intensified monitoring via loop recorder or even prophylactic permanent PM implantation might be considered.

VIII-7

Impact of electric cardioversion on 2-year incidence of recurrence, death and stroke in patients with atrial fibrillation

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Purpose: We have investigated the clinical and laboratory parameters predictive for success of electric cardioversion (CV) and recurrence of atrial fibrillation (AF).

Methods: Consecutive 190 patients (63 % male, 69 ± 10 years) with AF and subjected to CV between November 2011 and June 2012 have been included into the study and followed for 2 years for reoccurrence and clinical events. Echocardiographic data, medical history and treatment, level of N-terminal-proBNP and cardiac risk factors were statistically analyzed. Incidence of all-cause death and stroke was recorded. Logistic regression analysis was performed to analyze predictive factors for the success and recurrence of AF and occurrence of irreversible clinical events.

Results: CV was successful in 85.3 % of patients. There was no factor predicting the success or failure of the CV. One-hundred-one (62 %) patients (68 ± 9 years, 60 % male) suffered from recurrent AF while 62 (28 %) patients (70 ± 10 years, 62 % male) remained free from AF after successful CV. All echocardiographic parameter (diameter of the left or right atrium, diameter of left ventricle, ejection fraction, diastolic dysfunction, grade of mitral or tricuspidal insufficiency, pulmonary pressure) were similar in the groups. Interestingly, lower level of proBNP was found in patients with recurrent AF requiring repeated CV (1706 ± 1885 vs 2538 ± 3155 pg/ml, $p = 0.036$). The cardiac risk factors, such as diabetes mellitus, hypertension, hyperlipidaemia as well as cardiac history (eg. coronary heart disease, dilated cardiomyopathy) and cardiac medication were similar in the groups. Patients with repeated CV had a significantly lower incidence of death 1.6 vs 5.9 % ($p = 0.008$) but trend to higher stroke rate of 9.7 vs 5.9 % as compared with patients with persistence of sinus rhythm. Unsuccessful CV was not associated with increased incidence of stroke (7.4 %) or death (3.7 %). Logistic regression analysis could not find significant predictive factor for re-occurrence of AF.

Conclusions: Electrical CV is a useful and safe method for treatment of AF. To maintain the sinus rhythm, more than half of the patients required repeated CV and prophylactic antiarrhythmic drugs. Interestingly, sudden death was more frequent in patients without recurrence of AF suggesting that the death was caused by underlying disease.

Postersitzung IX: Rhythmologie II

IX-1

First clinical experience using a new fluoroscopy-integrated catheter positioning system (Mediguide) for ablation of ventricular tachycardias

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Introduction: Mediguide (MG) represents a new catheter positioning system integrated into the C-arm of a conventional fluoroscopic system. After initial recording of short fluoroscopic loops (usually in RAO and LAO position), the tip of Mediguide-enabled catheters is precisely visualized in these pre-recorded loops.

Methods: We assessed intraprocedural Mediguide related parameters for RF-ablation of ventricular tachycardias (VT) in patients with structural heart disease (SHD; ischemic or non-ischemic) or idiopathic VT.

40 consecutive VT-patients (20 treated with the MG-system, 20 non-MG) were compared to a case-matched cohort using a standard 3D system. 13 patients in the MG-group (11 ischemic, 2 non-ischemic) and 16 patients in the non-MG group (13 ischemic, 3 non-ischemic) showed SHD and 7 (MG) vs. 5 (non-MG) idiopathic VT. Procedural parameters were compared between both groups. The endpoint of non-inducibility was used for all patients.

Results: 10 (MG) vs. 13 (non-MG) patients had a history of recurrent ICD/CRTD shocks. Mean procedure duration could be reduced significantly by 32 min in mean. Furthermore, mean fluoroscopy time and dose were remarkably reduced by the use of Mediguide (Table 1 and Fig. 1).

66 % of the fluoroscopy-time in the Mediguide group was acquired in "non-Mediguide-dependant" situations (positioning of non-Mediguide-enabled reference catheters, introducing sheaths, performing transseptal punctures) showing a great additional potential in further decreasing fluoro-time if more specialized Mediguide tools become available. No procedure related complications occurred in both groups.

Conclusions: The use of the novel Mediguide catheter positioning system is feasible and safe in VT ablation, dramatically reducing procedure time as well as fluoroscopy time and dose compared to standard 3D systems.

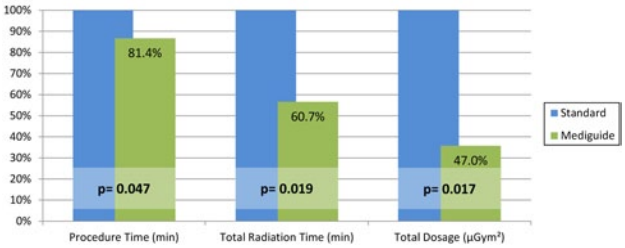

Fig. 1 Procedural Parameters in VT Ablation - Standard vs Mediguide

Table 1 Mean procedure duration, radiation time and dose

	Mean	Std. deviation	Sig (2-tailed)
Procedure time (min)	243,95	48,22	$p=0.047$
	211,5	51,48	
Total radiation time (min)	16,74	10,22	$p=0.019$
	9,47	3,26	
Total dosage (µGym²)	4787,87	4119,07	$p=0.017$
	1710,22	1866,5	

IX-2

Increased inducibility of atrial fibrillation in a porcine model of arterial hypertension

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Introduction: Arterial hypertension is the strongest risk factor for atrial fibrillation (AF). However, the underlying mechanisms are poorly understood, and integrative animal models are needed that allow to study early atrial remodeling during arterial hypertension. We previously established a porcine model of arterial hypertension by subcutaneous implantation of DOCA pellets (deoxycorticosterone acetate, an aldosterone analogon) and high-salt feeding. This model is characterized by an approx. 40 mmHg increase of systolic blood pressure, mild left atrial dilatation, left ventricular concentric hypertrophy, atrial and left ventricular cardiomyocyte hypertrophy, but no increase of atrial and left ventricular collagen content. Here, we tested whether these changes already increase the inducibility of atrial fibrillation.

Methods: Seven healthy pigs underwent subcutaneous implantation of DOCA pellets and high-salt feeding for 12 weeks. 8 weight-matched animals (65 ± 4 vs. 66 ± 6 kg) served as controls. The animals were anaesthetized and instrumented with a quadripolar stimulation catheter in the high right atrium and a decapolar catheter in the coronary sinus. Effective atrial refractory periods (AERP) were measured with a S1S2 stimulation protocol (1 ms pulse at twice diastolic threshold at cycle lengths 400, 300 and 240 ms). The inducibility of AF was assessed by burst protocols (1 ms pulse at four times diastolic threshold, cycle lengths 200/150/100/50 ms, 10 s duration, 5 repetitions). AF was defined as the onset of irregular atrial electrograms with an average cycle length shorter than 150 ms for more than 10 s.

Results: AERP did not significantly differ between both groups (S1 = 400 ms: 185 ± 27 vs. 187 ± 37 ms, S1 = 300 ms: 179 ± 29 vs. 147 ± 26 ms, S1 = 240 ms: 179 ± 26 vs. 140 ± 74 ms). The inducibility of AF (burst cycle length 50 ms) was significantly higher in DOCA treated animals compared to controls (69 ± 34 vs 25 ± 28 %, $p<0.01$). Mean AF duration was not different between groups (DOCA: 17 ± 2 s, control: 12 ± 5 s; n. s.).

Conclusion: DOCA-induced arterial hypertension increases atrial susceptibility towards fibrillation before structural changes and fibrosis become prominent. The underlying mechanisms in this model may therefore be reversible and serve as therapeutic targets to prevent the development and progression of atrial fibrillation.

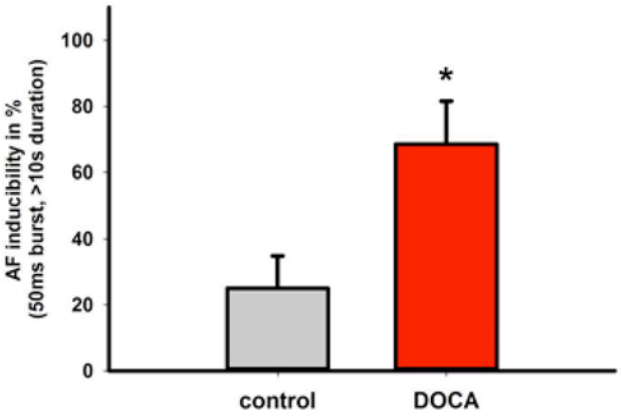

Fig. 1 The inducibility of atrial fibrillation is higher in hypertensive (DOCA, $n=7$) pigs than in controls ($n=8$). Error bars indicate SEM

IX-3

Long term results following catheter ablation using the Hansen Medical Sensei System in patients with atrial fibrillation

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Objectives: To evaluate the long-term outcomes of catheter ablation for atrial fibrillation (AF) using robotic navigation (RN) with the Hansen Medical Sensei System compared with manual catheter navigation.

Methods: Data on 185 robotic navigation and 109 manual navigation patients from a single center was retrospectively analyzed.

Results: The catheter ablation procedures were successfully completed in all patients. Ninety-seven percent (RN) and 99 % (manual ablation) of single pulmonary veins were successfully isolated. Procedural time was significantly reduced in the RN group compared to manual ablation (231.4 ± 51.8 vs 268.7 ± 61.0 min; $p<0.0001$). Mean fluoroscopy time was 26.6 ± 9.7 min in the RN group compared to 39.3 ± 12.7 min with manual ablation ($p<0.0001$). Peri-procedural complications were similar between the two groups. Mean follow-up was 27.7 months in the RN group and 42.4 months in the manual ablation group. Long-term success rates in patients treated for paroxysmal AF were comparable between the two treatment groups. Patients treated for persistent AF with robotic navigation had significantly improved outcomes compared to those treated with manual technique. At 12 and 24 months, the Kaplan-Meier estimate of freedom from recurrence of arrhythmia was 95.1 % ± 2.0 and 72.9 % ± 4.7 respectively for robotic navigation, compared to 63.9 % ± 8.0 and 40.7 % ± 8.3 for manual ablation ($p<0.0001$).

Conclusions: These long-term results show that robotic navigation with the Hansen Sensei X System can be achieved successfully, with an acceptable rate of peri-procedural and short-term complications, and favorable long-term success rates, particularly for treatment of persistent AF.

IX-4

Minimizing asymptomatic cerebral lesions in pulmonary vein isolation by modified heparin management and catheter introduction

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KH der Elisabethinen Linz, Kardiologie

Background: In a previous study our group reported an increased risk of asymptomatic cerebral lesions (12.2 %) after left atrial radiofrequency ablation. The aim of this study was to quantify the amount of silent cerebral lesions by changing two key-points during the ablation procedure:

1. immediate administration of a full 100IE per kilogram bolus of unfractionated heparin after the groin venous puncture (in comparison to our prior study, where half the bolus was given directly before and another half after the transseptal puncture);
2. all catheter insertions or exchanges through the transseptal sheath we performed having blood backflow or active suction over the sheath, thereby avoiding any air intake;

Methods: A total of 69 consecutive patients ($n = 55$; 79.7 % male) undergoing catheter ablation for paroxysmal ($n = 55$; 79.7 %) or persistent ($n = 14$; 20.3 %) atrial fibrillation were included in this study. Pulmonary vein antrum isolation was performed in all patients, additionally roofline and CFAE ablation were performed in persistent cases on operator's decision. We used 3.5 mm open-irrigated tip catheters as well as 3D electro-anatomic mapping systems in all patients. All patients underwent preprocedural and postprocedural cerebral MRI (within 24 h prior and 24 h after the procedure). Oral anticoagulation was continued throughout the procedure (91.3 % on therapeutic warfarin and 8.7 % on novel oral anticoagulants stopped after the morning dose the day prior to ablation).

Results: Only three postprocedural cerebral microembolism (3–4 mm; 2 patients on warfarin, one patient on a novel oral anticoagulant) were detected after left atrial radiofrequency ablation in this group of patients (4.3 %). Acute entry and exit block could be documented in 100 % of the pulmonary veins.

Conclusions: Early administration of full dose heparin and modified transseptal sheath management is able to significantly reduce silent cerebral lesions in left atrial radiofrequency ablation using open-irrigated tip catheters.

IX-5

Optimizing radiofrequency ablation of paroxysmal and persistent atrial fibrillation by direct catheter force measurement—a case-matched comparison in 198 patients

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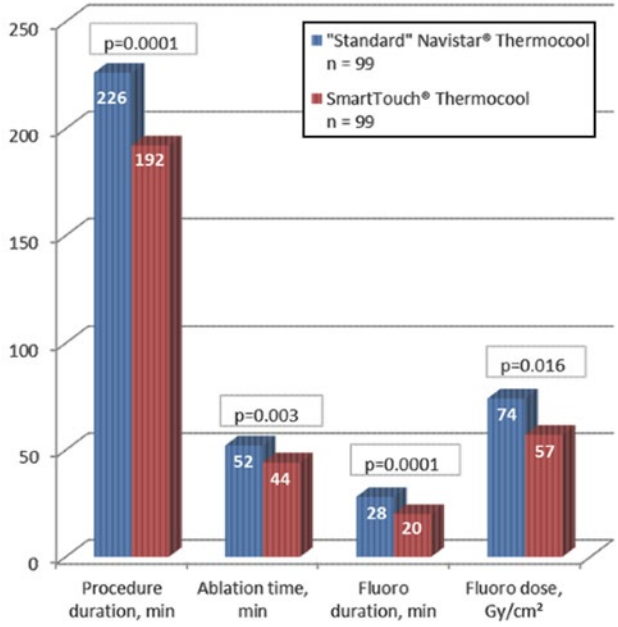
Background: Sufficient electrode-tissue contact is crucial for adequate lesion formation in radiofrequency catheter ablation (RFCA).

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

Methods: 99 consecutive patients (pts; 70 % male) with paroxysmal (63.6 %) or persistent AF underwent left atrial RFCA using a 3.5 mm open-irrigated tip (OIT) catheter with contact force measurement capabilities (group 1). For comparison a case-matched cohort with standard OIT catheters was used (99pts; group 2). Case-matching included gender, type of AF, number or RFCA procedures, and type of procedure.

Results: Procedural data showed a significant decline in radiofrequency ablation time from 52 ± 20 to 44 ± 16 min ($p = 0.003$) 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 from 28.5 ± 11.0 to 19.9 ± 9.3 min ($p = 0.0001$) as well as fluoroscopy dose from 74.1 ± 58.0 to 56.7 ± 38.9 Gy/cm² ($p = 0.016$). Periprocedural complications were similar in both groups.

Conclusions: The use of novel contact force sensing technology is able to significantly reduce ablation, procedure, and fluoroscopy times as well as dose in RFCA of AF in a mixed case-matched group of paroxysmal and persistent AF. Energy delivery is substantially reduced by avoiding radiofrequency ablation in positions with insufficient surface contact. Additionally, 12-months-outcome data showed increased efficacy. Such time saving and equally safe technology may have a relevant impact on laboratory management and increased cost effectiveness.



The use of CFM technology showed a significant reduction in ablation time, overall procedure duration, fluoroscopy time and dose

IX-6

Vernakalant: pharmacological cardioversion of atrial fibrillation

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Krankenhaus der Elisabethinen Linz, Kardiologie

Background: Intravenous Vernakalant has been approved in Austria in January 2011 as an atrial-selective antiarrhythmic drug for the acute conversion of recent-onset atrial fibrillation (£ 7 days). Due to its atrial-selective properties, Vernakalant prolongs the effective refractory period of the atria with minimal effects on the ventricles, being associated with a low proarrhythmic risk. Vernakalant is dosed by patient body weight to be infused over a 10 min period in a monitored clinical setting with an optional second dose after 15 min.

Methods: A total of 61 patients (pts.) (31 female/30 male) at the age of 66.5 ± 11.3 years were treated with Vernakalant at our institution. All of them had symptomatic recent-onset atrial fibrillation with a mean duration of 20.6 ± 20.9 h (47.5 % of pts. £ 12 h).

Results: Conversion of atrial fibrillation to sinus rhythm occurred in 37 pts. (60.7 %), in 30 pts. (49.2 %) already after the first dose and in 7 pts. (11.5 %) after a second dose applied 15 min after initial infusion. Conversion to sinus rhythm occurred rapidly (the median time to conversion was 18.4 ± 10.7 min from start of first infusion). In the remaining 20 pts. (32.8 %), electrical cardioversion was performed later on. Adverse reactions were seen at the end of infusion in 26 pts. (42.6 %), included cough, sneezing, flush, dysgeusia, and dizziness. These events were clustered around the time of infusion and transient. Clinically relevant hyper- or hypotension were not observed, mean systolic blood-pressure of 128 ± 19 mmHg at the beginning of the infusion changed to a mean systolic blood-pressure of 134 ± 22 mmHg at the end of administration.

Conclusions: In the conversion of atrial fibrillation to sinus rhythm Vernakalant is highly effective without clinically significant side effects. Vernakalant is nowadays recommended in the updated ESC-guidelines 2012 for medical cardioversion and has became an important antiarrhythmic drug for the rapid conversion of recent-onset atrial fibrillation in our department.

IX-7

Strahlendosisreduktion bei elektrophysiologischen Untersuchungen durch Verwendung einer neuen Detektortechnologie mit kristallinem Silizium und Optimierung der Durchleuchtungsparameter

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AKH Linz, I. Medizinische Abteilung mit Kardiologie

Hintergrund: Die im Vergleich zu anderen radiologischen Untersuchungsfragestellungen langen Durchleuchtungszeiten bei elektrophysiologischen Untersuchungen erfordern rigorose Maßnahmen zur Dosisreduktion im Sinne der Strahlenhygiene für Patient und Untersucher. Neue Detektorsysteme mit kristallinem Silizium sollen durch sensiblere Detektion und höhere Ortsauflösung eine geringere Strahlendosis ermöglichen.

Methodik: Wir verglichen die Dosiswerte der Durchleuchtungsanlage (DLA) unserer elektrophysiologischen Untersuchungseinheit (EPU) mit zwei anderen DLAs des gleichen Herstellers in unserem Haus (Vergleichs-DLA 1: Koronarangiographie, Vergleichs-DLA 2: Becken-Bein-Angiographie). Das DLA-EPU Detektorsystem war bereits mit kristallinem Silizium ausgestattet, während bei den anderen DLAs noch herkömmliche Detektoren mit amorphem Silizium in Verwendung standen. Die Messungen der Strahlendosis wurden unter Verwendung der im jeweiligen Einsatzbereich typischen Standardprogramme (Röhrenstrom, -spannung und Vorfilterung) durchgeführt. Es wurden die Objektseintrittdosis (OD) an einem Dummy (flüssigkeitsgefüllter Plexiglascontainer mit den Maßen 25 × 25 × 20 cm), die Detektoreingangsdosis (DD), das Fläche-Dosis-Produkt (DFP), die Streustrahlung (SS) sowie die Auflösung der DLA (Linienpaare/mm, LP) erhoben. Bei einem Bild-Objekt-Abstand von 5 cm und einem Strahlenquellen-Bild-Abstand von 105 cm wurde bei jeder DLA auf den Dummy (25 × 25 cm) eingeblendet. OD und DD wurden mit einem Diados T11003 Diagnostikdosimeter, die Streustrahlung in 2 m Abstand im rechten Winkel zum Zentralstrahl mit einer Automess Szintillatorsonde 6150 AD-b (Energiebereich: 23 keV-7 MeV) gemessen. Das DFP wurde direkt an der DLA abgelesen. Es wurden in jeder Einstellung 5 unabhängige Einzelmessungen mit denselben Parametern vorgenommen, die Werte gemittelt und Standardabweichungen berechnet.

Resultate: Im Durchleuchtungsmodus lagen die gemessenen Werte bei der EPU-Anlage mit kristallinem Silizium-Detektorsystem deutlich unter jenen, die bei den anderen beiden Anlagen erhoben wurden. EPU-DLA (74.2 kV, 17.9 mA, 0.9 mm Kupfer): DD 15.2 ± 0.1 nGy/Impuls(p), OD 262.3 ± 0.9 nGy/p, DFP 0.110 ± 0.004 μGym²/10p, S. 6.8 ± 0.3 μSv/h, 1.0 LP; Vergleichs-DLA 1 (68.4 kV, 46.2 mA, 0.3 mm Kupfer): DD 113.3 ± 0.2 nGy/p, OD 2538.8 ± 4.8 nGy/p, DFP 1.168 ± 0.003 μGym²/10p, S. 47.3 ± 0.9 μSv/h, 1.4 LP; Vergleichs-DLA 2 (65.0 kV, 94.6 mA, 0.6 mm Kupfer): DD 69.1 ± 0.5 nGy/p, OD 1311 ± 6.1 nGy/p, DFP 0.682 ± 0.004 μGym²/10p, S. 36.6 ± 0.8 μSv/h, 1.6 LP. Für den Film-Modus ergaben sich ähnliche Proportionen der Strahlendosiswerte. EPU-DLA (76.1 kV, 42.0 mA, 0.3 mm Kupfer): DD 121.1 ± 0.3 nGy/p, OD 2431.4 ± 6.0 nGy/p, DFP 1.214 ± 0.004 μGym²/10p, S. 58.9 ± 0.6 μSv/h, 1.4 LP; Vergleichs-DLA 1 (81.0 kV, 37.9 mA, kein Kupferfilter): DD 411.2 ± 1.2 nGy/p, OD 1426.8 ± 5.5 nGy/p, DFP 8.000 ± 0.007 μGym²/10p, S. 142.1 ± 24.6 μSv/h, 1.6 LP; Vergleichs-DLA 2 (65.4 kV, 400.9 mA, 0.2 mm Kupfer): DD 3010.8 ± 86.5 nGy/p, OD 134520 ± 216.8 nGy/p, DFP 80.288 ± 0.561 μGym²/10p, SS > 400 μSv/h, 2.2 LP.

Diskussion: Sowohl Detektortyp als auch Durchleuchtungsparameter (Röhrenspannung, -strom, Vorfilterung) beeinflussen die Strahlendosis unabhängig voneinander. Mit neuer kristalliner Silizium-Detektortechnologie kann unter Optimierung der Parameter während Durchleuchtung eine 7 bis 12-fache, beim Filmen eine 7 bis 67-fache Reduktion des DFP bei Inkaufnahme einer minimal geringeren Auflösung erreicht werden.

IX-8

Senkung der Infektionsrate nach Schrittmacher- und ICD-Generatorwechseln durch komplette Taschenexzision und Nekrosektomie

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Hintergrund: Da die Anzahl an Schrittmacher- und Defibrillatorimplantationen weltweit stark steigt, ist in Zukunft auch mit einer Zunahme von schwerwiegenden Komplikationen, wie Systeminfektionen (SI) zu rechnen. Die in der Literatur angegebenen Infektionsraten reichen von 0.13–12.6 %, wobei Konsens besteht, dass das Infektionsrisiko nach Generatorwechseln gegenüber Primärimplantationen 4–6 fach erhöht ist. Für die erhöhte Rate an SI nach Revisionen wird vor allem eine chronische Keimbesiedelung des Taschengewebes angeschuldigt, wobei der Zweiteingriff zu einer Freisetzung der Erreger und damit zur SI führt. So ergaben Kulturen von vermeintlich nicht infiziertem Taschengewebe in 45 % der Fälle eine Staphylokokkenbesiedelung. Unter Bedachtnahme dieser Umstände wird an unserer Abteilung seit 2001 zur Senkung der Infektionsrate bei allen Generatorwechseln eine komplette Taschenexzision mit Entfernung sämtlicher fibrotischer und nekrotischer Gewebsanteile durchgeführt.

Ziel dieser Untersuchung war es, die Rate an SI nach Generatorwechsel mit dieser Methode zu evaluieren.

Methoden: Wir führten eine retrospektive Analyse der Rate an SI nach Generatortausch durch. Die Nachsorge wurde von einem Arzt spätestens 12 Monate nach dem Generatorwechsel und anschließend jährlich durchgeführt und beinhaltete die Anamnese, eine physikalische Untersuchung, die Abfrage der Schrittmacherfunktion sowie die Dokumentation eventueller Komplikationen bzw. von Infektionszeichen.

Ergebnisse: Zwischen 2001 und 2014 führten wir 617 Generatorwechsel (244 weibliche, 373 männliche Patienten, mittleres Alter: 74+/−13 Jahre) durch. Die mittlere Operationsdauer betrug 38 ± 9 min. Es wurden die Generatoren von 334 (54 %) Zweikammerschrittmacher-, 123 (20 %) Einkammerschrittmacher-, 94 (15 %)

ICD-, 47 (8 %) biventrikuläre Schrittmacher- und 19 (3 %) biventrikuläre ICD-Systeme gewechselt. Der mittlere follow-up betrug 5, 1+/−3,3 Jahre. Hierbei traten insgesamt drei (0,5 %) SI auf, die eine komplette Systemexplantation erforderlich machten.

Schlussfolgerung: Die im Vergleich zur einschlägigen Landmarkstudie (REPLACE Registry, SI-Rate 1.25 %) noch geringere SI-Rate von 0.5 % in unserer Serie rechtfertigt unserer Ansicht nach die aufwändigere chirurgische Technik der kompletten Taschenexzision. Diese kann helfen, die Notwendigkeit kompletter Systementfernungen wegen SI nach Generatorwechseln zu reduzieren.

Postersitzung X: Risikofaktoren/Stoffwechsel/Lipide I

X-1

Body mass index significantly modulates the power of C-reactive protein to predict cardiovascular event risk among angiographied coronary patients

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Introduction: Epidemiological studies in various populations show that obesity is associated with inflammation and with increased cardiovascular risk, and that the inflammatory marker C-reactive protein (CRP) strongly predicts the incidence of cardiovascular events. Whether CRP is equally predictive of cardiovascular event risk in obese patients and in non-obese subjects is not known and is addressed in the present study.

Material and methods: Cardiovascular events were recorded over a follow-up period of 10 years in a large high-risk population of 1731 consecutive patients undergoing coronary angiography for the evaluation of established or suspected stable coronary artery disease (CAD). Obesity was defined as BMI ≥ 30 kg/m^2.

Results: At baseline, CRP surprisingly was significantly higher in non-obese subjects (n = 452) than obese individuals (0.6 ± 1.5 vs. 0.5 ± 0.8 mg/dl; p < 0.001). Prospectively, 27.8 % of our patients suffered vascular events. CRP proved to be a strong and independent predictor of vascular events in non-obese subjects (HR 1.13 [1.06 – 1.20]; p < 0.001) but not in obese subjects (HR 1.08 [0.94 – 1.235]; p = 0.262). An interaction term BMI x CRP was significant (p < 0.001), indicating that the body mass index significantly modulated the power of CRP to predict vascular events.

Discussion: From the results of this large 10-year prospective cohort study we conclude that obesity significantly modulates the power of CRP to predict cardiovascular event risk among angiographied coronary patients.

X-2

Presence of type 2 diabetes mellitus significantly modulates the power of thyroid stimulating hormone to predict cardiovascular mortality

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Introduction: Elevated thyroid stimulating hormone (TSH) is associated with an adverse cardiovascular risk profile, especially in patients with type 2 diabetes (T2DM). We investigated the association between TSH and cardiovascular mortality in patients with T2DM as well as in non-diabetic subjects.

Material and Methods: We measured TSH in a high-risk cohort of 1741 consecutive patients undergoing coronary angiography for the evaluation of established or suspected coronary artery disease (CAD). The incidence of vascular events was recorded over 10 years; T2DM was defined according to current ADA criteria.

Results: From our patients, 34 % suffered vascular events. TSH proved to be a strong and independent predictor of cardiovascular mortality in subjects without T2DM (n = 1220; standardized adjusted hazard ratio (HR) 1.11 [1.00–1.24]; p = 0.036), but not in patients with T2DM (n = 521; HR 0.99 [0.87 – 1.14]; p = 0.934). An interaction term TSH x T2DM was significant (p = 0.039), indicating that TSH was a significantly stronger predictor of vascular events in subjects without T2DM than in patients without T2DM.

Discussion: From the data of this prospective cohort study we conclude that presence of T2DM significantly modulates the power of TSH to predict cardiovascular mortality.

X-3

Haemoglobin as a predictor of diabetes incidence in obese and non-obese patients undergoing coronary angiography

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Introduction: The association of blood haemoglobin concentration (Hb) with the incidence of future diabetes in obese patients is unclear. In the present study we therefore addressed this issue.

Material and methods: We prospectively recorded diabetes incidence over a mean follow-up period of 10 years in a large consecutive series of 1479 patients, who did not have previously known diabetes and who underwent coronary angiography for the evaluation of established or suspected coronary artery disease. Obesity was defined as body mass index (BMI) ≥ 30 kg/m^2.

Results: During follow-up, the incidence of diabetes was 13 %. Hb at baseline was significantly higher in obese patients (n = 331) than in non-obese subjects (148 ± 12 vs. 145 ± 13 g/l). Prospectively, Hb strongly and significantly predicted diabetes incidence with a standardized adjusted odds ratio (OR) of 1.50 [1.05 – 2.16]; p = 0.025 in obese patients but not in non-obese individuals (OR 0.95 [0.75 – 1.19]; p = 0.658). An interaction term BMI x Hb was statistically significant (p = 0.024), indicating that the body mass index significantly modulated the power of Hb to predict incident diabetes in this population.

Discussion: We conclude that Hb is a strong predictor of diabetes incidence in obese patients undergoing coronary angiography and that the body mass index significantly modulates the power of Hb to predict incident diabetes in this population.

X-4

Impact of age on the cardiovascular event risk conferred by HbA1c in patients with established coronary artery disease

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Introduction: In the present study we tested the hypothesis that age modulates the impact of HbA1c on cardiovascular event risk in patients with established coronary artery disease (CAD).

Material and methods: We prospectively recorded cardiovascular events over a mean follow-up period of 4.4 ± 1.2 years in a large consecutive series of 816 patients with angiographically proven CAD, including 376 subjects < 65 years and 440 subjects ≥ 65 years.

Results: During follow-up, the incidence of cardiovascular events was 9.3 % among subjects < 65 years and 24.8 % among subjects ≥ 65 years ($p < 0.001$). Among the younger patients, HbA1c strongly and significantly predicted cardiovascular events (HR 1.54 [1.06 – 2.23]; $p = 0.022$), but not among in the older patients (HR 1.22 [0.94 – 1.59]; $p = 0.125$). An interaction term age × HbA1c was statistically significant ($p = 0.007$), indicating that HbA1c was a significantly stronger predictor of cardiovascular events among younger than among older CAD patients.

Discussion: We conclude that HbA1c is a significantly stronger predictor of cardiovascular events in younger patients than in older patients with established CAD.

X-5

Lipoprotein (a), type 2 diabetes and vascular risk in angiographied coronary patients

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Introduction: Lipoprotein (a) [Lp(a)] especially in young individuals is an important cardiovascular risk factor. However, data on the long-term vascular risk conferred by Lp(a) in patients with type 2 diabetes (T2DM) are scarce.

Material and methods: Lp(a) was measured in a cohort of 909 consecutive patients undergoing coronary angiography for the evaluation of established or suspected stable coronary artery disease; vascular events were recorded over 10 years.

Results: Median Lp(a) at baseline was significantly lower in patients with T2DM ($n = 260$) than in subjects without T2DM (10 [interquartile range 1–34] vs. 16 [1–54] mg/dl; $p = 0.017$). Prospectively, 27.8 % of our patients suffered vascular events. Lp(a) proved to be a strong and independent predictor of vascular events in total population with a standardized adjusted hazard ratio (HR) of 1.15 [1.03 – 1.27]; $p = 0.006$) as well as in subjects without T2DM (HR 1.22 [1.10 – 1.36]; $p < 0.001$) but not in patients with T2DM (HR 0.990 [0.79 – 1.22]; $p = 0.888$). An interaction term T2DM × Lp(a) was significant ($p < 0.001$), indicating that Lp(a) was a significantly stronger predictor of vascular events in subjects without T2DM than in patients with T2DM.

Discussion: Lp(a) in patients with T2DM 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 T2DM.

X-6

Leptin serum levels are independently determined by obesity and by the presence of the metabolic syndrome

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Introduction: Obesity is a major risk factor for the metabolic syndrome (MetS), but some obese individuals do not have the MetS while others have the MetS but are non-obese. The single and joint associations of the adipokine leptin with obesity and the MetS have not yet been investigated and are addressed in the present study.

Material and methods: We measured leptin in four groups of patients: subjects who were non-obese and did not have the MetS ($n = 196$), non-obese patients with the MetS ($n = 149$), obese subjects who did not have the MetS ($n = 13$) and obese patients with the MetS ($n = 77$). Obesity was defined as a BMI ≥ 30 kg/m^2; presence of the MetS was defined according to the current harmonized consensus definition.

Results: Compared to serum leptin in non-obese subjects who did not have the MetS (6.71 ± 7.83 ng/ml), leptin was significantly higher in non-obese subjects with the MetS (9.29 ± 7.53 ng/ml; $p < 0.001$), as well as in obese subjects without (11.15 ± 9.75 ng/ml; $p = 0.016$) or obese patients with the MetS (15.92 ± 11.61 ng/ml; $p < 0.001$), in whom leptin trended ($p = 0.127$) to be higher than in obese patients without the MetS and was significantly ($p < 0.001$) higher than in non-obese patients with the MetS. Analysis of covariance showed that both obesity and the MetS significantly and independently predicted serum leptin, with obesity being the stronger predictor (F = 17.016; $p < 0.001$) than presence of the MetS (F = 7.60; $p = 0.006$).

Discussion: Obesity and presence of the MetS are independent determinants of serum leptin, but obesity explains a larger amount of serum leptin variation than the presence of the MetS.

X-7

Association of small dense LDL serum levels and circulating monocyte subsets in stable coronary artery disease

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Background: Atherosclerosis is considered to be an inflammatory disease in which monocytes and monocyte-derived macrophages play a key role. Circulating monocytes can be divided into 3 distinct subtypes, namely in classical monocytes (CM; CD14++CD16–), intermediate monocytes (IM; CD14++CD16+) and non-classical monocytes (NCM; CD14+CD16++). Low density lipoprotein particles are heterogeneous in size and density, with small, dense LDL (sdLDL) crucially implicated in atherogenesis. The aim of this study was to examine whether monocyte subsets are associated with sdLDL serum levels.

Methods: We included 90 patients with angiographically documented stable coronary artery disease and determined monocyte subtypes by flow cytometry. sdLDL was measured by an electrophoresis method on polyacrylamide gel.

Results: Patients with sdLDL levels in the highest tertile (sdLDL ≥ 4 mg/dL;T3) showed the highest levels of pro-inflammatory NCM (15.2 ± 7 vs. 11.4 ± 6 % and 10.9 ± 4 %, respectively; $p < 0.01$) when compared with patients in the middle (sdLDL = 2–3 mg/dL;T2) and lowest tertile (sdLDL = 0–1 mg/dL;T1). Furthermore, patients in the highest sdLDL tertile showed lower CM levels than patients in the middle and lowest tertile (79.2 ± 8 vs. 83.9 ± 7 % and 82.7 ± 5 %; $p < 0.01$ for T3 vs. T2 + T1). Levels of IM were not related to sdLDL levels (5.6 ± 4 vs. 4.6 ± 3 % vs. 6.4 ± 3 % for T3, T2 and T1, respectively). In contrast to monocyte subset distribution, levels of circulating pro- and anti-inflammatory markers were not associated with sdLDL levels.

Conclusion: The atherogenic lipoprotein fraction sdLDL is associated with an increase of NCM and a decrease of CM. This could be a new link between lipid metabolism dysregulation, innate immunity and atherosclerosis.

X-8

High-density lipoprotein subfractions are associated with circulating monocyte subsets in patients with stable coronary artery disease

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Background: High-density lipoprotein (HDL) particles are highly heterogeneous in structure and the role of HDL subfractions in atherogenesis are not well understood. Recently, it has been suggested that small HDL (HDL-s) may be dysfunctional in patients with metabolic syndrome or coronary artery disease (CAD). Monocytes and monocyte-derived macrophages are considered to play a key role in atherosclerotic diseases. Circulating monocytes can be divided into three subtypes according to their surface expression of CD14 and CD16 in pro- and anti-inflammatory subtypes. Our aim was to examine whether monocyte subsets are associated with HDL subfractions in patients with atherosclerosis.

Methods: We included 90 patients with angiographically stable CAD. Monocyte subsets were defined as classical monocytes (CD14++CD16–; CM), intermediate monocytes (CD14++CD16+; IM) and non-classical monocytes (CD14+CD16++; NCM). HDL subfractions were measured by an electrophoresis method on polyacrilamide gel.

Results: Patients with HDL-s levels in the highest tertile (HDL-s ≥ 13 mg/dL; $n=37$; T3) showed the highest levels of pro-inflammatory NCM (14.7 ± 7 vs. 10.7 ± 5 % and 10.8 ± 5 %; $p<0.01$) when compared with patients in the middle (HDL-s = 9–12 mg/dL; $n=27$; T2) and the lowest tertile (HDL-s = 0–8 mg/dL; $n=26$; T1). Additionally, patients in the highest HDL-s tertile showed lower CM levels than patients in the middle and lowest tertile (79.3 ± 7 vs. 83.7 ± 6 % and 83.9 ± 6 %; $p<0.01$ for T3 vs. T2 + T1). Levels of IM were not associated with HDL-s levels (5.9 ± 3 vs. 5.6 ± 3 % vs. 5.3 ± 3 % for T3, T2 and T1, respectively). In contrast, intermediate and large HDL particles as well as total HDL were not associated with monocyte subset distribution.

Conclusion: High HDL-s levels are associated with an increase of pro-inflammatory NCM and a decrease of the more anti-inflammatory CM. This suggests that HDL-s could have dysfunctional anti-inflammatory properties in patients with established CAD.

Postersitzung XI: Akutes Koronarsyndrom II

XI-1

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 von September 2011 bis September 2013 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: Insgesamt wurden in diesem Zeitraum an unserer Abteilung 275 Patienten akut koronarangiographiert. Einhundert Patienten (29 % weiblich) mit einem mittleren Alter von 59 (34–91) Jahren wurden eingeschlossen. Einhundertfünfundsiebzig Patienten (64 %) wurden ausgeschlossen: 112 Patienten wurde in ein anderes Spital transferiert, 9 waren im kardiogenen Schock, 12 Patienten lehnten die Befragung ab, 8 sind kurz nach der Angiographie verstorben und 34 Patienten konnten aus organisatorischen Gründen nicht befragt werden.

Bei den eingeschlossenen Patienten zeigte die Koronarangiographie eine Eingefäßerkrankung bei 52 %, eine Zwei- und Mehrgefäßerkrankung bei 43 %, und keine Koronarstenosen bei 5 %. Eine Hypertonie fand sich bei 72 %, Hypercholesterinämie bei 63 %, Nikotinkonsum bei 59 % und Diabetes mellitus bei 23 %. Fünfundreißig Patienten (35 %) waren Migranten: Zwanzig kamen aus dem ehemaligen Jugoslawien, 5 aus Zentraleuropa, 3 aus der Türkei, je einer aus Bangladesh und Pakistan und 3 aus Südamerika. Die Migranten waren tendenziell jünger als Patienten mit österreichischer Herkunft (56 vs 62 Jahre, $p=0{,}06$) und hatten häufiger eine Zwei- oder Mehrgefäßerkrankung (52 vs 38 %, $p=0{,}3$). Keine Unterschiede gab es bei Hypercholesterinämie (60 vs 69 %), bei Nikotinkonsum (55 vs 65 %), arterieller Hypertonie (69 vs 79 %), und in der Geschlechtsverteilung (Frauenanteil: Migranten 27 %, Österreicher 31 %). Migranten hatten häufiger Diabetes mellitus (37 versus 10 %, $p=0{,}024$) und weniger häufig Berufe mit hohem„skill level" als Nicht-Migranten (27 vs 0 %, $p=0{,}005$). Es gab keinen Unterschied im Bildungsniveau zwischen Migranten und Nichtmigranten (Universitätsabschluß 24 vs 23 %). Migranten hatten häufiger ein monatliches Einkommen < 1000 € als Nicht-Migranten(41 vs 14 %, $p=0{,}028$).

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

XI-2

Einfluss der Nierenfunktion auf Management und Outcome von Patienten mit akutem Koronarsyndrom

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Einleitung: Niereninsuffizienz ist häufig bei Patienten mit Koronarer Herzkrankheit und hat einen ungünstigen Einfluss auf die Prognose. Wir untersuchten, ob eine eingeschränkte Nierenfunktion bei der KH-Aufnahme Management und Outcome von Pat. mit Akutem Koronarsyndrom (ACS) beeinflusst.

Material und Methode: Es wurden von 2007 bis 2012 alle Patienten unseres Krankenhauses mit der Entlassungsdiagnose ACS erfasst. Es wurden demographische und anamnestische Daten sowie Angaben zu Behandlung, intrahospitalem Verlauf und Kom-

plikationen erhoben. Zusätzlich wurde die glomeruläre Filtrationsrate (eGFR) bei KH-Aufnahme erfasst.

Ergebnisse: Von 3828 Pat. mit ACS war bei 448 Pat. kein initialer eGFR Wert verfügbar. Von den verbleibenden 3380 Patienten mit ACS hatten 776 einen ST-Hebungsinfarkt (STEMI), 1432 einen Nicht-ST-Hebungsinfarkt (NSTEMI) und 1172 wurden als instabile Angina (IA) klassifiziert. 2180 Pat. hatte zum Zeitpunkt der Aufnahme eine eGFR von ≥ 61 ml/min (Gruppe A), 1005 Pat. eine eGFR von 31–60 ml/min (Gruppe B) und 175 Pat. eine eGFR ≤ 30 ml/min (Gruppe C).

Der Anteil der Männer betrug in Gruppe A, B und C 77,2, 52,9 und 35,4 % ($p < 0{,}001$), das Patientenalter betrug 64,2 ± 10,8, 78,0 ± 7,6 und 81,8 ± 8,3 Jahre ($p < 0{,}001$). Diabetes lag in Gruppe A, B und C bei 24,4, 28,8 und 32,6 % ($p = 0{,}01$) vor. Der Anteil von Pat. mit STEMI betrug in Gruppe A, B und C 24,6, 19,3 und 22,9 %, einen kardiogenen Schock entwickelten 2,0, 4,3 und 2,9 % der Patienten.

Eine Koronarangiographie wurde in Gruppe A, B und C bei 96,2, 87,5 und 60,6 % ($p < 0{,}001$), eine Koronarintervention bei 73,3, 62,2 und 46,9 % ($p = 0{,}001$) durchgeführt. Patienten mit eingeschränkter Nierenfunktion erhielten seltener ASS ($p = < 0{,}001$), Prasugrel oder Ticagrelor ($p < 0{,}001$) und Abciximab ($p < 0{,}001$) jedoch häufiger Enoxaparin ($p < 0{,}001$). Für die Behandlung mit Clopidogrel war dagegen kein signifikanter Unterschied festzustellen.

Intrahospitale Insulte traten in Gruppe A, B und C in 0,3, 0,7 und 0,6 % auf ($p =$ n. s.), auch in Bezug auf Reinfarkte (0,8, 0,8 und 2,3 %) bestanden keine signifikanten Unterschiede.

Erythrozytenkonzentrate mussten in Gruppe A, B und C in 1,3, 3,0 und 6,9 %, verabreicht werden ($p < 0{,}001$). Die intrahospitale Mortalität betrug in Gruppe A, B und C 1,0, 4,6 und 9,1 % ($p < 0{,}001$). Bei Berücksichtigung aller einflussrelevanten Faktoren in einer logistischen Regressionsanalyse erwies sich die eingeschränkte Nierenfunktion als stärkster Prädiktor für die intrahospitale Mortalität.

Diskussion: Pat. mit Niereninsuffizienz sind älter und häufiger Frauen. Sie wurden in unserem Patientenkollektiv seltener invasiv mittels Koronarintervention und seltener mit neuen Plättchenhemmern behandelt. Niereninsuffizienz ist der stärkste unabhängige Risikofaktor für die intrahospitale Mortalität bei Patienten mit ACS.

XI-3

Geschlechterspezifische Unterschiede im Einsatz moderner Therapiekonzepte bei Akutem Koronarsyndrom

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Einleitung: Seit vielen Jahren werden geschlechterspezifische Unterschiede im Management des akuten Koronarsyndroms (ACS) beschrieben. Wir untersuchten, ob der Einsatz moderner Therapiestrategien geschlechterspezifische Unterschiede aufweist.

Material und Methode: Anhand der LKF-Diagnosen wurden retrospektiv alle Patienten erfasst, die in den Jahren 2007–2012 an unserem Krankenhaus mit der Diagnose ACS aufgenommen waren. Aus den Krankenakten der Patienten wurden zahlreiche Daten erfasst. Diese reichten von demographischen und anamnestischen Daten, Angaben zu Diagnose und Behandlung bis zur Erfassung von Aufenthaltsdauer, Komplikationen und intrahospitaler Mortalität.

Ergebnisse: Insgesamt wurden 3828 Patienten, 2603 Männer (68 %) und 1225 Frauen (32 %) erfasst. Männer mit ACS waren jünger (65,9 vs. 74,0 Jahre, $p < 0{,}001$), waren öfter Raucher (27 vs. 11,9 %, $p < 0{,}001$) und hatten öfter eine Hyperlipidämie (64,1 vs. 54,5 %, $p < 0{,}001$). Männer hatten häufiger eine KHK Anamnese (24,3 vs 17,8 %, $p < 0{,}001$).

Bei den Männern wurden 25,1 % als STEMI, 41,6 % als NSTEMI und 33,1 % als Instabile Angina (IA), bei den Frauen 21,8 % als STEMI, 45,3 % als NSTEMI und 32,8 % als IA klassifiziert ($p < 0{,}05$). Schock und Reanimationsstatus lagen bei 3,3 und 4,9 % der Männer und bei 2,9 und 3,8 % der Frauen vor ($p =$ n. s.).

Bei 93,3 % der Männer und 82,4 % der Frauen wurde eine Koronarangiographie veranlasst ($p < 0{,}001$). Eine Koronarintervention wurde bei 72,3 % der Männer, jedoch nur bei 58,5 % der Frauen durchgeführt ($p < 0{,}001$).

Männer erhielten häufiger folgende medikamentöse Therapien: ASS (97,7 vs. 95,2 %, $p =$ n. s.), Clopidogrel (77,8 vs. 76,8 %, $p =$ n. s.); Prasugrel (27,2 vs. 13,5 %, $p < 0{,}001$), und Abciximab (58,7 vs. 44,6 %, $p < 0{,}001$) bei STEMI; Ticagrelor (16,8 vs. 8,6 %, $p < 0{,}001$) und Fondaparinux (26,3 vs. 10,3 %, $p < 0{,}001$) bei NSTEMI. Frauen erhielten häufiger niedermolekulares Heparin (61,5 vs. 56,7 %, $p < 0{,}05$).

Intrahospitale Komplikationen (Blutungen, Insult, Reinfarkt) betrafen 3,2 % der Männer und 3,6 % der Frauen ($p =$ n. s.). Die intrahospitale Mortalität betrug 3,3 %, bei Männern und 4,2 % bei Frauen ($p =$ n. s). Die Mortalität war höher bei Männern mit STEMI (12 vs. 7,5 %, $p < 0{,}05$), zeigte jedoch keine geschlechterspezifischen Unterschiede bei NSTEMI (3,1 vs. 3,2 %, $p =$ n. s.) und IA (0,2 vs. 0,5 %, $p =$ n. s.).

Diskussion: Moderne Guideline-konforme Therapiekonzepte werden seltener bei Frauen umgesetzt.

XI-4

Lassen sich Vorteile von Fondaparinux gegenüber Enoxaparin auch in der klinischen Routineanwendung nachweisen?

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Einleitung: Die OASIS V Studie zeigte einen klinischen Benefit von Fondaparinux gegenüber Enoxaparin bei Patienten mit NSTEMI. Dementsprechend wird Fondaparinux auch als Erstlinientherapie in den rezenten Leitlinien empfohlen. An unserer Abteilung wurde Fondaparinux frühzeitig als Therapiestandard bei NSTEMI eingeführt. Wir analysierten, ob sich ein Vorteil von Fondaparinux auch in der klinischen Routineanwendung in einem nicht selektionierten Patientenkollektiv nachweisen lässt.

Material und Methode: Es wurden anhand der LKF-Diagnosen retrospektiv alle Patienten erfasst, die in den Jahren 2007–2012 an unserem Krankenhaus mit der Diagnose ACS aufgenommen waren. Aus den Krankenakten der Patienten wurden zahlreiche Daten erfasst. Diese reichten von demographischen und anamnestischen Daten, Risikofaktoren, Angaben zu Diagnose und Behandlung bis zur Erfassung von Aufenthaltsdauer, Komplikationen und intrahospitaler Mortalität.

Ergebnisse: Von insgesamt 3828 konsekutive Patienten mit ACS wurden 1639 Pat. (42,8 %) als NSTEMI klassifiziert. 352 dieser Pat. (21,5 %) wurden mit Fondaparinux und 999 Pat. (61,0 %) mit Enoxaparin behandelt. 40 weitere Pat. (2,4 %), die konsekutiv beide Substanzen erhielten, und 248 Pat. (15,1 %), die keine der beiden Substanzen erhielten, wurden in der weiteren Analyse nicht berücksichtigt.

Patienten in der Fondaparinux-Gruppe waren häufiger Männer (74,1 vs. 64,1 %; $p = 0{,}004$), unterschieden sich aber weder im Patientenalter, noch in Hinblick auf das Vorliegen von Risikofaktoren und die Verwendung der Koronarangiographie von mit Enoxaparin behandelten Patienten. Pat. mit Fondaparinux erhielten (entsprechend einem neuen Therapiestandard) häufiger Ticagrelor ($p < 0{,}001$) und seltener Clopidogrel ($p < 0{,}001$).

Patienten unter Fondaparinux benötigten seltener Blutkonserven (0,2 vs. 1,5 %; $p = 0{,}036$) und weniger chirurgische Revisionen an der Katheter-Punktionsstelle (0,1 vs. 0,4 %; $p = 0{,}027$). Reinfarkte und Insulte im Krankenhaus waren in den beiden

Gruppen nicht unterschiedlich, jedoch war die KH-Mortalität unter Fondaparinux tendenziell niedriger (0,1 vs. 2,1 %; p = n. s.)

Konklusion: Die berichteten Vorteile von Fondaparinux in Hinblick auf eine geringere Rate an Blutungskomplikationen lassen sich auch in der klinischen Praxis an einem nicht selektionierten Patientenkollektiv nachvollziehen.

XI-5

Renal failure in myocardial infarction with cardiogenic shock—comparison of established and novel biomarkers—a biomarker substudy of the IABP-SHOCK II-Trial

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Background: Impairment of renal function is an important prognostic factor in acute coronary syndromes. In cardiogenic shock loss of renal function is one important sign of inadequate end-organ perfusion. The role of the novel biomarkers Neutrophil Gelatinase-Associated Lipocalin (NGAL), Kidney Injury Molecule 1 (KIM1) and Cystatin C for renal injury in comparison to established serum creatinine has never been investigated before.

Methods: In the randomized Intraaortic Balloon Pump in Cardiogenic Shock II (IABP-SHOCK II)-trial 600 patients with cardiogenic shock (CS) complicating acute myocardial infarction undergoing early revascularization were assigned to therapy with IABP or no IABP. In 190 patients blood samples were collected directly during primary primary coronary intervention, on day one, and day two after randomization. Blood was centrifuged immediately after sample drawing and serum frozen at –87 °C. NGAL, KIM1 and Cystatin C were measured with standard ELISA-Kits, Creatinine was assessed with routine laboratory measurement. All-cause mortality at 30 days was used for outcome assessment.

Results: Survivors had lower levels of creatinine (109 [IQR 90;141] vs. 138 [IQR 102;186] µmol/L; $p<0.001$) and NGAL (915 [IQR 568;1415] vs. 1091 [IQR 769;2229] ng/mL; $p=0.01$) than non-survivors at baseline, whereas there was no significant difference for KIM1 (134 [IQR 119;164] vs. 123 [IQR 108;178] pg/mL; $p=0.82$) and Cystatin C (3084 [IQR 2510;3596] vs. 3366 [IQR 2626;3778] ng/mL; $p=0.16$). In repeated measures analysis of variance over all 3 measurements creatinine ($p=0.04$) and NGAL ($p=0.04$) showed significant differences in contrast to KIM1 ($p=0.21$) and Cystatin C ($p=0.42$). Receiver operator characteristics (ROC) showed highest values for the area under the curve (AUC) in prediction of 30 day mortality for creatinine at all 3 time points (AUC baseline 0.65; day one 0.75; day two 0.78), NGAL showed the second best performance (AUC baseline 0.62; day one 0.60; day two 0.66). In c-statistics creatinine showed significant higher AUC over NGAL on day one and day two ($p=0.003$; $p=0.03$; respectively) and significant higher AUC at all time points in comparison to KIM1 and Cystatin C.

Conclusion: Renal failure has significant impact on outcome in cardiogenic shock. Of novel markers of renal injury NGAL showed the best performance in prediction of 30 day mortality, but was inferior to established serum creatinine measurements.

XI-6

Serum lactate in cardiogenic shock: clearance vs. single values—a biomarker substudy of the IABP-SHOCK II-trial

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Background: Serum lactate is widely used and an important biomarker for disease severity assessment in critically ill patients including those with cardiogenic shock (CS) complicating acute myocardial infarction. In sepsis and septic shock percentage of lactate reduction over time—the lactate clearance (LC)—has been extensively investigated. In CS only limited data are available.

Methods: In the randomized Intra-aortic 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. Lactate levels at baseline (L1) and after 8 h (L2) were collected prospectively. LC was calculated for every patient (Fig. 1). The areas under the curves (AUC) of receiver operating characteristics for L1 vs. L2 vs. LC were compared with c-statistics for prediction of 30 day mortality. Youden index was used to gain best cut-off values. A multivariable Cox regression analysis for prediction of 30-day mortality was applied to assess possible independent impact for time to death prediction.

Results: For 529 of 600 patients (88.2 %) L1 and L2 and consequently LC values were available. The 30-day mortality in this cohort was 39.5 % (209/529). The AUCs (L1: 0.67; L2: 0.76; LC: 0.62) showed no statistical difference between L1 and LC ($p=0.20$). In contrast, L2 AUC was significantly higher than for both other parameters ($p<0.001$, respectively). Youden index calculated 3.7 mmol/L as best cut-off value for L2. In multivariable stepwise Cox regression analysis L2 ≥3.7 mmol/L and LC <–3.25 %/h remained independent predictive of time to death ($p<0.001$ for both) with L2 showing highest Chi²-score (103) and hazard ratio (3.03; 95 % confidence interval 2.25 – 4.08).

Conclusion: L2 seems to be superior in prediction of death in comparison to L1 and LC. A cut-off value of 3.7 mmol/L for L2 after 8 h showed the best discrimination for assessing early prognosis in CS.

XI-7

Specific risk factors of procedure-related major bleeding events in elderly patients with acute coronary syndrome

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Background: Major bleeding events following primary percutaneous coronary interventions (PCI) are associated with an unfavourable short- and long-term outcome in patients with acute coronary syndroms (ACS). Therefore, the CRUSADE risk score has been developed for specific assessment of bleeding risk in patients with ACS. Interestingly, though chronological age represents a major risk factor for in-hospital bleeding events in ACS, it has not been integrated in the CRUSADE score. We therefore aimed to assess whether

the CRUSADE risk score represents a robust instrument for stratification of bleeding risk in elderly patients (>80 years) presenting with ACS and further aimed to identify age-specific predictors of major bleeding events.

Methods: We retrospectively included 383 patients >80 years with ACS into our final study cohort. Bleeding events were defined according to recommendations of the International Society on Thrombosis and Haemostasis (ISTH). Binary logistic regression models were applied to assess the effect of variables on the occurrence of peri-procedural bleeding during the hospital stay. The multivariate model was adjusted for variables used in CRUSADE and further potential risk factors of bleeding. In addition, receiver operating characteristic (ROC) analysis was applied to evaluate the discriminatory power.

Results: Out of 383 patients (median age: 84.1, 95 % confidence interval [CI]: 81.3–86.9 years, 54.9 % male) in the final study cohort 72 patients (18.8 %) suffered from major bleeding. Bleeding was a major predictor of in-hospital mortality ($n=55$) with a hazard ratio (HR) of 1.91 (95 % confidence intervall [CI]: 1.00–3.65, $p=0.05$). The CRUSADE score was associated with bleeding in univariate logistic regression with a HR per 1 standard deviation (SD) of 1.32 (1.02 – 1.71, $p=0.032$), but only showed only a borderline discriminatory power (ROC area under the curve 0.57, $p=0.05$). In multivariate analysis including the variables of the CRUSADE score, a history of bleeding with an adjusted HR of 3.21 (95 % CI:1.29 – 8.03, $p=0.01$) and normotest with an adjusted HR per 1-SD of 1.42 (1.06–1.92) were additional independent predictors of major bleeding.

Conclusion: We identified a history of bleeding and normotest as strong and independent predictors of procedure-related major bleeding events in elderly patients with ACS. Both variables may improve the only moderate predictive value of the CRUSADE risk in elderly patients with ACS. These results point towards a specific risk profile for bleeding events in elderly patients with ACS.

Postersitzung XII: Basic Science II

XII-1

Hypoxia triggers the release of CD31+/ Annexin+ endothelial microparticles

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Introduction: We have previously shown that endothelial microparticles (EMPs) are released in great numbers into the circulation after ST-elevation myocardial infarction (STEMI). EMPs are small membrane vesicles and originate from activated, damaged or apoptotic endothelial cells. Although the exact mechanism of EMP function still is largely unknown, it has been shown that they modulate inflammatory processes, coagulation and vascular function. In this study we hypothesized that transient hypoxia may act as a trigger for the release of EMPs.

Materials and Methods: Fourteen healthy volunteers were subjected to transient normobaric hypoxia in an air-conditioned hypoxia chamber simulating an oxygen concentration of a height of up to 5500 meters. Serial venous blood samples were drawn over a period of eight hours. The collected blood samples were evaluated for levels of CD31+/Annexin+ and CD31+/Annexin- EMPs using flow cytometry. 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 a value equivalent to a height of 5500 meters to achieve hypoxic conditions with a peripheral O2 saturation of approximately 78 %. Baseline concentrations for CD31+/Annexin+ EMPs were 0.033 % (±0.011 SEM). During the first hours of the experiment simulating a height equivalent of 2000 and 4000 meters these levels increased to 0.036 % (±0.008 SEM) at 2000 meters and to 0.054 % (±0.018 SEM) at 400 meters. After eight hours and a height equivalent of 5500 meters a significant increase was evident, CD31+/Annexin+ EMP levels were 0.119 % (±0.043 SEM, p = 0.0188, n = 15). No significant differences were found for CD31+/Annexin- EMPs.

Conclusions: These experimental results could provide explanation for the elevated level of EMPs in STEMI patients, showing that temporary hypoxic conditions can trigger the release of the CD31+/Annexin+ EMPs also in healthy volunteers. In our previous studies we have shown that apoptotic bodies can confer pro-survival signals to cardiomyocytes during myocardial ischaemia. Based on the experimental results of this current study we believe that the release of CD31+/Annexin+ EMPs during hypoxia might act as an endogenous survival signal. However, future studies are warranted to further explore this cellular signaling mechanism.

XII-2

Increased cardiomyocyte diastolic calcium release in a model of heart failure with preserved ejection fraction

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Background: Heart failure with preserved ejection fraction (HFPEF) is increasingly common but the established heart failure (HF) drugs are not effective. The underlying cellular mechanisms are incompletely understood. Therefore we investigated cardiomyocyte function and intracellular Ca^{2+} homeostasis in a model of HFPEF.

Methods: Young male Wistar rats were subjected to subtotal nephrectomy (NXT) or sham operation (SOP). Serial blood/urine samples, echocardiography and pressure-volume loops at 8 and 24 weeks were performed. After sacrifice, left ventricular (LV) hypertrophy and NCX function (Caffeine induced Ca^{2+} transient, TAU) and protein expression (Western blot) were determined. Cardiomyocyte function (Ca^{2+} transients, sarcoplasmic reticulum (SR) diastolic Ca^{2+} leak (Ca^{2+} sparks) and SR Ca^{2+} content; Fluo4-AM) were quantified in isolated LV cardiomyocytes without and with the NCX inhibitor SEA0400 (300nM).

Results: NXT rats showed stable compensated renal impairment and significantly hypertrophied LV at 8 weeks with a further increase after 24 weeks. LV systolic function (EF, dP/dt) was preserved. End diastolic pressure (EDP) volume relationship was markedly shifted left- and upwards and lung weight was significantly increased, indicating HFPEF with pulmonary congestion. LV cardiomyocytes from NXT showed no significant differences in amplitudes of Ca2+ transients. However, time for early (50 %) decay of the Ca^{2+} transients at 8 weeks was significantly prolonged with a further increase after 24 weeks (RT50 17.2 ± 2.9 and 30.8 ± 2.7 vs. 27.6 ± 1.8 and 41.8 ± 2.6 ms; $n \geq 20$; $p<0.05$). Prolonged cardiomyocyte Ca decay was significantly correlated with diastolic dysfunction in vivo.

TAU was significantly prolonged at 8 and 24 weeks indicating reduced NCX forward mode activity, while NCX protein expression was upregulated. At 8 weeks, Ca^{2+} spark frequency tended to be increased ($p=0.07$) while SR Ca^{2+} content was unchanged. SEA0400 accelerated Ca^{2+} transient decay but did not affect Ca^{2+} spark frequency. At 24 weeks, Ca^{2+} spark frequency was increased (4.3 ± 0.7 vs. 11.5 ± 1.8 sparks/s/µm3; $n \geq 20$; $p<0.05$) and SR Ca^{2+} content was decreased ($p<0.05$). SEA0400 significantly accelerated Ca^{2+} transient decay and reduced Ca^{2+} spark frequency in NXT.

Discussion: In this model of HFPEF, cytosolic Ca^{2+} decay of the LV cardiomyocytes was slower. Diastolic Ca^{2+} leak increased significantly during diseases progression. Whereas NCX forward mode activity was already reduced early despite increased NCX protein expression. Acute treatment with NCX inhibitor SEA0400 normalized cytosolic Ca^{2+} transients in young NXT rats, suggesting a role of reverse mode NCX activity and decreased Ca^{2+} leak at later time points.

XII-3

Gene expression based secretome analysis of irradiated human peripheral blood mononuclear cells

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Background: Conditioned media obtained from cultured cells has been shown to exert in- vitro and in-vivo cytoprotectice effects. Depending on cell type and preconditioning strategies different soluble factors are secreted and can be detected in the cell supernatant. Our group has recently shown that paracrine factors secreted from apoptotic peripheral blood mononuclear cells (APOSEC) exert pro-angiogenic, anti-aggregative, vasodilative and immunomodulatory effects.

In previous studies, we used an irradiation dose of 60 Gy to induce apoptosis in human peripheral blood mononuclear cells (PBMC) as apoptotic PBMCs evidenced enhanced paracrine effects in comparison to non-irradiated PBMCs.

The aim of the study was first to analyze radio responsive biological processes in human PBMCs and second to characterize the secretome of irradiated and non-irradiated cultured human PBMCs using global gene expression profiling

Methods: Human PBMCs from 4 donors were irradiated with 60 Gy of γ-rays. 2, 4 and 20 h after radiation the RNA was isolated and prepared for microarray messenger RNA (mRNA) and micro RNA (miRNA) expression evaluation. Bioinformatic algorithms were used to detect genes coding for secreted proteins and selected transcripts were validated with RT-PCR.

Results: IR induced changes in mRNA and miRNA expression profiles as a function of time. Gene ontology analysis revealed that initial radiation responsive genes associated with the biological process "p53 signaling pathway" were enriched after 2 h. The full magnitude of IR expression changes became visible 4 h after exposure whereas after 20 h a huge number of cellular processes were deregulated in irradiated PBMCs.

A time dependent increase of differentially expressed genes coding for secreted proteins was observed. We identified several secreted factors with known cytoprotective effects. Bioinformatics based classification of secreted proteins confirmed their involvement in the biological process "positive regulation of angiogenesis", "vascular wound healing", "regulation of coagulation" and "regulation of cell proliferation".

Conclusion: In this study we were able to show that (1) IR alters expression of both mRNAs and miRNAs; (2) many transcripts are targeted by the same miRNA and (3) miRNAs are involved in the modulation of radio response pathways, (4) a large number of genes coding for secretory proteins are detectable in irradiated PBMC, (5) bioinformatic analysis of these secreted proteins reveals that they have the potential to modulate biological processes of angiogenesis, wound repair, vasodilatation, platelet aggregation, hematopoiesis and tissue repair. We conclude that human PBMC can be seen as a source of soluble factors with the potency to treat a variety of human diseases.

XII-4

In Vivo Cardiac Role of Migfilin during Experimental Pressure Overload

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Background: Increased myocardial wall strain triggers the cardiac hypertrophic response by increasing cardiomyocyte size, reprogramming gene expression, and enhancing contractile protein synthesis. The LIM protein migfilin is a cytoskeleton-associated protein that was found to translocate in vitro into the nucleus in a Ca^{2+}-dependent manner, where it co-activates the pivotal cardiac transcription factor Csx/Nk×2.5. However, the in vivo role of migfilin in cardiac function and stress response is unclear.

Methods and results: To define the role of migfilin in cardiac hypertrophy, we induced hypertension by transaortic constriction (TAC) and compared cardiac morphology and function of migfilin knock-out (KO) to wild-type (WT) hearts. Heart size and myocardial contractility were comparable in untreated migfilin KO and WT hearts, but migfilin-null hearts presented a reduced extent of hypertrophic remodeling in response to chronic hypertensile stress. Despite this reduced adaptation, migfilin KO mice maintained their cardiac function for a longer time period compared to WT mice, which experienced fibrosis and heart failure. Migfilin translocated into the nucleus of TAC-treated cardiomyocytes, and levels of ANP and BNP transcripts as readout of Csx/Nk×2.5 activity were reduced in migfilin KO hearts.

Conclusions: Our findings indicate an important role for migfilin in the regulation of cardiac compensatory hypertrophy upon experimental TAC.

XII-5

Influencing acute inflammatory response leads to decreased calcification of subcutaneously implanted decellularized porcine aortas in mice

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Introduction: Chronic inflammatory processes lead to progressive tissue deterioration of biological heart valve prostheses thereby limiting graft survival. Shock waves were shown to modulate inflammation via Toll-like receptor 3. We hypothesized that shock wave therapy directly after graft implantation leads to enhanced graft survival via the modulation of acute inflammatory response.

Material and methods: Pieces of ascending aorta were harvested from pigs and decellularized using sodium-deoxycholate and sodium-dodecyl-sulfate. 0.5×0.5 cm pieces were implanted subcutaneously into 10–12 week-old C57BL/6 mice ($n=6$ per group). Treatment group (SWT) received shock wave treatment (250 impulses at 0.1 mJ/mm^2, 5 Hz) for modulation of inflammatory response directly after implantation, control animals received sham treatment (CTR). Grafts were harvested 72 h and 4 weeks after implantation and analyzed for inflammatory cytokines, macrophage infiltration, tartrate-resistant acid phosphatase (TRAP)

positive cells and calcification. In addition, transmission electron microscopy was performed. In a next step, decellularized porcine aortic valve conduits were reseeded with HUVECs with and without SWT, fibroblasts as well as macrophages and put in a pulsatile flow perfusion system. Cell coverage was determined after 12 h.

Results: RT-PCR showed increased mRNA levels of proinflammatory TGF-ß (CTR 0.01103 ± 0.002020 vs. SWT 0.8615 ± 0.2566; $p = 0.0078$) and TNF-a (CTR 0.5150 ± 0.02778 vs. SWT 1.370 ± 0.4197; $p = 0.05$) in the treatment group, whereas anti-inflammatory IL-10 was decreased (CTR 0.0002669 ± 3.248e-005 vs. SWT, $p < 0.0001$). Enhanced repopulation with recipient cells could be observed after SWT (CTR 15.65 ± 1.697 vs. SWT 28.28 ± 4.933, $p = 0.02$). F4/80 immunofluorescence staining revealed higher numbers of macrophage infiltration in treated animals (CTR 42.53 ± 4.162 vs. SWT 67.72 ± 2.768; $p < 0.001$). TRAP staining showed enhanced recruitment of osteoclastic cells after treatment (CTR 67.60 ± 14.14 vs. SWT 154.6 ± 29.87; $p = 0.03$) located in close proximity to calcified tissue. Consequently, SWT resulted in decreased areas of calcification in treated animals (CTR 1098.8 ± 142.5 vs. SWT 236.4 ± 65.4; $p < 0.001$). The pulsatile flow perfusion experiment showed that valves repopulated with fibroblasts exhibited the highest amount of coverage valves repopulated with fibroblasts showed the highest amount of coverage (45.91 ± 5.52), followed by macrophages (6.64 ± 1.08, $p < 0.0001$ vs fibroblasts and HUVECs (1.70 ± 0.28, $p < 0.0001$ vs. fibroblasts).

Valves reseeded with HUVECs showed better cell coverage after SWT compared to untreated controls (CTR 1, 70 ± 0.28 vs. SWT 4.85 ± 0.87; $p = 0.0005$).

Discussion: Shock wave therapy reduces calcification of bioprosthetic grafts via the modulation of inflammatory response. Influencing acute inflammation may develop an important adjunct to biological heart valve replacement.

XII-6

Investigating the vasodilating potency of two COS Donators in an Isolated Mouse Heart Model

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Background: Drug induced vasodilatation is a promising therapeutic option for patients with cardiovascular disease. The aim of this study is to investigate the vasoactive potency of the carbonyl sulfide (COS) releasing substances MAH3HCL and SWS47HCL on coronary arteries in an isolated mouse heart model.

Methods: Hearts of adult male OF-1 mice were excised after heparinization and evaluated in a crystaloid perfused isolated Langendorff heart. Following 15' of baseline measurement, hearts were randomly perfused with the COS donator (MAH3HCL $n = 6$, SWS47HCL $n = 6$) or saline solution (control, $n = 7$ and $n = 7$) for 10'. Then recording of hemodynamics was continued for 50'. Coronary flow (CF) and heart rate (HR) were monitored under constant afterload. Data are presented as mean ± SEM compared to baseline. (recovery in %).

Results: Whereas HR remained stable, MAH3HCL significantly increased CF with the onset of treatment (control: 98 ± 1 % vs. treatment: 123 ± 6 %, $p < 0.01$). When infusion was stopped CF normalized for the rest of the experiment. SWS47HCL instead showed no increase in CF compared to the control group (control: 96 ± 10 % vs treatment: 93 ± 7 %, n. s.). HR remained stable as well.

Conclusion: While SWS47HCL did not improve the CF Recovery, MAH3HCL significantly enhanced CF during administration and did not interact with heart rate. Further experiments are necessary to evaluate the efficacy of COS donors in the setting of coronary malperfusion.

XII-7

Levels of Tenascin-C in blood plasma in geriatric mice after myocardial infarction

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Introduction: Aging is associated with a higher incidence, mortality, and complication rate of myocardial infarction (MI). Tenascin-C (TNC) is a glycoprotein produced in the infarction border zone. Previous studies discussed TNC as prognostic marker for outcome after MI.

Methods: In male geriatric (OM, age: 18 months) and young (YM, age: 11 weeks) OF1 mice MI was induced by permanent LAD ligation. In SHAM groups the procedure was performed without LAD occlusion. 32 days after MI, cardiac MRI was used for hemodynamic evaluation. TNC plasma levels were assessed by ELISA 3, 7, and 32 days after MI (IBL 27767).

Results: In a 2-way ANOVA MRI examination showed significant effects of age and of MI vs. SHAM on ejection fraction (age: $p < 0.001$; MI vs. SHAM: $p < 0.001$), stroke volume heart weight ratio (age: $p < 0.001$; MI vs. SHAM: $p < 0.001$), cardiac output heart weight ratio (age: $p < 0.05$; MI vs. SHAM: $p < 0.05$), end-systolic (age: $p < 0.01$; MI vs. SHAM: $p < 0.001$), and end-diastolic left ventricular volumes (age: $p < 0.05$; MI vs. SHAM: $p < 0.001$). Moreover, MI had a significant effect on stroke volume (age: n. s.; MI vs. SHAM: $p < 0.05$). No significant effects of age and of MI vs. SHAM were found on heart rate and cardiac output. Furthermore, no significant interactions between the two factors were found in any parameter.

TNC plasma concentration was significantly increased in mice with MI at all time points, and significantly decreased in geriatric mice 3 and 7 days after MI compared to young mice after MI (3 days: OM: 4.52 ± 0.94 µg/ml, YM: 11.11 ± 3.46 µg/ml; 7 days: OM: 4.22 ± 1.92 µg/ml, YM: 9.03 ± 4.09 µg/ml).

Conclusion: We have successfully implemented a geriatric mouse model of MI with common signs of heart failure. Confirmed by MRI, we found significant hemodynamic differences between MI and SHAM groups, and also between OM and YM. We could find first evidence for age dependent differences in TNC production. These alterations should be respected in clinical studies examining the prognostic role of TNC in MI and heart failure. Further experiments are planned to proof these first results.

XII-8

Low energy shock wave therapy induces angiogenesis and improves blood perfusion in acute hind-limb ischemia in mice

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Objectives: Low energy shock waves were shown to induce angiogenesis, improve left ventricular ejection fraction and decrease angina symptoms in patients suffering from chronic isch-

emic heart disease. Whether there is as well an effect in acute ischemia was not yet shown.

Methods: Hind-limb ischemia was induced in 10–12 weeks old male C57/Bl6 wild-type mice by excision of the left femoral artery. Animals were randomly divided in a treatment group (SWT, 300 shock waves at 0.1 mJ/mm^2, 5 Hz) and untreated controls (CTR), n = 6 per group. The treatment group received shock wave therapy immediately after surgery.

Results: Real-time PCR analysis revealed higher gene expression of angiogenic factors VEGF-A and PlGF, as well as their receptors Flt-1 and KDR. Consequently western blot analysis showed significant upregulation of VEGF-A protein. Receptor tyrosine kinase profiler revealed significant phosphorylation of KDR.

This resulted in significantly more vessels per high-power field in SWT compared to controls. Significant improvement of blood perfusion in treatment animals was confirmed by laser Doppler perfusion imaging.

Conclusions: Low energy shock wave treatment induces angiogenesis in acute ischemia and shows the same promising effects as known from chronic myocardial ischemia. It may therefore develop as an adjunct to the treatment armentarium of acute myocardial and limb ischemia.

XII-9

Shock waves induce postnatal vasculogenesis in infarcted myocardium by recruitment of bone marrow derived endothelial progenitors

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Introduction: Recently shock waves at low energy levels were described to induce angiogenesis and regeneration in ischemic tissue. Improvement of myocardial perfusion and relief of angina symptoms in human patients with severe coronary artery disease have been shown. We hypothesized that the recruitment of progenitor cells from bone marrow to infarcted myocardium may be involved as well.

Materials and methods: Sub-lethally irradiated C57Bl/6 wild-type mice received bone marrow transplantation (BmTx) from transgenic GFP mice (C57BL/6Tg(CAG-EGFP)1Osb/J) (n = 6 per group). 4 weeks after BmTx, myocardial infarction was induced by LAD ligation. Treatment group (SWT) received shock wave therapy (0.38 mJ/mm^2, 200 impulses, 3 Hz) 3 weeks after infarction, whereas control animals (CTR) underwent sham treatment. Hearts were harvested 3 weeks after therapy. GFP positive bone marrow derived cells in the heart were detected by immunofluorescence microscopy. Lectin counterstaining revealed endothelial progenitor cells (EPCs). Gene expression of pivotal factors SDF-1, CXCR4, VEGF receptors and others was performed. Functional outcome was measured with a pressure catheter inserted into the left ventricle. For further mechanistic findings an in-vitro migration assay using human umbilical vein endothelial cells (HUVECs) was performed.

Results: Higher numbers of bone marrow derived endothelial progenitor cells per high power field have been found in the treatment group (CTR 3.98 ± 0.6 vs. SWT 17.89 ± 1.6, $p < 0.0001$). The main chemoattractant for EPC recruitment SDF-1 mRNA, was increased (CTR 1.86 ± 0.68 vs. SWT 5.19 ± 1.18, $p = 0.02$). Migration assay revealed higher migration rates (CTR 171.9 ± 15.89 vs. SWT 234.5 ± 25.9, $p = 0.04$). Functional outcome as assessed by pressure catheter showed an increase in dPdtmax (CTR 1957 ± 343 vs. SWT 3007 ± 617.4, $p > 0.059$), a decrease in dPdtmin (CTR −1532 ± 251.3 vs. SWT −2603 ± 346.7, $p = 0.03$) and an increase in Tau (CTR 33.68 ± 5.99 vs SWT 124.7 ± 42.15, $p = 0.09$) indicating functional improvement after SWT.

Discussion: Low energy shock waves induce postnatal vasculogenesis in infarcted myocardium by the recruitment of bone marrow derived endothelial progenitor cells. Shock wave treatment may develop a regenerative adjunct or alternative treatment option to state of the art revascularization in myocardial infarction. Notably, it has already been applied in angina patients without causing any severe side effects.

Postersitzung XIII: Bildgebung II

XIII-1

Reproducibility of vascular strain analyses at different arterial sites in healthy subjects

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Background: Vascular strain analysis by duplex ultrasound (DUS) allows the detection of premature alterations of vascular elasticity. Whether and to which extent vascular strain differs between various sites of the vascular tree is not known. Further, data on the reproducibility of vascular strain analysis are scarce. The aim of this study was to compare vascular strain between various parts of the arterial tree and to assess its reproducibility.

Methods: The common carotid arteries (CCA), common femoral arteries (CFA), popliteal arteries and the abdominal aorta of healthy volunteers were investigated using DUS. To assess inter- and intraday-reproducibility cross-sectional DUS clips of the respective arteries were obtained on three consecutive days, three times each day. Vascular strain was determined offline and the inter-/intraday reproducibility as well as the components of variance of vascular strain were calculated.

Results: In total 93.5 % of the DUS clips acquired in ten healthy subjects (m:f = 7:3, mean age 28.3 ± 3.2 years) could be analysed. Vascular strain was highest in the abdominal aorta (7.2 ± 3.0 %) lower in the CCA (5.7 ± 2.1 %) and lowest in the CFA (2.1 ± 1.1 %) and popliteal artery (1.9 ± 1.1 %). Intraday reproducibility of vascular strain in the CCA and CFA was lower than interday reproducibility. In the popliteal artery and abdominal aorta similar strain values were observed within one day and between days (see Table 1). A variance component analysis showed that the variance of vascular strain mainly depended on the investigated vessel and subject, while individual clips of one vessel, the day of examination and the body side (right/left) only had low impact on the variance of vascular strain. The variance components were similarly distributed in the CCA, CFA, popliteal artery and abdominal aorta.

Conclusion: Vascular strain can reliably be determined at various arterial sites with an acceptable reproducibility. Importantly, vascular strain varies considerably between different arteries.

Table 1 Various arterial sites

	Coefficient of variation	
Vessel	Intraday	Interday
Common carotid artery	3.9	8.4
Common femoral artery	3.3	10.3
Popliteal artery	6.1	4.6
Abdominal aorta	6.2	5.9
Intra- and interday coefficients of variation are given as percentages		

XIII-2

Comparison of an Oscillometric Method with Cardiac Magnetic Resonance for the Analysis of Aortic Pulse Wave Velocity

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Objectives: Pulse wave velocity (PWV) is the proposed gold-standard for the assessment of aortic elastic properties. The aim of this study was to compare aortic PWV determined by an oscillometric device and cardiac magnetic resonance imaging (CMR).

Materials and methods: PWV was assessed in 41 healthy volunteers with the two different methods. The oscillometric method (PWV-OSC) is based on a transfer function from the brachial pressure waves determined by oscillometric blood pressure measurements with a common cuff (Mobil-O-Graph, I.E.M. Stolberg, Germany). CMR was used to determine aortic PWV-CMR with the use of the transit time method based on phase-contrast imaging on the level of the ascending and abdominal aorta on a clinical 1.5 T scanner (Siemens, Erlangen, Germany). Spearman correlation coefficients, coefficients of variation and Bland-Altman plots were used to study methods agreement.

Results: Median age of the study population was 35 years (IQR: 24–56 years, 11 females). Both methods showed a very strong correlation with age (PWV-OSC r: 0.886 and PWV-CMR r: 0.837; $p<0.001$) and systolic as well as diastolic blood pressure (r: 0.488–0.686, $p<0.001$). Median PWV-OSC was 6.00 m/s (IQR: 5.1–8.2 m/s) and median PWV-CMR was 5.60 (IQR: 4.66–7.33 m/s). A good agreement was found between PWV-OSC and PWV-CMR (r: 0.776, $p<0.001$) but the mean difference between both methods was 0.43 m/s ($p=0.001$). The coefficient of variation between both measurements was 20 %.

Conclusion: Both methods showed a strong association with established determinants of PWV. We found a good agreement between PWV-OSC and PWV-CMR, but the measurements differed significantly in absolute values.

XIII-3

Fetuin-A: relation to myocardial function and left ventricular remodeling after acute ST-segment elevation myocardial infarction

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Objectives: Fetuin-A, a glycoprotein synthesized by the liver, increases the solubility of calcium and phosphorus and plays a key role in anti-inflammatory processes. The relationship between circulating fetuin-A and cardiac remodeling has not been studied so far in STEMI patients. We therefore investigated the association between plasma fetuin-A concentrations and left ventricular function, infarct size and the occurrence of adverse remodeling at 4 months after mechanical reperfusion for STEMI.

Material and methods: All patients ($n=52$) underwent contrast-enhanced cardiac magnetic resonance imaging within the first week after STEMI and 4 months thereafter. Left ventricular dimensions and function were measured from cine true-FISP sequences. Infarct size was determined with the use of late gadolinium enhanced images. Fetuin-A levels were determined from blood samples drawn at a median of 2 days (IQR 1–3 days) after STEMI by a sandwich immunofluorescent assay. Adverse remodelling was defined as an increase in end-diastolic volume of ≥ 20 % after 4 months.

Results: Fetuin-A levels (mean: 700 ± 195 µg/ml) were significantly related with 4-months ejection fraction ($r=0.409$, $p=0.002$) and trended to correlate with baseline ejection fraction ($r=0.236$, $p=0.092$). Patients with adverse remodeling ($n=7$) showed significantly lower baseline fetuin-A levels (528 ± 88 vs 737 ± 190 µg/ml, $p<0.001$) compared to patients without remodeling ($n=45$). The area under the curve of fetuin-A (0.79, 95 % CI 0.67 to 0.92) with the optimal cut-off value of 670 µg/ml revealed 100 % sensitivity and 67 % specificity (PPV = 32 %, NPV = 100 %) in the prediction of adverse remodelling at 4 months follow-up. Fetuin-A levels were not associated with baseline or 4 months infarct size.

Conclusions: Circulating fetuin-A at day 2 after STEMI is a potential predictor of 4-months myocardial function and adverse remodeling. These findings highlight the possible role of fetuin-A as a robust biomarker predicting outcome after reperfused STEMI.

XIII-4

Predictive utility of high-sensitive troponin T for long-term left ventricular function and infarct scar after acute myocardial infarction

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Objectives: Data relating high-sensitive troponin T (hs-TnT) to long-term myocardial function and scar in patients after acute ST-segment elevation myocardial infarction (STEMI) are limited. This study aimed to investigate the association between peak levels of circulating hs-TnT and long-term myocardial function as well as infarct scar in individuals with first acute STEMI.

Materials and methods: STEMI patients ($n=64$) treated with primary percutaneous coronary intervention underwent contrast enhanced cardiac magnetic resonance imaging within the first week and 12 months after the index event. Hs-TnT levels were measured by a fourth generation immunoassay on admission and serially up to 5 days.

Results: Median left ventricular ejection fraction was 56 % at baseline and 55 % at 12 months. Median infarct size was 16 % at baseline and 9 % at follow-up. Peak concentration of hs-TnT (6455 ± 4008 ng/l) was significantly correlated to maximum creatine kinase level ($r=0.72$, $p<0.01$). Moreover, hs-TnT was significantly associated with left ventricular ejection fraction ($r=-0.30$, $p=0.01$ at baseline; $r=-0.44$, $p<0.01$ at follow-up) as well as infarct size ($r=0.54$, $p<0.01$ at baseline; $r=0.57$, $p<0.01$ at follow-up). In receiver-operator characteristics analysis, the area under the curve (AUC) of hs-TnT was high for the prediction of decreased 12 months left ventricular ejection fraction (< 55 %, $n=32$) and large 12 months infarct areas (> 9 %, $n=32$) (AUC = 0.77 and 0.93, respectively).

Conclusion: In patients with reperfused STEMI peak hs-TnT is an accurate estimator of long-term myocardial function as well as infarct size determined by cardiovascular magnetic resonance.

XIII-5

Real-time visualization of myocardial viability during ischaemic preconditioning

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Background: Regional myocardial ischemia results in progressive loss of amplitude of monophasic action potential, as evidenced by decreased endocardial unipolar voltage.

Methods: For the in vivo on-line visualization and quantification of the ischemic burden of the heart, endocardial unipolar voltage values (UPV) were recorded by NOGA endocardial mapping catheter during repetitive ischemia and reperfusion (I/R) using 3 cycles of 10 min percutaneous coronary occlusion and reperfusion of the mid left anterior descending coronary artery of domestic pigs ($n=7$) (area mapping). UPV of a single stable distal anterior left ventricular point within the ischemic area were recorded every 10 s, and compared to that of sham procedure animals ($n=3$) (single location mapping).

Results: The voltage values of the ischemic area immediately decreased during repetitive occlusion without normalizing during reperfusion (Fig. 1). Despite the restoration of normal coronary blood flow the ischemic burden persisted after final reperfusion. UPV of the localized left ventricular point decreased rapidly during the first occlusion, while the second and third occlusion led to a less rapid decline of the voltage values of the ischemic myocardium (Fig. 2). Interestingly the UPV increased slowly during coronary occlusion after 5 min of ischemia. Ten minutes reperfusion times post repetitive occlusions proved to be insufficient to reach the baseline pre-ischemic value, probably due to concomitant and accumulating reperfusion injury.

Conclusion: Intracardiac measurements of unipolar voltage signals during coronary occlusion and reperfusion offer on-line visualization and immediate assessment of ischemic burden, and might be helpful to assess the effect of cardioprotective approaches against I/R injury.

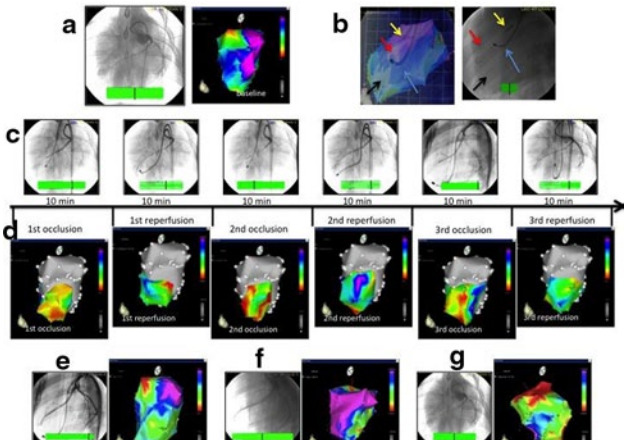

Fig. 1 UPV recorded by NOGA endocardial mapping during repetitive ischemia and reperfusion

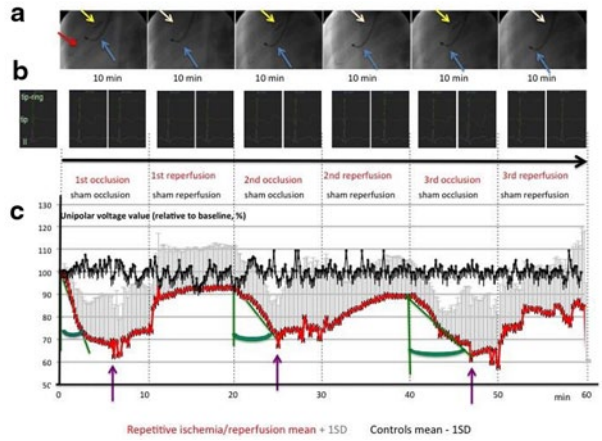

Fig. 2 The voltage values of the ischemic area

Postersitzung XIV: Chirurgie

XIV-1

Aktuelle Ergebnisse der Aortenwurzelrekonstruktion mit Aortenklappenreimplantation (David Operation)

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Einleitung: Für Patienten mit Aneurysma oder Dissektion der Sinus valsalvae und Aortenklappeninsuffizienz stellt die klappenerhaltende David Operation eine Alternative zur Bentalloperation mit Ersatz der Aortenklappe dar.

Patienten und Methoden: Es wurden von 2012 bis Feber 2014 22 Patienten (77 % Männer, Alter 50(27–74) Jahre) mittels Aortenwurzelrekonstruktion und Aortenklappenreimplantation (David Operation) operativ behandelt.

Ergebnisse: Die Indikation für die Operation waren ein Aortenaneurysma ($n=16$) oder Aortendissektion ($n=6$). In 50 % der Fälle wurde zusätzlich im hypothermen Kreislaufstillstand der Aortenbogen rekonstruiert. Die Aortenklappe war in 16 Fällen trikuspid, in 6 Fällen bikuspid. Die kardiopulmonale Bypasszeit betrug 203 (149–396) Minuten, die Aortenklemmzeit 154 (109–261) Minuten. Die postoperative Intensivstationsdauer war 1.5 (1–19) Tage. Die Hospitalmortalität war 0/22. Bei 2/22 (9 %) Patienten musste die Aortenklappe ersetzt werden, alle anderen Patienten hatten eine Restinsuffizienz Grad 1 ($n=3$) oder Grad 0–1 ($n=17$).

Diskussion: Die Rekonstruktion der Aortenwurzel mit Aortenklappenrekonstruktion kann bei geeigneten Patienten mit guter perioperativer Sicherheit und niedrigem Konversionsrisiko durchgeführt werden.

XIV-2

Der transaortale und transapikale Zugangsweg für Aortenklappen-Interventionen – die Grazer Erfahrungen

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Einleitung: Zwischen 2011 und 2013 konnten am Universitären Herzzentrum Graz 48 Patienten mit hochgradiger Aortenklappenstenose mittels Katheter-unterstützten Verfahren transapikal ($n=30$) bzw. transaortal ($n=18$) versorgt werden (mittleres Alter 83, 65 Jahre, weiblicher Anteil 43, 73 %, mediane NYHA-Klassifikation III). Als häufigste Komorbidität im Patientenkollektiv mit gesamtgesehen höhergradigen Frailty-Indices fand sich die renale Insuffizienz (10, 62 %), bei 12, 5 % eine CABG-Operation vorbestehend.

Resultate: Transaortal konnten 17 Medtronic CoreValves und eine Edwards Sapien-Prothese, sowie über den transapikalen Zugangsweg 27 Edwards Sapien und drei Symetis Acurate-Klappen implantiert werden.

Zu Blutungskomplikationen mit Notwendigkeit zur Reoperation kam es nach 3 Implantationen, zum offenen Verfahren musste in 2 Fällen (4,20 %) konvertiert werden. Bei einem Patienten erfolgte aufgrund einer postinterventionell höhergradigen Mitralklappeninsuffizienz eine Re-Operation inklusive Austausch der Aortenklappe auf eine biologische Prothese. Postoperativ

erfolgte bei großzügig gestellter Indikation in 14 Patienten (29,17 %) die Implantation eines permanenten Schrittmachersystems aufgrund eines höhergradigen AV-Blocks. Die 30-Tagesmortalität betrug 6,25 % ($n=3$), die Gesamtmortalität nach einem mittleren Beobachtungszeitraum von 14 Monaten 8,33 % ($n=4$), die Todesursache dabei nur in einem Fall bei intraoperativer Ventrikelruptur unmittelbar mit der Aortenklappenintervention assoziiert. Als weitere Todesursachen fanden sich Sepsis nach Sigmaperforation, respiratorische Insuffizienz nach nosokomialer Pneumonie und Multiorganversagen nach protrahiertem ICU-Verlauf.

Postoperativ konnte bei 22 Patienten (45,83 %) keine, bei 20 Patienten (41,66 %) eine gering-gradige sowie in 2 Patienten (4,20 %) eine gering- bis mittelgradige Aortenklappeninsuffizienz nachgewiesen werden.

Schlussfolgerung: Mittels Katheter-unterstützten Verfahren kann chirurgischen Hoch-Risiko-Patienten mit hochgradiger Aortenklappenstenose nicht nur zur Lebensverlängerung sondern vor allem zur Verbesserung der Lebensqualität eine Therapieoption geboten werden.

XIV-3

High-risk patients (EuroScore > 30 %) with impaired left ventricular ejection fraction

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Objective: Transcatheter aortic valve implantation (TAVI) was developed as an alternative treatment option for frail and conventional inoperable patients. Especially high-risk patients with severely compromised LVEF are deemed to be one of the most profiting patient population. We retrospectively studied the results of transapical TAVI (TA-TAVI) in comparison to surgical aortic valve replacement in very high-risk patients with severe symptomatic aortic stenosis reduced left ventricular function and multiple comorbidities...

Methods: Between Feb 2008 and March 2013, 70 concomitant patients with severe, symptomatic aortic stenosis who underwent either a successful TA-TAVI procedure ($n=35$, mean age 81+/–6, male 48.6 %) or open heart aortic valve replacement (AVR) ($n=35$, mean age 77+/–7, male 48.6 %) and reduced left ventricular function < 50 % were included in this study. Mean logistic Euroscore was 32.9 % +/– 15.9 for AVR and 39.5 % +/– 19.6 % for the TA-TAVI cohort. The median LVEF was 36 % in the TA_TAVI and 35 % in the AVR group.

Results: The 30-day-mortality was 14.3 % ($n=5$) in the AVR and 17.1 % ($n=6$) in the TA-TAVI group. The estimated overall postoperative survival rate using Kaplan-Meier-Analysis TA-TAVI vs. AVR was 84.8 vs. 76.6 % at 1 year 75.4 vs. 68.9 % at 2 years, and 62.8 vs. 68.9 % at 3 years.

Conclusion: In our concomitant patient cohort we observed similar outcomes regarding 30 days as well as the results of the mid-term follow up.

It seems that a highly professional team of anaesthetists, surgeons and a competent postoperative management can warrant good survival in these high-risk patients with either therapeutic strategy.

XIV-4

The Hospital Hietzing experience in transapical-transcatheter aortic valve implantation

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Introduction: Transcatheter aortic valve implantation (TAVI) has been proposed as a therapeutic option for high-risk or inoperable patients with severe symptomatic aortic valve stenosis. The aim of this singlecenter study was to assess short term outcomes of transapical aortic valve implantation (TA-TAVI) at our institution.

Method: From April 2010 through September 2013, a total of 101 patients were enrolled in our TA-TAVI program. Comprehensive clinical testing had been performed on baseline and on 30-day follow-up. As primary endpoints 30-day-mortality and -morbidity had been chosen.

Outcome: Our patients' median age at time of implantation was 80 years (61–92 years; n=101; 60.4 % female). All of them were considered as high risk patients. The Edwards SAPIEN ($n=89$) and the Symetis Acurate ($n=12$) prostheses were implanted by transapical access. 6 patients had to undergo a valve-in-valve implantation, whereas one had to be placed in mitral position. Median follow-up was 25 months (range, 12–44 months). Thirty-day device success was high (PVL ≤ I in 96 %; $n=97$). All-cause mortality at 30 days was 4.9 % ($n=5$). Life-threatening bleeding (7.9 %; $n=8$), and acute kidney failure (2.9 %; $n=3$) were further major adverse events after TAVI. Only one patient (0.9 %) showed postoperatively signs of a transient ischaemic attack that resolved completely during follow up. 6.9 % ($n=7$) needed a permanent pacemaker device after TA-TAVI.

Conclusion: Short term outcomes after TAVI were encouraging in this high-risk patient population group, were comparable to literature data and underlined the large potential of this hybrid surgical procedure. It also reflects the fact that TA-TAVI showed excellent neurological outcomes despite vigorous calcification of the vascular tree or the valve itself.

XIV-5

Große koronararterielle Fistel von der rechten Koronararterie in das systemvenöse Atrium bei einem Patienten mit Transposition der großen Arterien nach Vorhofumkehr-OP: What to do

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Hintergrund: Patienten mit Transposition der großen Arterien (TGA) nach Vorhofumkehr-OP haben eine im Verlauf zunehmende Einschränkung der Funktion des rechten Systemventrikels. Eine koronararterielle Fistel den rechten Ventrikel betreffend stellt somit ein Risiko für eine weitere auch akute Verschlechterung der rechtsventrikulären Funktion dar.

Fall: Bei einem 33-jährigen bekannten Patienten fällt in der Echokardiographie eine große rechte Koronararterie (RCA) auf. In einem daraufhin durchgeführten Cardiac CT zeigt sich eine koronararterielle Fistel, die von der prominenten RCA abgeht und in das systemvenöse Atrium mündet. Im Rahmen einer Spiroergometrie zeigen sich zunehmende VES und ST-Streckenveränderungen, zudem eine Entsättigung von 95 auf 83 % pulsoxymetrisch bei maximaler Belastung. Eine Herzkatheter-Untersuchung bestätigt die koronararterielle Fistel. Als Ursache der Entsättigung zeigt sich ein sog. Baffle-Leak mit Verbindung zwischen systemvenösem und pulmonalvenösem Atrium bei gleichzeitig vorliegender Stenose im systemvenösen Atrium. Zunächst wird das Baffle-Leak mit einem 10 mm Amplatzer Septal Occluder verschlossen. Im Anschluss wird ein gecoverter 39 mm CP Stent im systemvenösen Atrium über der Stelle der Einmündung der koronararteriellen Fistel platziert. Im

Anschluss wird eine Antikoagulation mit Marcoumar begonnen. In einer Spiroergometrie 6 Monate später findet sich keine Entsättigung mehr und nur ein ventrikuläres Couplet zu Beginn der Belastung. Ein Cardiac CT demonstriert eine deutlich kleinere RCA und nur mehr eine sehr kleine Fistelverbindung zum systemvenösen Atrium.

Konklusion: Eine koronararterielle Fistel von der RCA zum systemvenösen Atrium bei Patienten mit TGA nach Vorhofumkehr-OP wurde bisher nicht beschrieben. Ein Verschluss erscheint ratsam aufgrund möglicher Ischämien mit Beeinträchtigung der Funktion des rechten Systemventrikels und Triggerung ventrikulärer Arrhythmien. Das Überdecken der Fistel-Mündung im systemvenösen Atrium mittels gecovertem Stent erscheint eine geeignete Lösung. Bei einer Desaturierung unter Belastung muss an ein Baffle Leak gedacht werden.

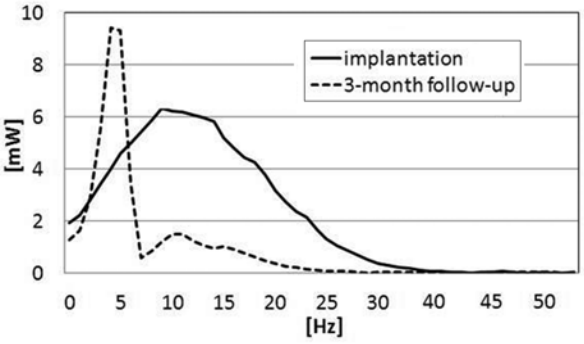

Fig. 1 Power spectral density of an individual responder to CRT

Postersitzung XV: Herzinsuffizienz II

XV-1

Correlation between clinical response to cardiac resynchronisation therapy and changes in frequency spectra recorded with an endocardial acceleration sensor—preliminary data

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Interne II—Kardiologie, Krankenhaus der Barmherzigen Schwestern Linz

Purpose: There is an ongoing search for early prognostic markers in patients with cardiac resynchronisation therapy (CRT). We initiated this pilot study to prove our hypothesis that dyssynchrony of the left ventricle leads to a wide range of frequencies in the endocardial acceleration signal (EAS) and that the frequency distribution becomes narrower during clinically successfull CRT.

Methods: Seven patients with chronic heart failure (LVEF ≤ 35 %, NYHA II—IV, QRS duration ≥ 130 ms in LBBB and ≥ 150 ms in non-LBBB, on stable optimal medical therapy) requiring CRT were enrolled. NYHA class, BNP, ECG, six-minute walk test and echocardiographic measurements were documented at implantation (IMP), pre-hospital discharge (PHD), at 3 months (3 M) and at 6 months (6 M) after implantation. The EAS was recorded for at least 3 consecutive cardiac cycles with different stimulation frequencies and different interventricular delays according to a standardized protocol at the same time points. The power spectral density and the main frequency components were calculated using a Fourier analysis.

Results: The frequency distribution became significantly narrower (IMP 23.1 ± 10.5 Hz; PHD 23.2 ± 11.2 Hz; 3 M 10.5 ± 4.9 Hz; 6 M 9.4 ± 3.6; $p < 0.001$) and the power of the main frequencies increased (area under the curve at IMP 19.0 ± 12.7 mW; PHD 25.1 ± 17.3 mW; 3 M 34.8 ± 19.3 mW; 6 M 27.5 ± 13.3 mW, respectively; $p < 0.001$) over time. Remarkably, there is a correlation between an improvement in NYHA class and a narrower frequency distribution combined with an increased power of the main frequencies.

Conclusions: It is possible to determine the synchronicity of the ventricular wall motion during a cardiac cycle by analyzing the frequency distribution with an EAS system. The observed correlation between a narrower frequency distribution combined with an increased power of the signal may be a marker of a beneficial clinical response to CRT. This method may enable continuous automatic monitoring of the reverse remodeling effect of CRT in the future.

XV-2

Detection of phrenic nerve stimulation with an endocardial acceleration sensor—a case series

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Interne II—Kardiologie, Krankenhaus der Barmherzigen Schwestern Linz

Introduction: Phrenic nerve stimulation (PNS) is a frequent finding in patients undergoing cardiac resynchronization therapy (CRT) that may require reprogramming of the stimulation vector and/or lead reposition. Although some technical advances have been made with a new quadripolar left ventricle (LV) lead incorporating different pacing configurations, the problem is still not solved.

Background: We report the first case series in which PNS could be visualized by an endocardial acceleration sensor (EAS). The sensor in the tip of the right atrial lead is designed to record infrasound in the range between 10 to 70 Hz by cardiac muscle vibrations related to the first heart sound (S1) which are mainly generated by the left ventricle. These signals are propagated well within the myocardium and reflect global contractility. Atrial contractions are in a lower frequency band with a maximum of 5 Hz. External sounds are filtered by the chest wall and do not alter the signal.

Case series: A 79-year-old man was complaining about a pulse-synchronous and rhythmic contraction of his epigastrium after implantation of a CRT-D device for ischemic cardiomyopathy with severely reduced left ventricular function. After 'electronic reposition' by changing the stimulation vector from LV tip to ring (T→R) to LV ring to coil (R→C) the patient was asymptomatic. Remarkably, we were able to record two different signals before and after changing the stimulation vector. In Fig. a there are vibrations in the EAS signal after the first heart sound S1 with the T→R pacing configuration resulting from the contraction of the diaphragm due to PNS. In contrast, these vibrations cannot be detected after changing the stimulation vector to R→C in Fig. b. Furthermore we were able to document these vibrations due to PNS in two other patients.

Discussion: PNS is frequently reported by patients at follow up and causes clinically relevant discomfort. Therefore changes of the pacing configuration and/or a reduction of the LV lead output is often required. An automatic detection of the contraction of the diaphragm might prove useful to develop an algorithm providing automatic switch of the pacing configuration to avoid PNS.

Conclusions: This case series demonstrates that detection of PNS with an endocardial acceleration sensor is possible. Further research is needed to prove that an automatic algorithm which changes the stimulation vector and/or reduces the LV lead output can avoid PNS in patients with CRT devices.

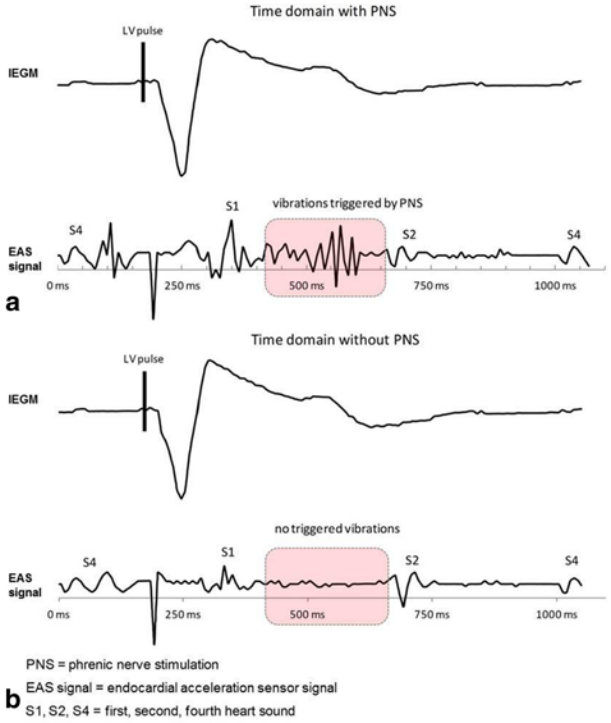

Fig. 1 Two different signals before and after changing the stimulation vector

XV-3

Evolution of electrocardiographic abnormalities in association with neuromuscular disorders and survival in left ventricular hypertrabeculation/noncompaction

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Background: Left ventricular hypertrabeculation/noncompaction (LVHT) is frequently associated with neuromuscular disorders (NMDs) and electrocardiographic (ECG) abnormalities. The prognostic relevance of newly developed ECG abnormalities and in LVHT and its dependency on NMD is largely unknown. Aim of the following retrospective cohort study in LVHT patients was thus to assess the development of new ECG-abnormalities and its dependency on NMD and survival

Methods: Included were patients in whom (a) LVHT was diagnosed between 1995–2011, (b) baseline ECG-recordings (bECG) and (c) follow-up ECG-recordings (fECG) were available. Survival status was assessed in June 2013.

Results: Included were 105 patients (mean age 55 years, 36 females, 67 with NMD). The interval between bECG and fECG was 3.6 years. ECG abnormalities increased in 46 %, were unchanged in 44 % and decreased in 11 %. Increase was associated with age (59 vs. 49 years, $p=0.0169$), exertional dyspnoea (79 vs. 53 %, $p=0.013$), heart failure (81 vs. 47 %, $p=0.0149$), a left ventricular enddiastolic diameter >57 mm (76 vs. 43 %, $p=0.004$) and a left ventricular fractional shortening <25 % (68 vs. 42 %, $p=0.0429$). New ECG-abnormalities were ST-T-wave abnormalities ($n=35$), left anterior hemiblock ($n=6$) and Q-waves ($n=6$). During 71 months, 40 patients died. Multivariate analysis identified age, male gender, "constant" (in bECG as well as fECG) atrial fibrillation, disappearance of atrial fibrillation, development as well as disappearance of low voltage ECG, increase of QRS width, constant QRS width >120 ms and constant tall QRS complexes were predictors for mortality.

Conclusions: LVHT-patients develop frequently new ECG-abnormalities of prognostic relevance.

XV-4

Fibroblast growth factor 23 is associated with disease severity and prognosis in chronic heart failure

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Background: Elevated levels of fibroblast growth factor 23 (FGF23) are associated with incident heart failure in individuals with or without chronic kidney disease. We aimed to investigate the association between serum FGF23 concentrations and disease severity and long-term outcome in patients with stable heart failure.

Materials and methods: Serum levels of C-term FGF23 (Ct-FGF23) concentrations, inorganic phosphate (Pi), parathormone (PTH), and 25-hydroxyvitamin D (25(OH)D) were measured in 208 patients with non-ischemic heart failure (age 48 ± 15 years; 70 % male; NYHA Class I 27.8 %, NYHA Class II 43.4 %, NYHA Class III/IV 28.8 %; LV-EF 34 ± 15 %; eGFR 85 ± 23.7 ml/min/1.73m^2).

Results: Median Ct-FGF23 levels were 18.2 RU/ml (7.5–40.8 RU/ml). A dose-response relationship was found between median Ct-FGF23 levels and increasing NYHA class (I: 11.9 RU/ml, II: 15.8 RU/ml, III/IV: 38.8 RU/ml; $p<0.001$). Ct-FGF23 correlated with NT-proBNP ($r=0.307$, $p<0.001$), central venous pressure (CVP), mean pulmonary arterial pressure, pulmonary capillary wedge pressure and inversely correlated with cardiac output (CO) after adjustment for renal function (eGFR) and Pi. Correlations with CO and CVP remained robust in multivariate regression analysis. Ct-FGF23 was associated with PTH ($r=0.238$, $p=0.001$), 25(OH)D ($r=-0.154$, $p=0.041$) and eGFR ($r=-0.345$, $p=<0.001$). LnCt-FGF23 was related with the combined endpoint of death or heart transplantation (hazard ratio 1.452 [1.029 to 2.048]; $p=0.034$) independent of Pi, PTH, 25(OH)D, age and sex.

Conclusion: The phosphatonin FGF23 is strongly associated with disease severity and long-term outcome in patients with non-ischemic heart failure. Further studies are needed to evaluate the pathophysiologic role of FGF23 and its potential as a biomarker in heart failure.

XV-5

Iron deficiency before and after diuretic therapy in congestive heart failure—results of a pilot study

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Background and aims: Iron deficiency (ID) is frequently found in patients with heart failure (HF). ID in HF is assumed to be caused by chronic inflammation, endocrine and/or immunologic disturbances. Dilution due to fluid overload has been implied to have an effect on anemia in congestive heart failure but whether it also has an effect on ID is unknown. The aim of this pilot study was to assess the influence of diuretic therapy on iron parameters in patients hospitalized with congestive HF using the body weight as a simple measure of fluid correction.

Methods: Consecutive patients admitted because of HF with systemic and/or pulmonary congestion who were treated with diuretics were included. The following parameters were measured after admission and before discharge: body weight, serum iron, ferritin and transferrin levels. ID was defined as ferritin < 100 µg/l and functional ID was defined as ferritin 100–299 µg/l and transferrin saturation < 20 %.

Results: Ten patients (4 females, mean age73 ± 15 years) were included. The etiology of heart failure was coronary artery disease in 5, valvular heart diseases in 2 and diastolic dysfunction in 3 patients. At the time of admission, mean values of body weight were 100 ± 35 kg, serum iron 51 ± 20 µg/dl, transferrin saturation 14 ± 6 % and ferritin 139 ± 121 µg/l. At discharge, mean body weight had decreased to 93 ± 33 kg ($p = 0.0002$), serum iron increased to 61 ± 21 µg/dl ($p = 0.07$), transferrin saturation to 15 ± 5 % ($p = 0.424$) and ferritin to 163 ± 154 µg/l ($p = 0.0905$). In 2 patients ferritin levels decreased from 145 to 130 µg/l, and from 50 to 43 µg/l. Of these 2 patients, one had hemoptysis during the hospitalization, the other did not show any signs of bleeding. According to the definitions, 5 patients showed ID and 3 functional ID at admission as well as at discharge.

Conclusion: In this small series of patients with congestive HF, a tendency could be observed that iron parameters are related to the amount of fluid overload. Whether ID could be normalised through diuretic therapy in certain patients should be investigated in a larger study.

XV-6

Left ventricular hypertrabeculation/ noncompaction and pregnancy

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Background: Left ventricular hypertrabeculation/noncompaction (LVHT) is characterized by extensive trabeculations and a two-layered structure of the left ventricular myocardium. Aim of the study was to summarize outcomes of pregnancies in a LVHT cohort.

Methods: All females in whom LVHT was diagnosed in one echocardiographic laboratory when they were younger than 45 years were contacted in July 2013. It was asked if pregnancy or delivery occurred after the diagnosis of LVHT had been established.

Results: From 1995–2013 LVHT was diagnosed in 207 patients. In 22 of the 63 female patients LVHT had been diagnosed when they were younger than 45 years. In January 2014, 5 of the 21 surviving females reported uneventful pregnancies and deliveries after LVHT had been diagnosed. Delivery was vaginal in 3, in the remaining 2 caesarean section was carried out because of breech presentation. These 5 females never suffered from heart failure and their systolic function was normal. Clinical and echocardiographic findings did not differ between the females who did and did not become pregnant.

Conclusions: LVHT per se is no contraindication for pregnancy. If LVHT is diagnosed in females of childbearing age, cardiac risk associated with pregnancy can be estimated by scores considering previous cardiac events or arrhythmia, NYHA class of heart failure, presence of left heart obstruction and left ventricular ejection fraction. Since the data about pregnancy and LVHT are still rare, patients should be encouraged for cardiological follow-up and their data, including neurological findings, should be collected in registries.

XV-7

Sind Patienten mit Linksventrikulären Unterstützungssystemen in ihrer Leistungsfähigkeit im Langzeitverlauf eingeschränkt?

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Einleitung: In den ersten Monaten nach Implantation eines Linksventrikulären Unterstützungssystems (Left Ventricular Assist Devices, LVADs) kommt es zur Verbesserung der Leistungsfähigkeit, jedoch Langzeitdaten diesbezüglich liegen nicht vor.

Methode: Daten von 12 Pat. (Alter 57 ± 10 J, weibl. 17 %, Heart Ware-HVAD 58 %, Thoratec-Heartmate II 42 %) von zwei stationären Rehabilitationsaufenthalten, einer unmittelbar postoperativ und ein weiterer mind. 1 Jahr später zwischen 1/2010 und 9/2013 wurden retrospektiv erfasst.

Die medizinische Trainingstherapie bestand aus Fahrradergometer- (Intervallmethode), Krafttraining, Gymnastik- und Wandergruppen. Die Zunahme des Trainingsumfanges und der Belastung beim Fahrradergometertraining (FET) (bestehend aus 12 Modulen mit ansteigender Belastung z. B. Modul 1 = 1/5 W, 60/30 s bis zum Modul 12 = 5/150 W, 60/20 s), der Wechsel in eine leistungsstärkere Wander- bzw. Gymnastikgruppe und der Kraftzuwachs wurde registriert. Jeweils am Ende wurde eine Spiroergometrie durchgeführt und der Verlauf des NT-proBNP dokumentiert.

Ergebnisse: Der erste Rehabilitationsaufenthalt (Dauer: 34 ± 6 Tage) war 6.1 ± 2.5 Wochen nach LVAD-Implantation und der zweite (Dauer: 27 ± 8 Tage) 1,7 ± 0,4 Jahre nach Implantation. Nach Ende des 2. im Vergleich zum Ende des 1. konnte eine Verbesserung der Intensität des FET (Module #8 ± 2 vs. #6 ± 2, $p = 0{,}027$), der Muskelkraft (Beinpresse: 58 ± 13 vs. 37 ± 15 kg $p = 0{,}001$, Beinstrecker: 13,9 ± 6,8 vs.10,8 ± 6,4, $p = 0{,}125$) und auch des Wander- und Gymnastiktrainings verzeichnet werden. Die maximal erreichten Watt in der Spiroergometrie konnte gesteigert werden, jedoch kam es zu keiner Verbesserung des VO2 peaks (11,1 ± 2,0 vs. 12,5 ± 2,9 ml/min/kg, $p = 0{,}223$), sondern aufgrund der Körpergewichtszunahme (95,8 ± 10:9 vs. 84,9 ± 11,1 kg, $p < 0.001$) sogar zu einer geringen, statistisch nicht signifikanten Reduktion.

Es kam zur Abnahme des NT-proBNP (1322 ± 1386 vs. 2769 ± 1861 pg/ml).

Zusammenfassung: Im Langzeitverlauf konnten Verbesserungen im submaximalen Leistungsbereich beobachtet werden. Die mangelnde Zunahme der aeroben Kapazität könnte Hinweis für eine nicht optimale Adaptation des Devices in Kombination mit der Pumpleistung des eigenen Herzens an körperliche Belastungen sein.

Eine Weiterführung eines strukturierten Trainingsprogramms nach der postoperativen stationären Rehabilitation in einem ambulanten Setting ist unbedingt anzustreben, um die Möglichkeit der Verbesserung der aeroben Kapazität im Langzeitverlauf besser beurteilen zu können.

Postersitzung XVI: Interventionelle Kardiologie III

XVI-1

Effect of apoptosis inhibitor on expression level of apoptotic, proliferative and inflammatory genes in porcine coronary arteries after stenting or balloon dilation

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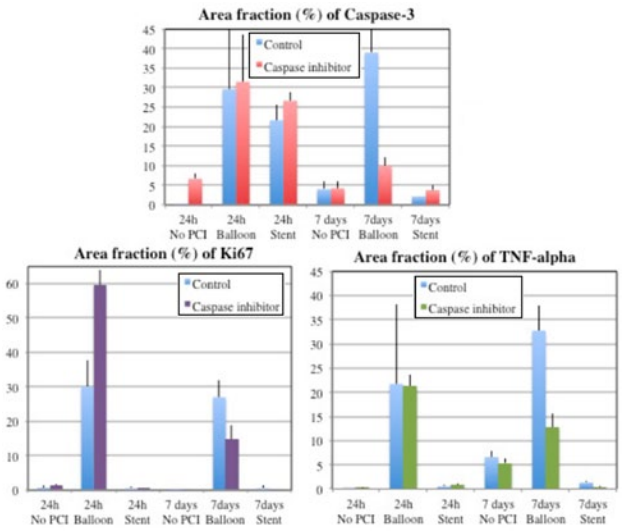
Background: Short exposure of atherosclerotic plaque to antiproliferative and antiinflammatory substances (such as paclitaxel released from drug-eluting balloon or stent) decreases the restenosis after coronary intervention. We have analysed expression of apoptotic (caspase-3), inflammatory (TNF-α) and proliferative (Ki67) genes in porcine coronary arterial segments treated with short intracoronary infusion of Ac-YVAD-cmk (IL-1-beta convertase and caspase-1 inhibitor) before stenting or balloon dilation.

Methods: Under general anaesthesia domestic pigs received selective intracoronary infusion of 5 mg Ac-YVAD-cmk (diluted in DMSO and Phosphate puffer for 3% DMSO solution) into the left anterior coronary artery (LAD) before coronary intervention. The mid part of the LAD underwent balloon dilation and the distal part received a bare metal stent. After 24 h and 7 days follow-up (FUP), the following arterial samples were investigated: proximal LAD (no intervention, drug infusion), mid LAD (balloon dilated, drug infusion), distal LAD (stented, drug infusion), proximal RCA (no intervention, no infusion), mid RCA (balloon dil. no infusion), distal RCA (stenting, no infusion). The expression patterns of Caspase-3, TNF-α and Ki67 (apoptosis, inflammatory and proliferation marker, respectively) were measured by immunofluorescence staining and quantified by planimetry using software ImageJ 1.47v.

Results: Intracoronary infusion of apoptosis inhibitor resulted in differential expression of apoptotic, proliferation and inflammation genes. The highest effect was seen after balloon dilation related arterial injury (Figures). Caspase-3 expression was in mid segment of LAD 4-fold higher against segment of RCA after 7 days FUP. Similarly, TNF gene was expressed 2-fold higher in mid segment of LAD (drug- affected) opposed to RCA (control). Expression of proliferation marker Ki67 was 2- fold higher in drug-treated vessels after 24 hours compared to control vessels. Conversely, expression of Ki67 was significantly downregulated after 7 days FUP.



Conclusion: Pharmacological inhibition of apoptosis by Ac-YVAD-cmk causes alteration in expressions of genes involved in apoptosis, proliferation and inflammation mechanism in arterial segments of porcine model. It may have a potential beneficiary approach to decrease neointimal proliferation associated to coronary interventions.

XVI-2

Gender-related differences in the rate of coronary angiography in elderly patients with acute coronary syndrome

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Background: The number of elderly patients with Acute Myocardial Infarction (AMI) is continuously rising due to demographic changes in the western world. Intervention rates are considerably lower in patients ≥80 years mainly due to concerns of procedure-related adverse events. However, recent evidence suggests that despite the increased risk profile of elderly patients this group is likely to benefit from an interventional approach. Based on a general gender gap in coronary interventions the underuse may be particularly high in elderly women. We therefore investigated (1) gender-related differences in the frequency of coronary angiographies, (2) gender-specific outcomes after coronary interventions, and (3) differences in the risk profile for procedure-related adverse events in elderly women and men with ACS.

Methods: We retrospectively identified 594 ACS patients <80 years (47.1% female, 66.3% ST-elevation myocardial infarction [STEMI]) and 453 ACS patients ≥80 years (54.3% female, 66.4% STEMI) referred to the General Hospital in Vienna, a tertiary care center, between January 1997 and December 2009. A comprehensive set of risk factors for procedure-related adverse events was assessed including the following variables: age, weight, height, BMI, frailty, a history of bleeding, prior stroke/TIA, cardiovascular disease, c-reactive protein, cardiogenic shock, creatinine, normotest, comorbidities, and home medication. Major bleeding was defined according to the definition of ISTH. Cox regression hazard analysis was used to assess the influence of coronary interventions on survival during a median follow-up of 4.6 years.

Results: Coronary angiography was performed in 323 patients ≥80 years (78.6%) and 575 patients <80 years (96.8%). We found that women had a significant lower rate of coronary angiography compared to men in patients ≥80 years (71.9 vs. 86.3%, $p<0.001$) but not in patients <80 years (97.1 vs. 96.5%, $p=0.655$). However, in patients who underwent coronary angiography no difference was found in the rate of percutaneous coronary interventions ($p=0.429$) or any interventions (plus fibrinolysis or coronary artery bypass graft surgery, $p=0.378$) between elderly women and men. The rate of in-hospital major bleeding in elderly women and men who underwent coronary angiography was comparable (female: 28.7%, male: 26.3%, $p=0.664$). Any intervention was associated with a higher reduction of long-term mortality in elderly women with a hazard ratio (HR) of 0.58 (95% confidence interval [CI] 0.38–0.88, $p=0.01$) than in elderly men with a HR of 0.69, 95% CI 0.45–1.06, $p=0.10$). When comparing elderly women and men with ACS no significant differences in risk factors for procedure-related events were found except for a lower height ($p<0.000$) and weight ($p<0.000$) in women.

Conclusion: Elderly women with ACS had a lower angiography rate than elderly men indicating a lower intention for coronary interventions. Though, the benefit of coronary interventions was even higher in elderly women. The distribution of risk factors in elderly women and men who did not undergo coronary angiography does

not explain the gender gap. Particularly elderly women may benefit from an objective risk assessment for the decision whether coronary angiography should be performed.

XVI-3

Krankenhausmortalität der ungeschützten Hauptstammrevaskularisation bei über 80-jährigen Patienten

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Hintergrund: Aufgrund der demographischen Verschiebung wird das Patientenkollektiv der über 80-jährigen in Zukunft stetig wachsen. Bei Patienten dieser Altersgruppe mit signifikanter Stenose des linken Hauptstammes ist die operative Revaskularisation mittels aortokoronarem Bypass aufgrund von oft bestehender Multimorbidität mit einem hohen Risiko behaftet. Wenn auch nicht als primäre Strategie empfohlen, erscheint die interventionelle Revaskularisation daher häufig sinnvoll. Ziel unserer Analyse war es, die Effektivität und Sicherheit der ungeschützten Hauptstammintervention in diesem Alterskollektiv an unserer Abteilung zu evaluieren.

Methodik: Es wurden retrospektiv alle Patienten mit einem Alter über 80, bei denen an unserer Abteilung in den letzten 10 Jahren eine interventionelle ungeschützte Hauptstammintervention durchgeführt wurde, ausgewertet. Hierbei wurden das Setting (akut vs. elektiv), die Komorbiditäten und kardialen Risikofaktoren sowie das Überleben bis zur Krankenhausentlassung (primärer Endpunkt), Komplikationen nach Revaskularisation, Koronarmorphologie, Stenttyp und Revaskularisationtechnik erhoben.

Resultate: Insgesamt erfolgte zwischen 2003 und 2013 bei 57 Patienten (39 % Frauen, Alter 82,9 ± 2,9, 21 % 3-Gefäß-Erkrankung, CCS Stadium 3,2 ± 0,8) eine ungeschützte Hauptstammintervention (11 im Rahmen eines ACS, 2 bei iatrogener Hauptstammdissektion, 44 elektiv). Unsere Patienten wiesen folgende Komorbiditäten auf: 26 % frühere Koronarintervention, 14 % früherer Herzinfarkt (MCI), 23 % Vorhofflimmern, 18 % Krebserkrankung in der Anamnese, 77 % arterielle Hypertonie, 14 % Diabetes mellitus, 51 % Hypercholesterinämie, 5 % COPD, 28 % früheres zerebrovaskuläres Ereignis und 11 % pAVK. Der Kreatininwert war im Mittel 1,1 ± 0,3 mg/dl, die linksventrikuläre Auswurffraktion 53,8 ± 15,7 %. 65 % der Patienten wurden nach Besprechung in einem Zweiteingriff interveniert, 35 % bereits im Rahmen des Ersteingriffes. Die Stenose des Hauptstammes war in 72 % der Fälle distal lokalisiert, in 12 % im mittleren Schaft und in 16 % am Ostium. Alle Patienten bis auf fünf (9 % bare metal Stents) erhielten einen drug-eluting Stent (21 % Sirolimus, 7 % Paclitaxel, 19 % Everolimus, 44 % Zotarolimus). 72 % der Eingriffe wurden in 1-Stent-Technik durchgeführt, die restlichen 28 % in 2-Stent-Technik. Bei fünf Revaskularisationen (9 %) war aufgrund massiver Kalzifikationen eine Rotablation vor Stentimplantation notwendig. In allen Fällen konnte das Gefäß erfolgreich revaskularisiert werden. Eine Mehrgefäßintervention erfolgte in 54 % der Eingriffe. Die Krankenhausmortalität betrug für die elektiven Eingriffe 4.5 % (2 Pat.: subakute Stentthrombose, target vessel MCI) und für die Akutinterventionen (ACS und iatrogene Hauptstammdissektionen) 15.4 % (2 Pat.: Akutintervention bei MCI mit kardiogenem Schock, iatrogene Hauptstammdissektion bei höhergradiger Aortenklappenstenose vor geplanter Core Valve® Implantation). Nach dem Eingriff kam es zu keinen neurologischen Komplikationen. Kein Patient erhielt eine intraaortalen Ballonpumpe.

Diskussion: Die Krankenhausmortalität der aortokoronaren Bypass-Operation bei über 80-jährigen mit Hauptstammbeteiligung liegt in der Literatur bei 5.7 %. Die Mortalität nach interventioneller Hauptstammrevaskularisierung bei 100 %iger Erfolgsrate an unserem Zentrum war mit 4.6 % bei elektiven Eingriffen vergleichbar. Auch bei einer Akutintervention zeigte sich in einem polymorbiden Patientengut eine günstige Mortalität.

XVI-4

Long-term effects of renal denervation on day- and night-time blood pressure in patients with resistant hypertension by the use of ambulatory blood pressure measurements

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Introduction: In patients suffering from resistant hypertension, renal denervation (RDN) is an auspicious treatment option in addition to medical antihypertensive therapy. Up to now, only few long-term data on blood pressure (BP) changes in ambulatory blood pressure measurements (ABPM) after RDN are published.

Methods: We systematically investigated the effects of RDN with the Simplicity Catheter System (Medtronic) on ABPM in a consecutive series of patients with resistant hypertension (mean systolic office BP [OBP] >160 mmHg despite treatment with at least three antihypertensive drugs).

OBP measurements and ABPM were performed in all patients before, 3, 6, 12, and 24 months after the procedure, respectively. Patients with mean systolic OBP reduction of more than 10 mmHg 6 months after RDN were classified as responders.

Results: We treated 32 patients with RDN between June 2010 and May 2011. Six months after RDN, 21 patients (65.6 %) were classified as responders. In these patients the mean 24- hour BP in ABPM decreased from 146.8 ± 17.0/89.1 ± 11 mmHg at baseline to 136.8 ± 15.0/83.2 ± 10.7 mmHg ($p = 0.034/p = 0.014$) 24 months after RDN. Mean Day-time BP decreased from 149.5 ± 17.5/91.5 ± 10.8 to 138 ± 16.2/84.4 ± 11.5 mmHg ($p = 0.017/p = 0.007$) and night-time BP decreased non significantly from 138.2 ± 17.6/80.9 ± 12.3 mmHg to 133.5 ± 12.0/77.9 ± 11.1 mmHg ($p = 0.223/p = 0.132$) respectively.

Conclusions: By the use of ABPM, we found a significant and sustained 24-months BP reduction in about two-thirds of the patients treated with RDN for resistant hypertension. BP reduction was mainly driven by the significant reduction of daytime blood pressure levels.

XVI-5

Long-term follow up in patients after MitraClip procedure due to severe symptomatic functional mitral regurgitation

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Introduction: Percutaneous mitral valve repair using the MitraClip system has gained increasingly acceptance in patients with significant mitral regurgitation who are inegible or with disproportionately high-risk for surgical intervention. However, data about long-term follow up are rare, especially in those who are treated for functional mitral regurgitation (FMR).

Methods and results: From August 2009 to March 2013 we treated 50 patients with a percutaneous catheter-based MitraClip

system. In 45 patients significant FMR grade 3+/4+ was the indication of index procedure and in 95 % (43/45) we could place 1 or more clips. Up to now we have hemodynamic and clinical outcome data available in 30 sufficiently treated patients beyond at least 24 month after MitraClip procedure. 60 % were male, median age was 73.5 years (IQR;66, 5–80), the logEuroscore I was mean 23.9 ± 13.0 % and NT-proBNP was median 5421 pg/ml(IQR 2877–12633). All of them were highly symptomatic in NYHA class III/IV and 6 min walktest (6 MWT) was mean 181 ± 141 m. The mean LVEF was 30.68 ± 12.2 % and even 8 patients had an LVEF ≤ 25 %. Survival rate at 24 month was 70 % (21/30). The proportion of patients with residual MR ≤ 2 was 90 %. One patient underwent heart transplantation due to persistant heart failure symptoms although the Clip procedure was successful and residual MR was grade < 2. After 24 month the 6 MWT increased and symptoms and NT-proBNP decreased both significantly. Even in a subgroup of 7/30 patients with a higly reduced LVEF ≤ 25 % surprisingly the survival rates was 62.5 % (5/8).

Conclusion: In the vast majority of high-risk patients with severe FMR, MitraClip treatment was effective in durably reducing MR at a follow-up exceeding 24 months. Survival rates were low in consideration of the multimorbidity of these patient group. The results confirm adequateness of percutaneous mitral valve repair as an important non surgical option for high-risk FMR patients and provide evidence for lasting efficacy of MitraClip treatment.

XVI-6

Percutaneous transcatheter aortic-valve implantation (TAVI) for severe aortic stenosis: changes in outcome after introduction of the Edwards Sapien device in addition to the Medtronic CoreValve device—the St. Poelten experience

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Background: Untreated severe, symptomatic aortic valve stenosis is associated with a high mortality of up to 50 % per year. Although the treatment of choice is surgical valve replacement, more than 30 % of these patients are deferred from surgery due to high surgical risk. Percutaneous transcatheter aortic valve implantation (TAVI) as a non-surgical treatment option for high-risk patients has been established in our center since 2008. Initially, the Medtronic CoreValve device has been used for all patients until the Edwards Sapien device was introduced in 12/2012. The aim of this study was to compare the performance of these two TAVI-devices with respect to 30-day-outcome measures.

Methods: We studied all patients undergoing a percutaneous TAVI at the Department of Internal Medicine III, (Cardiology and Emergency Medicine), Landesklinikum St. Poelten between 01/2008 and 12/2013. Patients receiving a Medtronic CoreValve were compared to those receiving an Edwards Sapien. Endpoints were new implantation of a cardiac rhythm device (pacemaker, cardiac resynchronization therapy, or implantable cardioverter defibrillator) and all-cause death after 30 days, respectively.

Results: Among a total of 279 patients (62 % female, mean age 82 ± 6yrs), 183 (66 %) received a CoreValve (176 transfemoral, 7 transsubclavian approach) and 96 (34 %) a Sapien (all transfemoral). As regards patient characteristics and comorbidities no significant differences were found between patients undergoing TAVI with CoreValve versus Sapien. Accordingly, no differences were found between estimated surgical risk (logistic EuroSCORE CoreValve: 19.9 ± 11.7, Sapien: 19.3 ± 10.9). Procedural success rate was 95 and 97 % for CoreValve and Sapien, respectively. The high rate of 27.9 % of cardiac rhythm device implantation 30 days after CoreValve Implantation dropped to 16.7 % after introduction of the Sapien valve in our TAVI program ($p = 0.037$). Likewise, 30-day-mortality after TAVI dropped from 11.5 % with CoreValve to 3.1 % with Sapien ($p = 0.020$).

Conclusion: After almost five years of experience with Medtronic CoreValve at our center, 30-day-outcome significantly improved after introduction of Edwards Sapien in our TAVI program with respect to the need for short-term cardiac rhythm device implantation and all-cause mortality. This improvement could not be explained by differences in patient characteristics or surgical risk.

XVI-7

The St. Poelten experience of percutaneous transcatheter aortic-valve implantation (TAVI) for severe aortic stenosis: Descriptive comparison to results from the PARTNER trial

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Background: Symptomatic aortic valve stenosis, the most common valve disease in adults, is associated with a high mortality of up to 50 % per year. Surgical valve replacement is the treatment of choice in symptomatic patients. However, more than 30 % of these patients do not undergo surgery due to high surgical risk. Recently, percutaneous transcatheter aortic valve implantation (TAVI) has been established as a non-surgical treatment option for patients with symptomatic aortic valve stenosis at high surgical risk and is used in our center since 2008. The short- and long-term mortality benefit of TAVI compared to conservative therapy has been clearly demonstrated in the randomized, controlled PARTNER-trial arm B. However, clinical trial data do not always reflect everyday clinical practice and the outcome of such interventions should also be evaluated in "real world" patients aside clinical trials. We therefore performed a retrospective analysis of all TAVI implantations in our center and descriptively compared their outcome to data from the PARTNER trial arm B.

Methods: In this retrospective, single-center, mono-cohort study all patients undergoing TAVI at the Department of Internal Medicine III (Cardiology and Emergency Medicine), Landesklinikum St. Poelten from 01/2008 to 12/2013 were included. Endpoints were all-cause death after 30 days and one year. Baseline characteristics and outcome were descriptively compared to the TAVI cohort of the PARTNER trial arm B (PTB: $n = 179$).

Results: Among a total of 279 patients (62 % female [PTB: 54 %], mean age 82 ± 6yrs [PTB: 83 ± 9yrs],) 183 (66 %) received a self-expandable Medtronic CoreValve (176 transfemoral, 7 transsubclavian approach) and 96 (34 %) a balloon expandable Edwards Sapien valve (all transfemoral). Procedural success rate was 96 %. The logistic EuroSCORE was 19.7 ± 11.4 % (PTB: 26.4 ± 17.2 %). Thirty-day and one-year all-cause mortality ($n = 185$, patients with completed one year follow-up) were 8.6 % (PTB: 5.0 %) and 29.7 % (PTB: 30.7 %), respectively.

Conclusion: Even in our real-world population in a non-academic environment, TAVI outcome measures with respect to mortality are comparable with randomized controlled trial data. This suggests that the benefit for patients known from clinical TAVI trials might be transferable into clinical practice.

XVI-8

Renale Sympathikusdenervation (RSD): Effekte auf 24h-Blutdruck (BD) und Gefäßsteifigkeit nach einem Jahr

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Einleitung: Die interventionelle RSD ist ein neues Therapieverfahren, das mittels perkutaner Ablation sympathischer Nervenfasern in der Adventitia der Nierenarterien eine BD-Senkung durch Reduktion der Sympathikusaktivität bewirkt (1). Das Verfahren wird bei Patienten (Pat) mit therapierefraktärer Hypertonie und Ausschluss einer sekundären Hypertonie angewandt. Die BD-Daten der internationalen Studien beziehen sich großteils auf Ordinationsmessungen. In der vorliegenden Untersuchung werden die an der Kardiologie Graz denervierten Pat mit 1 Jahres Follow-up vorgestellt und anhand der 24h-BD-Werte und der Messung der arteriellen Gefäßsteifigkeit hinsichtlich des Therapieerfolges analysiert.

Methoden: Bei allen Pat wurden zur Baseline und nach 1 Jahr (375 ± 56 Tage nach der Prozedur) eine 24h-Blutdruckmessung (ABDM), sowie eine Messung des zentralen BD und der Gefäßsteifigkeits-Parameter mittels Mobil-O-Graph® (ARCSolver Algorithmus) (2) durchgeführt. Die RSD wurde beidseits mit dem Simplicity® Katheter durchgeführt, es traten keine Komplikationen auf.

Ergebnisse: 32 Pat mit einem mittleren Ordinationsdruck von 169 ± 12/99 ± 11 mmHg erhielten eine renale Sympathikusdenervierung. Dadurch kam es zu einer signifikanten BD-Reduktion in der Auswertung des 24-h-BD von systolisch 153±16 mmHg auf 133±14 mmHg ($p < 0{,}001$) und diastolisch von 93 ± 17 mmHg auf 82 ± 12 mmHg ($p < 0{,}001$). Auch die Auswertungen des Tages- und Nacht-BD zeigten eine signifikante Blutdruckreduktion (Baseline Tag: 154 ± 17/91 ± 14; Nacht: 141 ± 24/80 ± 15; FU-1 J Tag: 135 ± 13/84 ± 12; Nacht 125 ± 18/75 ± 14; p jeweils < 0,01). Keinen Effekt zeigte die Methode auf den Mittelwert der Herzfrequenz über 24 h (68 ± 9 vs 68 ± 10/min; $p = 0{,}903$). Der zentrale systolische BD, der ein Maß für die Steifigkeit der großen Gefäße darstellt, wurde signifikant verringert (130 ± 36 vs 121 ± 13; $p > 0{,}001$). Keine signifikante Verbesserung konnte in der Analyse der Pulswellengeschwindigkeit (PWV) (8,3 ± 2,5 vs 9 ± 1 m/s; $p = 0{,}469$) sowie des Augmentationsindex (AIx75) (26 ± 9 vs 29 ± 12 %; $p = 0{,}382$) gezeigt werden.

Schlussfolgerung: Die RSD kann bei gut selektionierten Patienten mit therapierefraktärer Hypertonie den Blutdruck signifikant senken, was hier durch die vom Untersucher unabhängige 24-h-Blutdruckmessung verifiziert werden konnte. Auch der nächtliche BD, der mit einer besonders hohen kardiovaskulären Mortalität einhergeht, konnte signifikant gesenkt werden. Weiters wurde eine signifikante Reduktion des zentralen systolischen BD gezeigt. Jedoch kam es in unserem Patientenkollektiv zu keiner Reduktion der Herzfrequenz und keiner Verbesserung der PWV und des AIx.

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Postersitzung XVII: Pulmonale Hypertension

XVII-1

Elevated left ventricular filling pressures in chronic thromboembolic pulmonary hypertension

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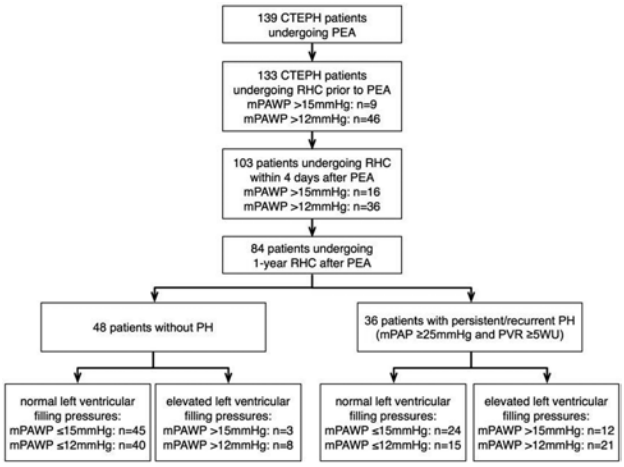
Purpose: Chronic thromboembolic pulmonary hypertension (CTEPH) is characterized by non-resolving thromboemboli in the pulmonary arteries, with elevation of right ventricular (RV) afterload, RV failure and eventually death. CTEPH is surgically curable by pulmonary endarterectomy (PEA). According to the European CTEPH registry 16.7 % of patients experience persistent or recurrent pulmonary hypertension (PH) after PEA. We hypothesized that a significant proportion of patients with persistent/recurrent PH after PEA suffer from post-capillary PH.

Methods: 139 consecutive CTEPH patients undergoing PEA were analyzed. Right heart catheterization (RHC) was performed (1) prior to PEA, (2) within 4 days after PEA and (3) 1 year after PEA. Persistent/recurrent PH was defined as mean pulmonary artery pressure (mPAP) ≥ 25 mmHg and pulmonary vascular resistance (PVR) ≥ 5 WU 1 year after PEA. Elevated LV filling pressures were defined as (1) mean pulmonary arterial wedge pressure (mPAWP) > 15 mmHg, according to the most recent ESC/ERS guidelines on diagnosis and treatment of PH, as well as (2) mPAWP > 12 mmHg, according to the latest heart failure with preserved ejection fraction (HFpEF) guidelines.

Results: Hemodynamics of 133 of 139 CTEPH patients undergoing PEA were available for analyses. Prior to PEA, 9 (6.8 %) patients presented with mPAWP > 15 mmHg and 46 (34.6 %) with mPAWP > 12 mmHg. RHC performed within 4 days after PEA in 103 patients showed that 16 (15.5 %) patients had mPAWP > 15 mmHg, while 36 (35 %) patients had mPAWP > 12 mmHg. Hemodynamic data 1 year after PEA were available in 84 patients. 36 patients were identified as having persistent/recurrent PH. Of those, 12 (33.3 %) had mPAWP > 15 mmHg and 21 (58.3 %) had mPAWP > 12 mmHg. Patients with recurrent/persistent PH and mPAWP > 12 mmHg were more likely to be male (63 vs. 20 %; $p = 0.012$) and to develop atrial fibrillation after PEA (31 vs. 0 %; $p = 0.12$), compared to those with mPAWP ≤ 12 mmHg.

Conclusions: CTEPH patients sustain or even increase elevated left-ventricular filling pressures immediately postoperative and 1 year after PEA. Increased LV filling pressures seem to play an important role in the persistence or recurrence of PH after PEA.



XVII-2

Parenteral treprostinil upregulates fibrocyte BMPRII expression in pulmonary hypertension patients

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Introduction: Pulmonary hypertension (PH) is characterized by remodeling of pulmonary resistance vessels with fibrosis and thrombosis, eventually causing right heart failure. Fibrocytes are progenitor cells derived from monocytes and have been implicated in wound repair, atherosclerosis and fibrotic diseases. Circulating fibrocytes have been found to be increased in children and young adults with PH. Prostacyclin analogues, e.g. treprostinil, an established treatment for PH, were shown to inhibit adhesion and differentiation of fibrocytes in a murine model. We aimed to investigate fibrocytes in PH patients treated with treprostinil.

Methods: Peripheral blood samples from PH patients ($n=9$, female = 66.6 %, age = 70 ± 10.7 years) were obtained at baseline, 1 week and 1 month after initiation of treatment with treprostinil. Flow cytometry was employed to characterize circulating fibrocytes based on the expression of CD45, CD34, Collagen I, CD11b and BMPRII.

Results: Treprostinil significantly increased BMPRII expression on fibrocytes (baseline mean fluorescence intensity (MFI) = 26,495 ± 18,861, one month MFI = 55,988 ± 34,727, $p=0.05$). Total numbers of fibrocytes were decreased (baseline = 0.27 ± 0.16 ‰ of CD45+ cells, one month = 0.13 ± 0.03 ‰ of CD45+ cells, $p=0.004$), and also CD34 expression (baseline 44,701 ± 36,124. One month 20,173 ± 12,074, $p=0.033$).

Conclusions: The restoration of the BMPRII pathway may normalize a pro-inflammatory state and thus inhibit recruitment of fibrocytes to the circulation.

XVII-3

Parenteral treprostinil leads to a shift in the myeloid to plasmacytoid dendritic cell ratio

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Introduction: Pulmonary arterial hypertension (PH) is characterized by remodeling of pulmonary resistance vessels with fibrosis and thrombosis, eventually causing right heart failure. Dendritic cells (DCs), specialized antigen-presenting cells, migrate to lung tissue in idiopathic PAH. Prostacyclin analogues, e.g. treprostinil, are established treatments for PH which decrease antigen uptake and pro-inflammatory cytokine production of DCs in vitro. However, the role of DCs, especially of monocyte-derived DC precursors, in the setting of PH is still poorly understood. We aimed to investigate the effect of treprostinil on DC subsets in PH patients.

Methods: Peripheral blood samples from PH patients ($n=9$, female = 66.6 %, age = 70 ± 10.7 years) were obtained at baseline, 1 week and 1 month after initiation of treatment. Flow cytometry was employed to characterize circulating DC precursors based on the expression of CD45, CD33, CD123, CD85k and CCR7.

Results: Treprostinil significantly decreased the percentage of CD123- myeloid DCs (mDCs), whereas the percentage of CD123+ plasmacytoid DCs (pDCs) significantly increased (mDCs baseline: 65.5 ± 10.2 %, one month follow-up (FUP): 56.4 ± 13.0 %, $p=0.01$; pDCs baseline: 34.5 ± 10.4 %, one month FUP: 43.6 % ± 12.9, $p=0.009$). This was expressed as a decreased mDC:pDC ratio (baseline: 2.11 ± 0.89, one month FUP: 1.45 ± 0.68, p = 0.029). Total DC count remained unchanged. CD85k, CCR7 and CD33 expression on DCs was not affected by treprostinil treatment.

Conclusions: The shift towards plasmacytoid DCs under treatment with treprostinil may be due to suppression of the monocytic differentiation pathway towards mDCs. pDCs have been implicated as drivers of a Th2 response, which have been shown to mediate pulmonary arterial muscularization, a hallmark feature of PH. We aim to clarify whether this immunologic effect of treprostinil is implicated in therapeutic outcome.

XVII-4

Phenprocoumon dose requirements and genetic polymorphisms in chronic thromboembolic pulmonary hypertension

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Background: Chronic thromboembolic pulmonary hypertension (CTEPH) is caused by large fibrotic thrombus in the pulmonary arteries, likely originating from pulmonary embolism. Inadequate anticoagulation is one of the suspected mechanisms of disease in CTEPH.

The aim of our study was to assess phenprocoumon dosing in relation to genetic polymorphisms of vitamin K epoxide reductase complex subunit 1 (VKORC 1) and cytochrome P-450 2C9 (CYP2C9).

Patients and methods: The ratio of weekly mean phenprocoumon dose in relation to mean INR levels was assessed in CTEPH patients on phenoprocoumon oral anticoagulation for at least 6 months, compared with PAH patients. VKORC 1 (−1639, −3730) and CYP2C9 (*2, *3) single nucleotide polymorphisms (SNPs) were determined by polymerase chain reaction (PCR).

Results: In 72 consecutive patients were observed (46 CTEPH, 26 PAH; mean treatment duration 51.7 ± 44.7 months, mean age 63.4 ± 12.2 years (63 % female). Mean dose of phenprocoumon per week was 15.8 mg (4.5 to 42 mg). The mean ratio of weekly phenprocoumon dose and INR levels showed statistically significant differences between CTEPH (mean ratio 6.58 ± 3.3) and PAH (mean ratio 4.87 ± 1.7; $p=0.013$). As expected, patients with CTEPH and VKORC1–1639 GG homozygous wild type required significantly higher phenprocoumon doses compared with VKORC1–1639 AA homozygous mutants ($p<0.05$). The distribution of the two subsets of CYP2C9 (*2, *3) was not different from the normal population.

Conclusions: CTEPH patients require more phenprocoumon in relation to INR levels than PAH patients. Unmet phenprocoumon dosing requirements may be one mechanism of disease in CTEPH.

XVII-5

Pulmonary artery occlusion waveform analysis for the assessment of pulmonary vascular disease 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 arterial wedge pressure (mPAWP) >15 mmHg. In the 5th World Symposium on Pulmonary Hypertension in Nice, PH due to LHD (post-capillary PH) was subdivided into two phenotypes, „isolated" post-capillary PH (IPCPH, diastolic pulmonary vascular pressure gradient [DPG] <7 mmHg) and „combined" pre-capillary and post-capillary PH (CPCPH, 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. Pulmonary artery occlusion technique assesses the decay from pulmonary artery pressure to PAWP to approximate the pressure in pre-capillary small pulmonary arteries (POCCL). With POCCL, pulmonary vascular resistance can be partitioned into larger arterial (upstream, Rup%) and small arterial plus venous (downstream) components. The aim of the present study was to assess the accuracy of pulmonary artery occlusion waveform analysis (PAOWA) in patients with CPCPH.

Methods: PAOWA was performed in 37 patients undergoing right and left heart catheterizations at rest and after inhalation of 40 ppm nitric oxide (NO). 10 patients were classified as IPCPH with a transpulmonary gradient >12 mmHg, 20 as CPCPH and 7 as pre-capillary pulmonary arterial hypertension (PAH).

Results: The lowest Rup% was observed in patients with iPAH (67.1±12.1%) and CPCPH (74.56±13.7%; $p=0.57$), while patients with IPCPH showed higher Rups% (94.5±5.3%). While iPAH patients (0.52±11.5, $p=0.91$) did not show a change in Rup% upon NO, an increase in Rup% could be observed in patients with CPCPH (6.6±7.35%, $p=0.054$). A significant correlation between DPG and Rup% was observed ($r=-0.41$; $p=0.011$).

Conclusion: PAOWA confirms that patients with PH due to LHD and a DPG ≥7 mmHg (CPCPH) have pulmonary vascular disease similar to iPAH. In contrast to iPAH, a proportion of patients with CPCPH show a significant increase in Rup% upon NO, which might be due to reactive vasoconstriction in this condition.

XVII-6

Soluble platelet endothelial cell adhesion molecule-1 (sPECAM-1) plasma levels in venous thromboembolism

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Introduction: Misguided thrombus resolution after an acute episode of venous thromboembolism (VTE) leads to post-thrombotic syndrome (PTS) and/or chronic thromboembolic pulmonary hypertension (CTEPH). Platelet endothelial cell adhesion molecule-1 (PECAM-1) is a transmembrane receptor that is involved in leukocyte migration and angiogenesis, which are key components of venous thrombus resolution. In our previous study we have shown that cell surface cleavage of PECAM-1 raises soluble PECAM-1 (sPECAM-1) plasma levels and leads to a lack of functional PECAM-1 at the site of venous thrombosis. Consequently, in patients with elevated sPECAM-1 plasma levels, venous thrombus resolution is impaired, which favours clot persistance and the development of PTS after acute deep vein thrombosis (DVT).

Our objective for the present study was to evaluate plasma sPECAM-1 levels in patients with acute, symptomatic pulmonary embolism (PE) and chronic thromboembolic pulmonary hypertension (CTEPH) to identify a similar mechanism as seen in patients developing PTS after acute DVT.

Methods: sPECAM-1 plasma levels were analysed in patients with acute PE ($n=26$) and in patients with confirmed CTEPH ($n=41$) using a sandwich ELISA.

Results: Plasma levels of sPECAM-1 in patients with acute PE decreased from 80.14 (63.06/96.30) ng/mL (median, 25th/75th percentile) at the time of diagnosis to 71.76 (56.14/86.16) ng/mL one month after the event. In patients with CTEPH sPECAM-1 plasma levels remained elevated (83.00 (71.02/100.1) ng/mL; $p=0.301$) at a significantly higher level than values one month after acute PE ($p=0.029$).

Discussion: Sustained elevation of sPECAM-1 plasma levels in CTEPH patients mirror a status of persistant endothelial dysfunction. Our results suggest that sPECAM-1 may serve as a biomarker for CTEPH development after acute PE.

XVII-7

Subcutaneous treprostinil for the treatment of post-capillary ("reactive") pulmonary hypertension: a prospective, academic study

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Background: Post-capillary pulmonary hypertension (PH) is the most common cause of PH. The "reactive" form of post-capillary PH has recently been labeled as Combined pre- and post-capillary pulmonary hypertension (CPCPH), and defined as PH with a mean pulmonary arterial wedge pressure of >15 mmHg, a transpulmonary gradient (TPG) ≥12 mmHg and a diastolic pulmonary gradient DPG) ≥7 mmHg. Currently, no specific treatments are available and approved for this hemodynamic entity. The objective of our prospective cohort study was to investigate the efficacy and safety of subcutaneous (sc) treprostinil (TRE) in patients with severe CPCPH.

Patients and methods: Data were collected at the time of diagnosis and one year after the initiation of scTRE. Primary endpoints were the change from baseline of 6-minute walking distance (6MWD) and time to first clinical worsening at one year. Secondary endpoints included the change from baseline in WHO functional class (FC), NT-proBNP and Borg dyspnea score at one year follow up.

Results: Baseline TPG was 18.4±2.7 mmHg and DPG 8.6±1.9 mmHg (mean age 66 years, 44.1% female) (Tables 1 and 2). There were no treatment discontinuations.

Table 1 Baseline characteristics

Characteristic	$n=34$
Mean age (range), y	66 (31–82)
Sex, n (%)	
Male	19 (55.8)
Female	15 (44.1)
DANA Point classification, n (%)	
II	
Left heart disease	6 (17.6)
Mitral valve disease	6 (17.6)
Tricuspid valve disease	5 (14.7)
Aortic valve disease	1 (2.9)
Diastolic dysfunction	9 (26.5)
III	
COPD	5 (14.7)
Lung fibrosis	1 (2.9)
WHO FC, n (%)	
III	17 (50)
IV	17 (50)
Mean 6MWD (SD), m	256.8 (93.4)
Mean BDS (SD)	6.1 (2.2)
Median proBNP (IQR), pg/mL	2929 (1478–5548)

Table 2. Baseline hemodynamics

Hemodynamics	$n=34$
HR, beats/min, mean (SD)	73 (15.5)
BP systolic, mmHg, mean (SD)	134 (15.7)
mRAP, mmHg, mean (SD)	14.6 (6.6)
mPAP, mmHg, mean (SD)	55.7 (13.7)
mPAWP, mean (SD)	21 (2.9)
TPG, mmHg, mean (SD)	18.4 (2.7)
DPG, mmHg, mean (SD)	8.6 (1.9)
CO, L/min, mean (SD)	3.6 (0.9)
CI, L/min/m^2, mean (SD)	2.0 (0.4)
PVR, dyn.s.cm^{-5}, mean (SD)	880.1 (436.1)

3 patients (8.8 %) died from heart failure and 5 patients (14.7) were hospitalized due to worsening of PH. One year after initiation of scTRE 6MWD had improved by 45.3 meters from baseline (95 % CI 21.9 to 68.7 m; $p<0.001$). WHO FC decreased by 1.1 from baseline (95 % CI – 1.42 to – 0.74; $p<0.001$). Borg dyspnea score also decreased by 2.47 from baseline (95 % CI – 3.77 to – 1.16; $p<0.001$)

Conclusion: In patients with severe CPCPH scTRE is a safe and tolerable treatment option that is efficacious at one year.

XVII-8

Vitamin D and pre-capillary pulmonary hypertension

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Background: Vitamin D regulates a multitude of biological processes and its deficiency is reemerging as an important public health issue. Vitamin D plays a role in thrombotic disease and inflammation. However, no data are available on the vitamin D status in patients with pre-capillary pulmonary hypertension (PH). The aim of this study was to assess the role of vitamin D status in the pathogenesis of PH.

Patients and methods: Data were collected from patients suffering from pulmonary arterial hypertension (PAH) and chronic thromboembolic PH (CTEPH). Serum 25-hydroxyvitamin D concentrations were measured at time of diagnosis, and associations of vitamin D deficiency with markers of systemic inflammation and thrombosis were assessed.

Results: Mean serum 25-hydroxyvitamin D was 39.67 ± 21.36 nmol/L ($n=133$, mean age 55 ± 17 years; 61.7 % female). 51 patients (38.3 %) had PAH and 82 patients (61.3 %) suffered from CTEPH. Mean concentrations of serum 25:hydroxyvitamin D showed no statistical significant differences between these two PH subsets (PAH 41.74 ± 20.28 mmol/L, CTEPH 38.39 ± 22.03 mmol/L, $p=$ ns). Strong correlations were found between exercise capacity (rho = 0.513, $p<0.001$), Borg dyspnea score (rho = :0.518, $p<0.001$), high:sensitive C-reactive protein (hsCRP; rho = 0.433, $p=0.002$), mean right atrial pressure (rho = :0.288, $p=0.040$), and vitamin D deficiency in PAH patients.

Conclusion: Serum 25-hydroxyvitamin D concentrations were reduced in PAH, and correlated with prognostic parameters. Vitamin D status may play a role in the pathogenesis of PAH.

XVII-9

Tenascin-C deficiency and the development of Pulmonary Arterial Hypertension

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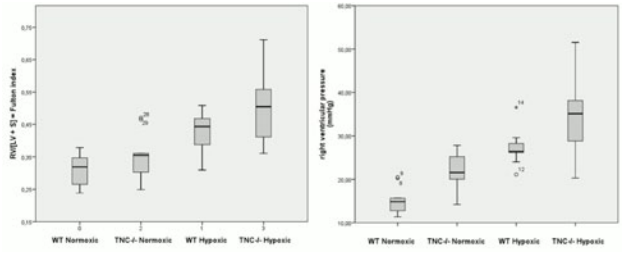
Background: Pulmonary arterial hypertension (PAH) is a severe and progressive disease entailing a deteriorating pulmonary vasculopathy with obstruction of small pulmonary arteries, smooth muscle cell hypertrophy and intimal fibrosis. It has been proposed that Tenascin-C (TnC), a key mediator of smooth muscle cell growth and survival is critically involved in the pathogenesis of PH. Aim of our study was to investigate the effect of TnC inhibition by direct gene manipulation on the development of PH.

Methods: We utilized mice with a homozygous TnC knock-out (TnC KO) and A/J wild types (WT). Both TnC KO and WT littermates were held in an environmental chamber with FiO2 of 10 % or under normoxia for 4 weeks. We investigated the effect of TnC deletion and chronic normobaric hypoxia on parameters of pulmonary vascular resistance such as right ventricular systolic pressure (RSVP) and right ventricular hypertrophy (Fulton Index/right to left ventricular- ratio). To assess the degree of smooth muscle cell hyperplasia, alpha-smooth muscle actin antibody staining was performed.

Results: TnC KO mice showed significantly increased right ventricular pressures after 4 weeks under normoxic conditions, compared with wild type controls. Both TnC KO and WT mice showed increased right ventricular pressures under normobaric hypoxia. TnC KO mice revealed significantly higher right ventricular pressures (Fig.) and Fulton indices than controls.

Conclusion: TnC a extracellular matrix glycoprotein prominent during tissue remodelling and wound healing may play a pivotal role in the early pathogenesis of pulmonary hypertension.



Postersitzung XVIII: Rhythmologie III

XVIII-1

Dabigatran-induced lupus temporarily preventing blood group determination

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Epistaxis led to severe anemia in an 89-year-old Caucasian female under a therapy with dabigatran since 12 months because of atrial fibrillation. Correction of the anemia was difficult because it was impossible to assess her blood group due to polyagglutination. Since hospital records disclosed that in 2011 her blood group was 0 positive, acquired polyagglutination was assumed. After 66 days, it was again possible to assess the blood group as 0 positive. Immunologic investigations disclosed that antinuclear antibodies and anti-histone antibodies were elevated, and antibodies to double-stranded DNA were negative. Drug-induced lupus was diagnosed due to the autoantibody profile detected. It is quite likely that dabigatran had induced polyagglutination and drug-induced lupus.

Immunologic side effects of therapy with dabigatran, a small lipophilic molecule with a molecular weight of 472 DA, are rarely reported. In the RE-LY study, drug hyper-sensitivity, allergic oedema, anaphylactic reaction, and anaphylactic shock were reported in <0.1% of patients receiving dabigatran. We conclude that dabigatran may impede determination of the blood group due to drug-induced lupus with polyagglutination.

XVIII-2

Familial Himalayan P-wave and left ventricular hypertrabeculation/ noncompaction

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Background: Giant P-waves in the ECG, also termed "Himalayan P-waves", are reported in congenital heart disease and cardiomyopathies. We report a family, in whom the father underwent heart transplantation because of hypertrophic cardiomyopathy and his two daughters showed Himalayan P-waves, extensive focal right atrial wall thickening and LVHT

Case presentation: The father received a pacemaker at age 33 years and underwent heart transplantation because of hypertrophic cardiomyopathy. His two daughters showed Himalayan P-waves and extensive, focal right atrial wall thickening. Left ventricular hypertrabeculation/noncompaction (LVHT) was diagnosed in sister A at age 23 years and developed in sister B between the ages of 42 to 46 years. In sister A the heart rate continuously declined during follow-up. She refused implantation of a pacemaker and died suddenly at age 49 years. Sister B, now 47 years, suffers from bradycardia and refuses implantation of a pacemaker.

Conclusion: Himalayan P-waves are due to focal right atrial wall thickening, may be familially and associated with LVHT. Focal right atrial hypertrophy in LVHT may be associated with bradyarrhythmia and sudden death.

XVIII-3

Repeated radiofrequency ablation of atrial tachycardia in restrictive cardiomyopathy secondary to myofibrillar myopathy

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Myofibrillar myopathy is characterized by non-hyaline and hyaline lesions due to mutations in nuclear genes encoding for extra-myofibrillar or myofibrillar proteins. Cardiac involvement in myofibrillar myopathy may be phenotypically expressed as dilated, hypertrophic or restrictive cardiomyopathy. Radiofrequency ablation of atrial fibrillation and flutter has so far not been reported in myofibrillar myopathy. We report the case of a young female with myofibrillar myopathy and deteriorating heart failure due to restrictive cardiomyopathy and recurrent atrial fibrillation and atrial tachycardias intolerant to pharmacotherapy. Cardiac arrhythmias were successfully treated with repeat radiofrequency ablations and resulted in regression of heart failure thus postponing the necessity for cardiac transplantation.

XVIII-4

Left ventricular substrate mapping in a patient with electrical storm and dilated cardiomyopathy due to Emery-Dreifuss muscular dystrophy

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Background: Emery-Dreifuss muscular dystrophy (EDMD) is a progressive muscle-wasting disorder defined by early contractures of the Achilles tendon, spine, and elbows. EDMD is also distinctive for its association with cardiac manifestations like defects of the cardiac conduction system and dilated cardiomyopathy.

Methods: We report on a 45-year-old male patient with an X-linked EDMD who was admitted to our hospital after successful cardiopulmonary resuscitation in the setting of electrical storm and endstage dilated cardiomyopathy. EDMD was diagnosed histologically fifteen years ago. A pacemaker was implanted seven years ago in the setting of complete AV block, and a CRT-D upgrade was done three years ago.

The patient underwent electrophysiological examination. In the bipolar voltage map of the left ventricle using the CARTO technology, a small endocardial inferior scar was detected, where late potentials could be recorded. The unipolar voltage map revealed an extensive scar extending from the basal inferior wall to the septum, and an extensive intramural septal scar. An ablation of all endocardial late potentials was successfully performed. However, the QRS

morphologies during pacemapping from the endocardial inferior scar did not match the QRS morphologies of the clinical ventricular tachycardias (VT). Two months after ablation, the patient had a VT recurrence, successfully shocked by the ICD. As the patient is listed for heart transplantation, we refrained from an epicardial ablation attempt.

Discussion: This is the first report of VT substrate mapping in a patient with dilated cardiomyopathy due to EDMD. Left ventricular mapping revealed a scar pattern typical for patients with non-ischemic cardiomyopathy, namely a small endocardial inferior scar and an extensive scar extending from the basal inferior wall to the septum, and an extensive intramural septal scar. Most likely, the septal scar contributed to the complete AV block.

XVIII-5

"Patient pathway"—guided management of atrial fibrillation: a pilot study

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Background: Atrial fibrillation (AF) is the most frequent heart rhythm disorder and is associated with a significantly increased risk of stroke, heart failure and death. Despite improvements in prevention and treatment, the prognosis has not changed significantly. The aim of our study was to establish a pathway to improve drug adherence as well as quality and safety of treatment.

Methods: Initiated by the "Wiener Krankenanstaltenverbund" (KAV) and in collaboration with the "human information systems" group (Systema) we conducted a prospective pilot analysis of patients admitted to hospital because of AF. From September 2012 to February 2013, 88 patients (female 44 %, male 56 %, age 69.5+/−12.4) with AF were included. Detailed written description of disease was provided and medical and AF history were recorded from baseline to hospital discharge. The primary endpoints were drug adherence, serious adverse events (SAE) and level of information after 6 months follow up period (FUP). State of knowledge on AF was evaluated based on school grading system (1–5).

Results: Regarding the stroke risk, 88 % presented with a CHA2DS2VASc of ≥ 2 (Fig. 1a). 33 % of patients were already anticoagulated at study inclusion, 78 % were discharged with oral anticoagulation (OAC). The mean duration of hospital stay was 10 ± 8 days. Complete follow-up was only obtained in 32 patients (36 %), mainly due to rejection of telephone questionnaire (22.7 %), poor health condition (10.2 %) and invalid telephone numbers (13.6 %). 3.4 % ($n = 3$) died within FUP period. Of the 32 participants analysed, 87.5 % were anticoagulated after 6 months. In 3 patients (9.4 %) oral anticoagulation (OAC) was terminated by the general practitioner. Stroke under OAC was recorded once, drug incompatibility was mentioned in 2 cases. 94 % of participants rated their state of knowledge ≤ 3 at FUP (Fig. 1b).

Conclusion: 6 months after discharge, state of knowledge concerning the own disease was satisfactory. Moreover, drug adherence among those with completed FUP was excellent. To further analyze whether a pathway-guided AF management improves long-term safety and quality of care, a prospective randomized-controlled trial is needed.

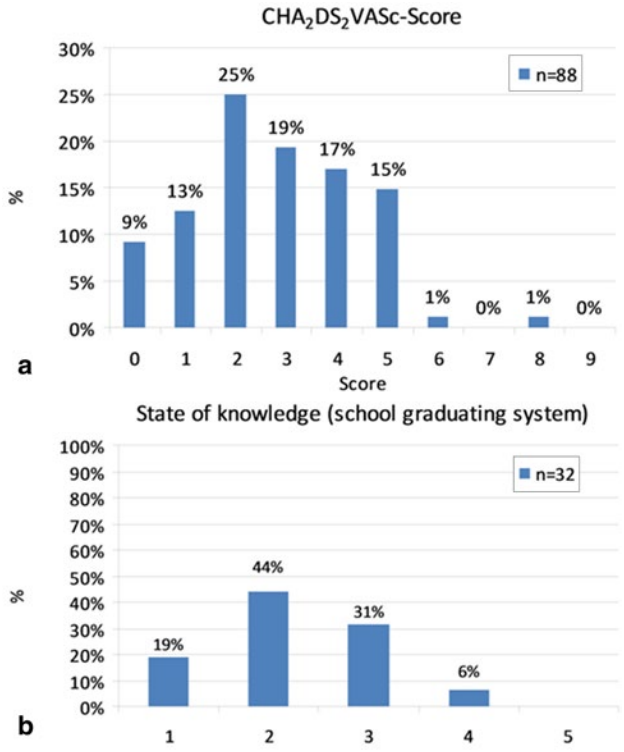

Fig. 1 Level of information after 6 months FUP

XVIII-6

Early Repolarization mit horizontaler ST-Strecke als unabhängiger Risikoparameter für das Auftreten von Kammerflimmern nach STEMI

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Einleitung: Beim Early Repolarization (ER) Phänomen, auch bekannt als „J-point elevation", handelt es sich um eine Erhöhung des J-point von ≥ 0, 1 mV in 2 benachbarten Ableitungen, deszendierend oder gekerbt. Da die EKG-Veränderung häufig bei Athleten und jungen gesunden Menschen zu finden ist, galt sie lange Zeit als benigne. 2009 wurde erstmals gezeigt, dass bei Patienten mit idiopathischem Kammerflimmern (VF) signifikant häufiger eine ER zu beobachten ist[1]. Insbesondere fand sich bei diesen Pat. die maligne Form mit horizontaler EKG-Strecke (Abb. 1). Im Rahmen einer akuten Koronarischämie ist eine ER mit horizontaler ST-Strecke ein Risikomarker[2]. Beides, Bestehen der EKG-Veränderung schon vor dem ersten Myokardinfarkt (MI) oder Auftreten nach dem MI sind mit einer höheren Inzidenz von VF verbunden.

Material und Methodik: Ein 57-jähriger Mann wird 2 h nach Schmerzbeginn mit den Zeichen eines Vorderwand-STEMI aufgenommen und akut interveniert. Eine proximale, langstreckige 90 %-ige und eine 95 %-ige MID-LAD-Stenose werden mit 2 DES, ein 80 %-ig stenosierter Ramus diagonalis mit 1 DES versorgt.

Ergebnisse: In den ersten 30 nach Intervention treten nicht anhaltende ventrikuläre Runs auf. Das EKG am Tag nach dem akuten Ereignisses zeigt neben infarkttypischen Veränderungen auch ST-Veränderungen in den inferioren Ableitungen im Sinne einer ER mit horizontalem Muster (Abb. 2); die EKG-Veränderung ist in

den Folge-EKGs nicht konstant zu sehen. Echokardiographisch findet sich eine VW-Akinesie, die LVEF ist gering reduziert. Nach telemetrischer Überwachung wird der Pat. am Tag 9 entlassen. Am nächsten Tag erleidet der Pat. zu Hause vor dem PC sitzend einen SCD (VF). Er wird erfolgreich reanimiert und 24 h gekühlt. Im EKG ist wieder eine ER mit horizontaler ST-Strecke zu sehen. In der Aufwärmphase kommt es zu rezidivierenden ventrikulären Tachykardien, die Kontrollangiographie zeigt einen anhaltend guten PCI-Erfolg, es wird die Indikation zur ICD-Implantation gestellt.

Diskussion: Ein Zusammenhang zwischen ER und ventrikulären Arrhythmien beim akuten STEMI wurde erstmals 2012 von Patel[3] bei 50 Patienten gezeigt. Ventrikuläre Tachykardien traten in den ersten 72 h signifikant häufiger auf, wenn eine ER-Veränderung im EKG zu beobachten war (26 vs. 4 %, $p = 0{,}01$). Das größte Risiko bestand bei Patienten, wenn die typischen EKG-Veränderungen (horizontales Muster) in den inferioren Ableitungen bereits vor dem ischämischen Ereignis dokumentiert wurden. Ein solches EKG stand uns im beschriebenen Fall nicht zur Verfügung.

Konklusion: In Zukunft sollte bei der Beurteilung des Infarkt-EKGs auch das Augenmerk auf das Vorliegen einer Early Repolarization mit horizontalem Muster geachtet werden, da bei diesen Patienten ein erhöhtes Risiko für das Auftreten von ventrikulären Arrhythmien bis hin zu Kammerflimmern besteht. Wie lange das Risiko nach MCI besteht, ist dzt. völlig unklar. Daher existieren keine Empfehlungen, wie Patienten mit ER in der Post MI-Phase zu managen sind. Ob durch eine prolongierte Monitorphase, durch eine bestimmte antiarrhythmische Therapie oder eine frühzeitige ICD-Implantation die Prognose dieser Patienten günstig beeinflusst werden kann, sollte dringlich untersucht werden. Bis Ergebnisse und Empfehlungen vorliegen, könnte die Verordnung einer Defibrillatorweste (LifeVest) in diesen Fällen eine gute Option sein.

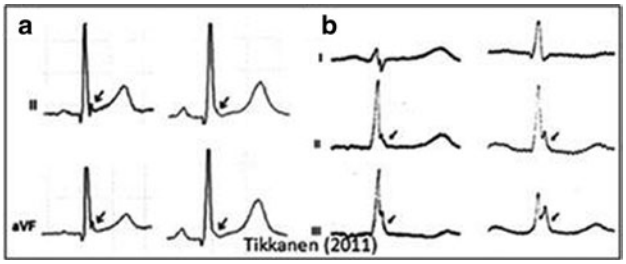

Abb. 1 Beispiele einer Early Repolarization mit (**a**) rasch ansteigende ST-Strecke (benigne Form) und (**b**) horizontaler ST-Strecke (maligne Form)

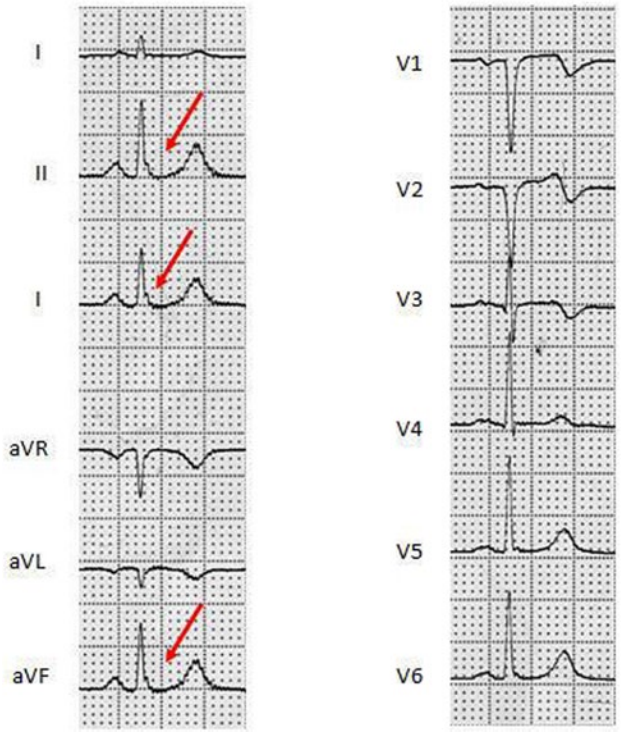

Abb. 2 J-wave in II, III, aVF (Early Repolarization) mit horizontaler ST-Strecke

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XVIII-7

Focal impulse and rotor modulation (FIRM) using a novel rotor mapping system

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Introduction: Atrial fibrillation (AF) can be perpetuated by rapidly activating spiral waves, so called "rotors". Recent studies demonstrated, that rotors identified with computational mapping can be mapped and that AF can be successfully treated by rotor elimination.

We present the first in human experience of focal impuls and rotor modulation (FIRM) using a novel 64-electrode basket catheter (FIRMap, Topera Inc., CA).

Methods: 15 patients (10 male, 63 ± 8 years, left atrium 45 ± 5 mm, hypertension in 6 pts) underwent FIRM guided mapping and ablation for paroxysmal AF ($n = 8$) or persistent AF ($n = 7$).

After double transseptal puncture, two long sheath were advanced into the left atrium (LA). In patients presenting in sinusrhythm, AF was induced by burst pacing. Rotor mapping was performed after AF sustained for a minimum of five minutes using the RhythmView mapping system in combination with the FIRMap catheter. After rotor identification, irrigated radiofrequency current was applied for 300 s at each rotor. Rotor mapping was repeated until all rotors were identified and ablated in both atria. After rotor ablation, pulmonary vein isolation was performed. Esophageal temperature monitoring was performed and RF delivery was stopped at an esophageal temperature of > 41 °C.

Results: AF was occurred spontaneous in 4 pts and required induction in 11 pts.

A mean of 2.8 ± 1.9 rotors per patients (LA 2.1 ± 2.0, RA 0.5 ± 0.6) could be identified with computational mapping. All rotors could successfully be eliminated with a mean of 887 ± 553 s of RF delivery. AF terminated during ablation in three pts into sinus rhythm and in 1 patient into atrial tachycardia during ablation. These 4 patients suffered from paroxysmal AF and AF was induced at the beginning of the procedure.

RF current delivery was stopped because of an esophageal temperature rise of > 41 °C in one ptn during rotor ablation and in seven pts during PVI.

No acute complication occurred.

Results: Computational mapping of the left atrium in combination with this novel basket catheter identifies AF rotors. Rotor ablation leads to AF termination in a subset of patients. AF rotors can successfully be eliminated by catheter ablation. Clinical outcome data is lacking.

Postersitzung XIX: Risikofaktoren/ Stoffwechsel/Lipide II

XIX-1

Barostimulation: therapy in patients with resistant hypertension – First experience in Austria

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Introduction: Systemic arterial hypertension is one of the main cardiovascular diseases and a major risk factor for coronary artery disease, cerebrovascular disease and heart and renal failure. Despite the availability of a wide variety of pharmacotherapies, resistant hypertension (HTN) persists as a significant public health issue, comprising approximately 10 % of all hypertensive patients.

In recent years beside pharmacological agents, device therapies evolved in the treatment of resistant hypertension. Primarily renal denervation developed as a widespread and promising therapy. However, conflicting results regarding benefit have raised concerns of this technique. Baroreflex Activation Therapy (BAT) is a unique approach to HTN therapy wherein electrical stimulation of carotid sinus baroreceptors evokes coordinated reductions in sympathetic traffic to the heart, vasculature and kidneys, as well as augmented parasympathetic activity. BAT is applied by implanting a stimulator similar to a pacemaker along with one lead attached to the carotid sinus.

We report the first experience in Austria after BAT-Implantation in two patients with resistant hypertension.

Methods: We considered two patients with resistant hypertension for BAT-Implantation after a second hypertension was ruled out.

The first patient was a 44-year old male with resistant HTN, who even suffered of end organ damage in terms of a cerebral stroke. Despite a medication of seven different antihypertensive agents the ambulant blood pressure measurement (ABPM) showed a mean blood pressure of 154/98 mmHg. As mentioned before secondary hypertension was ruled out.

The second patient was a 76-year old female with a history of HTN for decades with end organ damages in terms of left ventricle hypertrophy and a fundus hypertonicus II°. Furthermore she suffered of recurrent hypertensive crises with blood pressure measurements of 230/110 mmHg. Although taking several combinations of antihypertensive medications, recommended blood pressure goals were never reached.

Procedure: BAT-Implantation (Rheos Barofelex Hypertension Therapy System CVRx, Inc) is accomplished by a team of a surgeon, anaesthiologist and a cardiologist. In general anaesthesia the neck was incised on the right side to expose the carotid bifurcation. Intraoperatively, up to nine electrode positions at the level of the carotid bifurcation were tested to identify a suitabel electrode position.

The electrode position of choice is where stimulation provides reduction of blood pressure and heart rate with fast recovery after stimulation is stopped. Once the location eliciting optimal hemodynamic response had been identified, the electrode was sutured in place. The pulse generator was placed in a subcutaneous pocket and the lead was tunneled subcutaneously. Similar to cardiac pacemaker, pulse generation settings can be programmed transcutaneously. The stimulator remains switched off for 2 weeks due to possible interference with wound healing.

In our patients intraoperative blood pressure could be reduced by approximately 20/10 mmHg.

Conclusion: Baroreflex Activation Therapy acutely decreases arterial blood pressure in hypertensive patients and is a promising tool in treating patients with resistant hypertension. However, careful patient selection is mandatory. Especially secondary hypertension should be ruled out before patients are considered for such a device therapy.

XIX-2

Cotinin als Marker zur Prädiktion von Mortalität in der Ludwigshafen Risk and Cardiovascular Health Study (LURIC)

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Einleitung: Zigarettenrauchen ist ein wichtiger und vermeidbarer Risikofaktor für kardiovaskuläre Erkrankungen und zeigt eine starke Assoziation zu Morbidität und Mortalität weltweit. Cotinin ist eines der Hauptabbauprodukte von Nikotin im Körper und kann als Laborparameter zu Abschätzung des Rauchverhaltens dienen. Ziel dieser Studie war die Untersuchung von Cotinin als Marker für eine individuelle Risikoprädiktion bei Teilnehmern der Ludwigshafen Risk and Cardiovascular Health (LURIC) Studie sowie ein Vergleich mit der Angabe des Zigarettenkonsums in Packyears.

Material und Methoden: Die Blutabnahme durch Venenpunktion erfolgte morgens in nüchternem Zustand. Cotinin wurde mittels eines Radioimmunassays (Nikotin Metabolit RIA, DPC Biermann GmbH, Bad Nauheim, Germany) bestimmt. Anhand der Cotininkonzentration wurden die Studienteilnehmer in Quartilen aufgeteilt. Die Verteilung anderer Risikofaktoren in den Quartilen wurde mittels ANOVA untersucht. Die Assoziation von Cotinin und Packyears mit Gesamtmortalität (GM) und kardiovaskularer Mortalität (KVM) wurde mittels Cox Regression analysiert. Für die statistischen Tests wurde SPSS v22 verwendet.

Ergebnisse: Cotininwerte über der Nachweisgrenze von 0.2 µg/l lagen für 840 LURIC Teilnehmer vor, davon waren selbstberichtet 591 aktive Raucher, 158 ehemalige Raucher und 91 lebenslange Nichtraucher. Höhere Cotininkonzentrationen waren signifikant assoziiert mit niedrigerem Alter und HDL-Cholesterin sowie höherem C-reaktivem Protein. Im unadjustierten Modell zeigte Cotinin im Gegensatz zu Packyears eine signifikante Assoziation zu frühzeitiger Herzerkrankung mit einem OR (95 % KI) von 1,38 (1,18 – 1,62) pro Standardabweichung (SD), welche aber in Modellen adjustiert für andere kardiovaskuläre Risikofaktoren verlorenging. Beide Parameter zeigten signifikante Assoziation mit GM und KVM mit HR (95 % KI) von 1,30 (1,17 – 1,44) und 1,25 (1,08 – 1,45) pro SD für Cotinin und HR von 1,19 (1,06 – 1,34) und 1,18 (1,00 – 1,38) pro SD für Packyears in Modellen adjustiert für Alter, Geschlecht, LDL-C, HDL-C, BMI, Hypertension und Diabetes. In Cox-Modellen, die sowohl Cotinin als auch Packyears enthielten, blieben für die GM beide Variablen signifikant, für die KVM dagegen nur Cotinin.

Diskussion: Cotinin ist in LURIC ein stärkerer Prädiktor für Gesamtmortalität und kardiovaskuläre Mortalität als der selbst angegebene Zigarettenkonsum in Packyears. In einem Modell mit beiden Parametern bleibt nur Cotinin signifikant mit KVM assoziiert. Dies könnte sich dadurch erklären, dass auch bei einigen der Teilnehmer, die angegeben hatten niemals geraucht zu haben, deutlich erhöhte Cotininwerte über 100 µg/l gemessen wurden.

Dies könnte sich durch eine fehlerhafte Selbstangabe oder starke Belastung durch Passivrauchen erklären lassen. Wir würden somit empfehlen Cotinin als objektiv messbaren Parameter der Angabe Packyears für die Risikoprädiktion vorzuziehen.

XIX-3

HDL quality in heart failure with preserved ejection fraction

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Purpose: Heart failure with preserved ejection fraction (HFPEF) is a pathophysiologically complex disease with intertwined contributing factors, including systemic inflammation and various metabolic abnormalities. Advanced disease stages are characterized by backward failure with pulmonary congestion and chronic kidney disease, which in turn may propagate the inflammatory state. The protein composition of high-density lipoprotein (HDL) has been demonstrated to be severely altered in various diseases with increased cardiovascular risk characterized by chronic inflammation. Therefore, we assessed HDL quality by analysis of two critical HDL-bound proteins, serum amyloid A (SAA) associated with systemic inflammation and surfactant protein B (SP-B) related to pulmonary congestion, to represent indicative clinical and diagnostic HFPEF features.

Methods: Consecutive HFPEF patients ($n=105$) diagnosed according to current ESC guidelines (1. signs or symptoms of heart failure, 2. a left ventricular ejection fraction over 50 % and 3. evidence of abnormal left ventricular relaxation, filling or diastolic stiffness) were recruited in our prospective registry. Diagnosis was confirmed by right heart catheter in all study participants. We developed a simple, laboratory assay to measure the amount of HDL-bound SAA and SP-B directly from serum. Patient samples were subjected to this assay at the time of clinical diagnosis. SAA and SP-B levels were correlated with functional and clinical parameters in the cohort, grouped by occurrence of cardiac events during the follow-up period of up to 3 years (defined by hospitalization due to heart failure and/or cardiac death).

Results: HFPEF patients showed clearly increased levels of HDL-bound SAA and SP-B compared to controls. High levels of SAA(HDL) were found to correlate with parameters of inflammation (C-reactive protein: $r=0.490$, $p=0.003$) and kidney function (glomerular filtration rate: $r=-0.525$, $p=0.001$; serum creatinine: $r=0.463$, $p=0.005$). SP-B(HDL) was inversely associated with pulmonary functions, such as DLCO ($r=-0.478$, $p=0.018$), FEV1 ($r=-0.378$, $p=0.033$). Importantly, these correlations were independent of HDL-cholesterol levels and only found in patients who experienced cardiac events after inclusion.

Conclusion: Substantially increased levels of HDL-bound SAA and SP-B demonstrate systemic inflammation and pulmonary congestion as cardinal features of HFPEF and might serve as novel biomarkers of diagnostic value. Moreover, these proteins can be related to properties predictive of cardiac events, which is central to advance our understanding of the pathophysiology of HFPEF.

XIX-4

Macht die kardiologische Rehabilitation Patienten dick?

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Adipositas ist einer der wichtigsten Risikofaktoren bei kardialen Patienten in der ambulanten kardiologischen Rehabilitation. Über Änderungen in einem 6-wöchigen Trainingsprogramm wurde bisher kaum berichtet.

In dieser systematischen prospektiven Studie analysierten wir alle Patienten, die 2013 am ambulanten Phase II-Rehabilitationsprogramm des Instituts Cardio-Vital Wels teilnahmen, hinsichtlich Ihrer demographischen Daten, der zugrundeliegenden Erkrankung, des Risikoprofils und der Veränderungen durch die Rehabilitation.

Von Jänner bis Dezember 2013 nahmen in 19 Gruppen 189 PatientInnen an dem Programm teil. Die Indikationen waren wie folgt: akutes Koronarsyndrom 54 %, Stentimplantation bei stabiler Angina pectoris 18 %, Kardiomyopathie 7 %, aortokoronare Bypassoperation 5 %. Bei 175 Personen (76 % Männer, 59 + 11 Jahre) wurde das Körpergewicht vor und nach dem Programm gemessen. Das Körpergewicht veränderte sich wie folgt: Beginn: 84,7 + 19 kg, Ende 84,4 + 19 kg; Unterschied − 0, 3 + 2,7 kg. Patienten mit Migrationshintergrund nahmen im Schnitt um 0,5 kg an Körpergewicht zu. 5 Personen nahmen um mehr als 10 kg ab, 120 zwischen 0 und 5 kg, während 48 bis zu 5 kg zunahmen (1 Person > 10 kg). Das regelmäßige Ergometertraining ergab eine signifikante Korrelation zwischen Leistung und Änderung des Körpergewichts. Jene, die abnahmen, steigerten die Leistung,. Die, die zunahmen konnten am Ende weniger Watt leisten ($p<0,05$). Andere Parameter wie das Geschlecht, Zigarettenrauchen, Blutdruck, Lipidstatus und auch die LDL-Cholesterin-Änderung zeigten keine signifikanten Korrelationen zur Körpergewichtsveränderung.

Obwohl doch ein größerer Prozentsatz an Herzpatienten durch die Rehabilitation moderat an Gewicht verliert und damit auch fitter wird, bleibt ein großer Nachholbedarf hinsichtlich der Rehabilitationsziele bestehen.

XIX-5

Partikeldurchmesser der Low Density Lipoproteine als Mortalitätsfaktor – Ergebnisse der Ludwigshafen Risk and Cardiovascular Health Study (LURIC)

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Einleitung: Kardiovaskuläre Erkrankungen stellen vor allem in Industrieländern eine wesentliche Ursache der Morbidität und Mortalität dar. Wichtige Risikofaktoren sind Veränderungen von Parametern des Lipidstoffwechsels, insbesondere ein Anstieg des Low density lipoprotein Cholesterols (LDL-C). Ziel unserer Studie war die Analyse des Zusammenhanges zwischen LDL-Partikeldurchmesser und koronararterieller Erkrankung (CAD) und Mortalität in Patienten der Ludwigshafen Risk and Cardiovascular Health Study (LURIC).

Material und Methoden: In der LURIC Studie eingeschlossen wurden 3266 koronarangiographierte Patienten; von diesen wurden 1643 Patienten, die keine lipidsenkende Therapie erhielten, in die Auswertung eingeschlossen, davon 1070 mit und 573 ohne koronarangiographisch nachgewiesene CAD. Die Bestimmung der mitt-

leren Durchmesser der LDL erfolgte nach kombinierter Ultrazentrifugation-Präzipitation (β-quantification; VLDL, LDL, HDL) und Berechnung aus den Konzentrationen von ApoB und der Lipide (Baumstark et al. Biochim. Biophys. Acta 1990). Die statistische Auswertung erfolgte mittels SPSS 19.0.

Ergebnisse: Die Studienteilnehmer wurden nach ihrem mittleren LDL-Partikeldurchmesser in drei Gruppen eingeteilt (< 16,5 nm, $n = 704$; 16,5–16,8 nm, $n = 470$, Referenzgruppe; > 16,8 nm, $n = 469$) und die Hazard Ratios (HR) mit denen der Referenzgruppe verglichen. Die adjustierten HR für Todesfälle insgesamt betrug 1,71 (95 % CI 1,31 – 2,25) bei Personen mit großen und 1,24 (95 % CI 0,95 – 1,63) bei Personen mit kleinen LDL. Die entsprechenden Werte für die kardiovaskuläre Mortalität betrugen 1,89 (95 % CI 1,32 – 2,70) und 1,50 (95 % CI 1,06 – 2,12). Die Equilibrium density gradient Ultrazentrifugation zeigte typische und unterschiedliche Profile der LDL-Partikel bei Personen mit großen LDL (nahezu gleichmäßige Verteilung von IDL und LDL-1 bis LDL-6), mittelgroßen LDL (Peakkonzentration bei LDL-4) und kleinen LDL (Peakkonzentration bei LDL-6).

Diskussion: Die Berechnung des mittleren Partikeldurchmessers der LDL erlaubt eine Identifizierung von Individuen mit unterschiedlichem Verteilungsmuster der LDL-Subfraktionen und unterschiedlicher Partikelzusammensetzung. Sowohl das Vorliegen einer erhöhten Konzentration großer LDL als auch eine Zunahme der Konzentration kleiner LDL geht dabei im Vergleich zu LDL mittlerer Größe mit einer erhöhten Gesamtmortalität und einer Steigerung der kardiovaskulären Mortalität einher, was auf einen Einfluss des LDL-Metabolismus hinweist. Bei der Ermittlung des individuellen Risikos sollte daher neben der Bestimmung der Konzentration, insbesondere der Konzentration des LDL-C, auch eine Untersuchung der Parameter des LDL-Metabolismus erfolgen.

XIX-6

Prevalence of cardiovascular disease risk factors from a health check program in an Austrian company

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Background: Austria has a high mortality rate due to diseases of the cardiovascular system (43 % of all deaths in 2012). The aim of this investigation was to establish the prevalence of cardiovascular disease (CVD) risk factors amongst Austrian workers enrolled in a workplace health-promotion program.

Methods: Worksite employees in the region of Salzburg were screened for their health status, between 2006 and 2013. Respondents were classified as normotensives, pre-hypertensives and hypertensives according to their blood pressure levels, as defined by the JNC 7 guidelines. Body height, weight, waist circumference (WC), total cholesterol, HDL, LDL, and triglyceride (TG) were measured. Self-reported information regarding smoking was collected. We used the European risk chart from the European Society of Cardiology (based on gender, age, cholesterol, systolic blood pressure and smoking status) to assess the 10 year risk of fatal CVD.

Results: In total, 1129 respondents, 913 men and 216 women, were recruited, with a mean (SD) age of 38.3 (10.1) years and a BMI of 25.5 (3.8) kg/m^2. Of all respondents, 58.2 % were identified as hypertensives and 34.9 % as pre-hypertensives. Only 6.9 % had normal blood pressure levels. All anthropometric (weight, WC) and laboratory parameters on lipids differed significantly between these three groups (Table 1). The CVD risk factors were high blood lipids (83.9 %), overweight (38.3 %), obesity (11.5 %), abdominal obesity (17.2 %), hypertension (58.2 %), smoking (24.6 %), and diabetes mellitus (1.2 %). In participants with a BMI above 25 kg/m^2, compared to those with below 25 kg/m^2, we could observe a 3-fold higher risk for hypertension [odds ratio (OR) 2.72; 95 % confidence interval (CI): 1.38 – 5.35, $p = 0.004$; adjusted for age, gender and waist circumference]. Moreover, pre- and hypertensive persons showed a 2-fold increased risk to demonstrate higher CVD risk scores [OR 2.25; 95 % CI: 1.32 – 3.83, $p = 0.003$; adjusted for BMI and WC].

Conclusions: A high proportion of relatively young and apparently healthy Austrian employees demonstrated pre- and hypertension. BMI, WC and lipids were significantly higher among individuals with pre- or hypertension compared to normotensives. The current investigation showed that a workplace CVD risk screening process was effective in identifying the relatively high prevalence of CVD risk factors amongst Austrian employees. Consequently, it draws attention to the need for the adoption of workplace programs to encourage a healthy lifestyle and to prevent diseases.

XIX-7

The LOW-BP-VIENNA (Lowering Blood Pressure in Primary Care in Vienna) trial—rationale and design

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Rationale: Hypertension is the single largest contributor to death, accountable for a variety of severe and costly diseases, such as heart attack and stroke, chronic kidney disease and dementia. Approximately 30 % of the adult population suffer from hypertension and of those diagnosed and treated, only 30–50 % have adequately controlled blood pressure. At present, the importance of hypertension as fundamental risk factors is inadequately addressed among many patients and physicians.

Table 1 Anthropometric and laboratory parameters on lipids

	Normotensives			Prehypertensives			Hypertensives			*p* value
	Mean	*SD*	*n*	*Mean*	*SD*	*n*	*Mean*	*SD*	*n*	
Age (year)	32	9		36	9	391	40	10	651	0.000
Weight (kg)	70.0	13.8	77	77.5	13.1	389	82.6	13.8	652	0.000
BMI (kg/m^2)	22.7	2.9		24.8	3.4	388	26.2	3.8		0.000
WC (cm)	83.3	9.3	75	89.4	10.8	382	93.8	11.5	630	0.000
Cholesterol (mg/dl)	177.7	30.8	74	189.8	37.6	385	202.4	38.2	641	0.000
HDL (mg/dl)	60.4	12.9	73	52.5	15.6	378	50.8	15.9	627	0.000
LDL (mg/dl)	89.6	31.2	70	100.4	33.8	361	110.6	35.7	590	0.000
TG (mg/dl)	154.1	93.7	74	178.3	108.5	383	206.8	123.9	642	0.000

Design: The aim of this prospective, randomised, open-label, multicentre clinical trial is to enhance blood pressure control in primary care by introducing a standardised and simplified titration regime with single pill combinations (SPC), comprising an angiotensin receptor blocker, calcium channel blocker and hydrochlorothiazide.

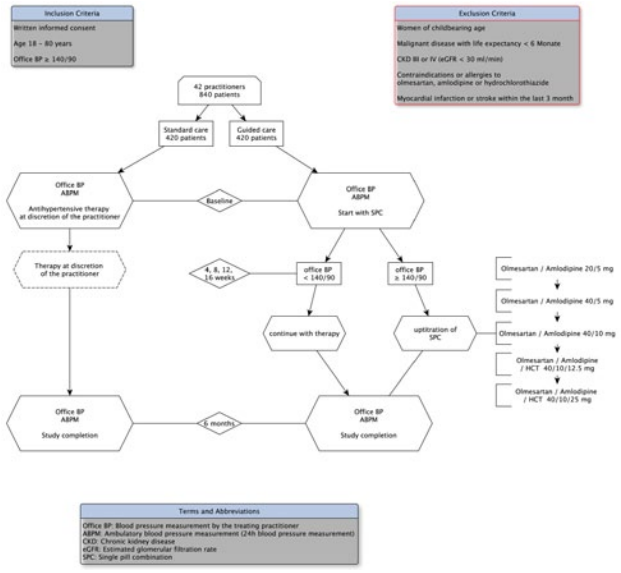
The trial will randomise 42 family doctors or resident specialists for internal medicine (enrolling 840 patients with treated or untreated hypertension) to either experimental care or standard care for hypertension, latter according to the 2013 European Society of Cardiology Guidelines for the Management of Arterial Hypertension.

Practitioners randomised to experimental care will up-titrate antihypertensive therapy with SPCs in 4-week intervals if the target blood pressure of < 140/90 mmHg is not reached at the respective follow-up (Fig. 1).

Study outcomes: The primary efficacy endpoint will be the proportion of patients achieving the target office blood pressure after 6 months of follow-up. The main secondary endpoint will be the improvement of 24h ambulatory blood pressure (ABPM) profile, measured at inclusion and after 6 months of follow-up.

Safety assessments include the evaluation of treatment emergent adverse events, particularly hospitalisation, worsening of renal function, peripheral oedema and hypotension.

Moreover, the study will collect data on the quality of blood pressure control in primary care in Vienna, unavailable until today, identify patients with treatment resistant hypertension, investigate the cost-effectiveness of antihypertensive treatment with SPCs in Austria and evaluate parameters associated with cardiovascular events, such as pulse wave velocity and arterial stiffness.



XIX-8

Trans-Fettsäuren und kardiovaskuläre Mortalität – Ergebnisse der Ludwigshafen Risk and Cardiovascular Health Study (LURIC)

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Einleitung: Kardiovaskuläre Erkrankungen stellen eine wichtige Ursache der Morbidität und Mortalität dar. Ein Risikofaktor sind Veränderungen von Parametern des Lipidstoffwechsels. Trans-Fettsäuren, d. h. ungesättigte Fettsäuren mit einer Doppelbindung in trans-Konfiguration, die sowohl natürlich vorkommen als auch industriell durch Härtung von Pflanzenfetten hergestellt werden, werden ebenfalls als Risikofaktoren für kardiovaskuläre Erkrankungen diskutiert. Ziel der Studie war die Analyse des Einflusses der Konzentration von trans-Fettsäuren auf die Mortalität von in die Ludwigshafen Risk and Cardiovascular Health Study (LURIC) eingeschlossenen Patienten mit kardiovaskulären Erkrankungen.

Material und Methoden: Bei 3259 Patienten erfolgte eine Untersuchung der Fettsäurezusammensetzung der Erythrozytenmembran aus eingefrorenem Material unter Verwendung der HS-Omega-3 Index Methodik. Hierbei erfolgten eine Umesterung, eine Auftrennung mittels Gaschromatographie und ein Vergleich mit einer Standardmischung von Fettsäuren. Die statistische Auswertung erfolgte mittels SPSS 20.0.

Ergebnisse: Der Anteil von trans-Fettsäuren an den Gesamtfettsäuren der Erythrozytenmembran betrug 0,96 ± 0,26 % (MW±Stdabw., Range: 0,27 – 2,4 %). Bei Auswertung über die Tertilen der Konzentration an trans-Fettsäuren war diese mit einem höheren Alter, höherem LDL-Cholesterol, höherem HDL-Cholesterol und höherer Eicosapentaensäure, sowie geringerem Body Mass Index (BMI), geringeren Gesamttriglyceriden, geringeren HDL-Triglyceriden, geringerem diastolischem Blutdruck und geringerer Nüchternglucose assoziiert ($p = 0{,}006$ für HDL-C, übrige $p < 0{,}001$). Patienten mit höherer Konzentration von trans-Fettsäuren waren häufiger weiblich, litten seltener an koronararteriellen Erkrankungen oder Diabetes mellitus, rauchten seltener und nahmen seltener lipidsenkende Medikamente ein ($p < 0{,}001$). Eine Untersuchung der Mortalität in den einzelnen Tertilen über einen Beobachtungszeitraum von 10 Jahren zeigte zudem, dass eine erhöhte Konzentration an trans-Fettsäuren mit einer Abnahme des Risikos für kardiovaskuläre Todesfälle (HR (95 % CI); 3. Tertile vs 1. Tertile 0,79 (0,64 – 0,98)) bzw. plötzlichem Herztod (3. Tertile vs 1. Tertile: 0,68 (0,50 – 0,92)) einherging. Ursächlich war hierfür vor allem ein Anstieg von trans-Palmitoleinsäure (C16:1n7t; 3. Tertile vs 1. Tertile: 0,75 (0,62 – 0,91) bzw. 3. Tertile vs 1. Tertile: 0,55 (0,41 – 0,76)), die natürlicherweise in Wiederkäuern gebildet wird. In schwächerer Ausprägung zeigte sich auch ein protektiver Effekt von C18:1t in der zweiten Tertile bei kardiovaskulärer Mortalität (0,82 (0,67 – 0,99)) und plötzlichem Herztod (0,70 (0,51 – 0,96)).

Diskussion: LURIC Patienten weisen geringere Konzentrationen der trans-Fettsäuren als U.S. Amerikaner auf, obwohl auch bei diesen in den letzten Jahren die Konzentration abnahm. Eine höhere Konzentration von trans-Fettsäuren ist mit niedrigerem BMI, Blutdruck, Nüchternglucose, Diabetes mellitus und niedrigerer Häufigkeit für das Auftreten von kardiovaskulären Erkrankungen, kardiovaskulärer Mortalität und plötzlichem Herztod assoziiert. Auffällig ist, dass diese Effekte mit der Konzentration natürlicher trans-Fettsäuren in Verbindung stehen, während die in der vorliegenden Studie in geringen Konzentrationen gemessenen industriell hergestellten trans-Fettsäuren keinen Einfluss auf das Risiko aufwiesen.

Postersitzung XX: Risikofaktoren/ Stoffwechsel/Lipide III

XX-1

Plasma chemerin is a strong and independent predictor of cardiovacular event risk

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Introduction: Associations of the adipokine chemerin with the metabolic syndrome (MetS) and with chronic kidney disease (CKD), two important indicators of increased cardiovascular event risk, have been described. However, the power of chemerin to predict cardiovascular events has not been investigated so far and is addressed in the present study.

Material and methods: We measured plasma chemerin in a high-risk cohort of 495 patients undergoing coronary angiography for the evaluation of suspected or established coronary artery disease (CAD) in which cardiovascular events were prospectively recorded over 3.5 ± 1.1 years. Significant baseline CAD was diagnosed in the presence of coronary artery stenoses ≥ 50 %.

Results: At baseline, plasma chemerin was significantly higher in patients with the MetS as defined by the current harmonized consensus definition ($n = 147$) than in non-MetS subjects (201 ± 71 vs. 163 ± 62 ng/ml $p < 0.001$) and was inversely correlated with estimated glomerular filtration rate (eGFR; r = – 0.33, $p < 0{,}001$). During follow-up, chemerin significantly predicted cardiovascular events ($n = 82$) univariately, after adjustment for age, gender, BMI, and eGFR, and also after additional adjustment for the presence of significant baseline CAD, with standardized hazard ratios of 1.83 [1.19 – 2.83], $p = 0.006$; 1.77 [1.12 – 2.80], $p = 0.015$; and 1.69 [1.07 – 2.67], $p = 0.024$, respectively.

Discussion: From this first prospective evaluation of the cardiovascular event risk associated with chemerin we conclude that chemerin is strongly predictive of cardiovascular events independently from standard risk factors, from the MetS, and from the baseline presence of CAD.

XX-2

Albuminuria significantly predicts cardiovascular events irrespective of the metabolic syndrome and the baseline coronary artery state

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Introduction: Albuminuria is an important indicator of cardiovascular risk. Whether albuminuria predicts cardiovascular events independently of the baseline coronary artery state in patients with the metabolic syndrome (MetS) and in subjects who do not have the MetS has not been investigated yet.

Material and methods: We measured urinary albumin and creatinine concentrations in 872 consecutive patients undergoing coronary angiography for the evaluation of established or suspected 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 3.1 ± 1.2 years.

Results: During follow up, 17.5 % of our patients suffered cardiovascular events. In the total study population, albuminuria significantly predicted the incidence of major cardiovascular events after adjustment for age, gender, BMI, T2DM, smoking, blood pressure, LDL cholesterol, HDL cholesterol and the eGFR (adjusted HR = 1.84 [1.30–2.61]; $p = 0.001$). Further adjustment for the angiographically determined presence of CAD at baseline did not significantly attenuate the predictive power of albuminuria (HR 1.82 [1.28 – 2.59]; $p = 0.001$). In analyses with respect to the MetS, the presence of albuminuria strongly and significantly predicted cardiovascular events in patients with the MetS ($n = 390$; HR 1.80 [1.12 – 2.88]; $p = 0.015$) as well as in those without the MetS (2.02 [1.18 – 3.48]; $p = 0.011$). An interaction term MetS*albuminuria was not significant ($p = 0.619$), indicating that the cardiovascular risk conferred by the presence of albuminuria was not significantly different in subjects with the MetS compared to patients without the MetS.

Discussion: We conclude that albuminuria significantly predicts cardiovascular events both in patients with and in subjects without the MetS independently of established cardiovascular risk factors and of the baseline coronary artery state.

XX-3

ProBNP strongly predicts future macrovascular events in angiographied coronary patients with as well as in those without the metabolic syndrome

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Introduction: Pro-B-type natriuretic peptide (proBNP) is a prognostic biomarker for patients with congestive heart failure as well as in other patient populations. The power of proBNP to predict cardiovascular endpoints in patients with the metabolic syndrome (MetS) is unclear and is addressed in the present study.

Material and methods: We measured serum proBNP in 722 patients undergoing coronary angiography for the evaluation of stable coronary artery disease (CAD). Significant CAD was diagnosed in the presence of coronary stenoses with lumen narrowing of ≥ 50 %. Prospectively, we recorded vascular events over 3.2 ± 1.2 years.

Results: ProBNP was significantly higher in patients with ($n = 386$) than in subjects without significant CAD at baseline (711 ± 1287 vs. 663 ± 1565 pg/ml; $p = 0.001$). Prospectively, we recorded 121 cardiovascular events. The incidence of vascular events significantly increased over tertiles of proBNP in patients with the MetS (10.7, 18.5, and 28.8 % respectively; $p = 0.004$) as well as in those without the MetS (10.4, 11.5, and 22.0 %, respectively; $p = 0.011$). Similarly, serum proBNP significantly predicted the incidence of major cardiovascular events after adjustment for age, gender, BMI, smoking, systolic and diastolic blood pressure, LDL cholesterol, HDL cholesterol and the eGFR both in subjects with the MetS (standardized adjusted HR 1.48 [1.21 – 1.80]; $p < 0.001$) and in those without the MetS (HR 1.21 [1.04 – 1.40]; $p = 0.011$). These results were not attenuated after further adjustment for the angiographically determined baseline CAD state (HRs 1.50 [1.23 – 1.83]; $p < 0.001$ and 1.26 [1.09 – 1.47]; $p = 0.003$ in subjects with the MetS and in those without the MetS, respectively).

Discussion: Serum proBNP predicts cardiovascular events independently of established cardiovascular risk factors and of the baseline coronary artery state both in patients with and in subjects without the MetS.

XX-4

Plasma omentin significantly predicts cardiovascular events independently from the presence and extent of angiographically determined baseline coronary artery disease

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Introduction: No prospective data on the power of the new adipocytokine omentin to predict cardiovascular events are available. We therefore aimed at investigating (i) the association of plasma omentin with cardiometabolic risk markers, (ii) its association with angiographically determined coronary atherosclerosis, and (iii) the power of plasma omentin to predict cardiovascular events.

Material and methods: We measured plasma omentin in a series of 295 patients undergoing coronary angiography for the evaluation of established or suspected stable CAD; presence of baseline CAD was defined as the presence of any lumen irregularities at angiography; the extent of baseline CAD was defined as the number of significant coronary stenoses ≥ 50 %; prospectively cardiovascular events were recorded over a mean follow-up period of 3.5 years.

Results: During this period, 17.6 % of our patients suffered cardiovascular events, corresponding to an annual event rate of 5.3 %. Plasma omentin did not differ significantly between patients with and subjects without significant CAD ($p = 0.783$), but prospectively omentin significantly predicted cardiovascular events after adjustment for age, gender, BMI, diabetes, hypertension, LDL cholesterol, HDL cholesterol and smoking with a standardized adjusted hazard ratio (HR) of 1.41 [95 % CI 1.16 – 1.72], $p < 0.001$, as well as after additional adjustment for the presence and extent of CAD at the baseline angiography (HR 1.52 [95 %CI 1.23 – 1.86], $p < 0.001$).

Discussion: From this first prospective evaluation of the cardiovascular risk associated with plasma omentin we conclude that elevated omentin is a strong predictor of cardiovascular events independently from the presence of baseline CAD.

XX-5

Impaired kidney function is a diabetes risk equivalent in patients with established coronary artery disease

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Introduction: Type 2 diabetes (T2DM) is a paramount risk factor for cardiovascular disease, in particular among patients with established coronary artery disease (CAD). Similarly, chronic kidney disease (CKD) confers a high risk of cardiovascular events. We aimed at investigating the single and joint effects of T2DM and of CKD on cardiovascular risk in patients with angiographically proven CAD.

Material and methods: We prospectively recorded cardiovascular events over 10 years in a cohort of 1423 patients with angiographically proven CAD. CKD was defined as an estimated glomerular filtration rate (eGFR) < 60ml/min/1.73m^2.

Results: The risk of cardiovascular events was significantly higher in T2DM patients ($n = 171$) than in non-diabetic subjects (39.1 vs. 28.7 %; $p < 0.001$) and also was higher in patients with CKD ($n = 116$) compared to those with an eGFR ≥ 60 ml/min/1.73m^2 (47.2 vs. 28.7 %; $p < 0.001$). When both, T2DM and CKD were considered, 841 subjects had neither T2DM nor CKD, 336 had T2DM but not CKD, 145 did not have diabetes but had CKD, and 101 had both diabetes and CKD. When compared with the event rate among patients with neither T2DM nor CKD (26.3 %), event rates were significantly higher in patients with T2DM who did not have CKD (34.8 %; $p = 0.007$) and in non-diabetic patients with CKD (42.8 %; $p = 0.020$) and were highest in patients with both, T2DM and CKD (53.5 %; $p < 0.001$). Further, patients with both, T2DM and CKD were at a significantly higher event risk than those with T2DM but no CKD ($p = 0.011$) and those without T2DM but with CKD ($p = 0.048$). Event rates were similar in patients with T2DM but not CKD and in non-diabetic patients with CKD ($p = 0.798$).

Discussion: We here report the novel findings that CKD and T2DM contribute synergistically to cardiovascular event risk and that CKD is a T2DM risk equivalent in patients with established coronary artery disease.

XX-6

Single and joint effects of obesity and of the metabolic syndrome on cardiovascular event risk

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Introduction: Obesity is a major risk factor for the metabolic syndrome (MetS), but some obese individuals do not have the MetS while others have the MetS but are non-obese. We prospectively investigated the single and joint effects of obesity and of the MetS on cardiovascular event risk.

Material and methods: Cardiovascular events were prospectively recorded over 10 years in a large cohort of 1705 patients undergoing coronary angiography for the evaluation of established or suspected stable coronary artery disease. Obesity was defined as a BMI ≥ 30 kg/m^2; presence of the MetS was defined according to the current harmonized consensus definition.

Results: From our patients, 827 were non-obese and did not have the MetS, 443 were non-obese but had the MetS, 113 were obese but did not have the MetS, and 322 were obese and had MetS. Cardiovascular event risk was 34.1 % in non-obese patients with the MetS. It was significantly higher in this patient group when compared to non-obese subjects without the MetS (25.3 %; $p < 0.001$), when compared to obese subjects without the MetS (22.1 %; $p = 0.036$), and even when compared to obese subjects with the MetS (25.2 %; $p = 0.006$).

Discussion: We conclude that non-obese patients with the MetS face a particularly unfavourable cardiovascular prognosis.

XX-7

Diabetes is not a coronary artery disease risk equivalent among women

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Introduction: Diabetes per se is widely considered a coronary artery disease (CAD) risk equivalent, particularly among women. We aimed at investigating the contribution of baseline coronary atherosclerosis to the risk of diabetic women for future vascular events in a prospective cohort study on subjects who were characterized by coronary angiography at baseline.

Material and methods: Vascular events were recorded over 10 years in 598 consecutive women undergoing coronary angiography for the evaluation of established or suspected stable CAD.

Results: From our women, 271 had neither type 2 diabetes (T2DM) nor significant CAD (i.e. coronary stenoses ≥ 50 %) at the baseline angiography, 79 had T2DM but not significant CAD, 152 did not have T2DM but had significant CAD, and 96 had both T2DM and significant CAD. Non-diabetic women without significant CAD had an event rate of 12.5 %. The event rate was similar in T2DM women without significant CAD (15.2 %; $p = 0.749$), but higher in non-diabetic women with significant CAD (32.9 %; $p < 0.001$). Women with both T2DM and significant CAD had the highest event rate (43.8 %; $p < 0.001$). Importantly, T2DM women without significant CAD had a significantly lower event rate than non-diabetic women with significant CAD ($p = 0.003$).

Discussion: We conclude that T2DM per se is not a CAD risk equivalent among women. Moderate-risk diabetic women without significant CAD and very high-risk diabetic women with significant CAD add up to a grand total of high-risk diabetic women. This is why diabetes seems to be a CAD risk equivalent in many epidemiological studies.

XX-8

Impact of gender on the risk of coronary atherosclerosis and cardiovascular events conferred by HbA1c in subjects without known diabetes

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Introduction: Diabetes confers a larger increase in the relative risk of cardiovascular events among women than among men. Whether gender also affects the association of HbA1c with coronary atherosclerosis and cardiovascular events among subjects without known diabetes is unknown.

Material and Methods: We enrolled a large consecutive series of 1479 patients undergoing coronary angiography for the evaluation of established or suspected coronary artery disease (CAD), including 495 women and 984 men who did not have previously known diabetes Significant CAD was diagnosed in the presence of significant coronary stenoses ≥ 50 %. Prospectively, we recorded cardiovascular events over 4.4 ± 1.2 years.

Results: Among women, 36.4, 56.2, and 7.4 % and among men 44.2, 46.6, and 9.1 % had 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), respectively. The prevalence of angiographically diagnosed significant CAD 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). An interaction term gender × HbA1c was statistically significant ($p < 0.001$), indicating that the association of HbA1c with CAD was significantly stronger among women than among men. During follow-up, the incidence of cardiovascular events was 21.5 % in women and 28.5 % in men ($p = 0.002$). Among women, HbA1c strongly and significantly predicted cardiovascular events (adjusted OR for a 1 % increase in HbA1c (HR 2.08 [1.24 – 3.03]; $p < 0.001$), but not among among men (HR 1.12 [0.94 – 1.53]; $p = 0.145$). An interaction term gender x HbA1c again was statistically significant ($p = 0.011$), indicating that HbA1c was a significantly stronger predictor of cardiovascular events among women than among men.

Discussion: We conclude that gender significantly modulates the risk of coronary atherosclerosis and cardiovascular events conferred by HbA1c in subjects without known diabetes.